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Added Value of Diffusion-Weighted Magnetic Resonance Imaging in Characterization and Staging of Rectal Cancer

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ABSTRACT

Background: Approximately 15% of all cancers are found in the rectum. Rectal cancer is one of the most common malignant tumors in patients. According to the National Cancer Institute, it's the third most frequent cancer in males and the second most prevalent cancer in women. About 96 percent of all colon cancers are adenocarcinomas, with lymphoma, gastrointestinal stromal tumors, and carcinoid among the more uncommon malignancies.

Aim of the study: to discuss the accuracy of MRI at staging cancer rectum using high-resolution MRI sequences and to give a brief review about more emerging important aspects of rectal cancer staging, such as the circumferential resection margin, extramural vascular invasion, and the staging of low rectal cancers.

Patients and Methods: Our study was done in the Radiodiagnosis Department, Zagazig University Hospital, with 24 patients with primary rectal cancer referred from the Surgery Department for preoperative local staging of cancer rectum; the results of MRI were compared to pathologic findings.

Results: Patients included in the study were 16 females and eight males; their ages ranged from 45 to 75 years with a mean age of 60 years. Adenocarcinoma comprised about 83.3 % of all of our cases. T3 and N1 tumors were found to be the most common stages in our cases.

Conclusion: Preoperative MRI utilizing high-resolution sequences is an accurate modality for preoperative grading of rectal carcinoma, delineation of affection of mesorectal fascia, circumferential resection margin, and extramural vascular invasion.

Keywords: Cancer, MRI, Rectal, Tumors.

INTRODUCTION

Rectal cancer is one of the most common clinical malignant tumors, which accounts for about 15% of all malignant tumors [(1)]. It is the third most common cancer in men and the second most common cancer in women [(2)]. Adenocarcinomas comprise approximately 96% of all colorectal cancers, whereas the uncommon malignancies include lymphoma, gastrointestinal stromal tumors, and carcinoid [(3)].

The prognosis of rectal cancer is directly related to tumor infiltration into the mesorectum and the ability to surgically achieve negative circumferential resection margins (CRMs) [(4)]. The use of total mesorectal excision (TME) as the standard treatment of rectal cancer and the adoption of neoadjuvant chemoradiotherapy for patients with locally advanced rectal cancers, diagnosed on the basis of MRI features, has led to substantial improvement in local disease control [(5)].

There is a need for accurate clinical staging of rectal cancer to optimize individualized treatment [(6)]. Rectal cancer is staged based on the TNM classification system. The T stage refers to local tumor extent, the N stage refers to regional lymph node status, and the M stage refers to the presence or absence of distant metastatic disease [(7)].

Currently, MRI is the preferred imaging modality for local staging of rectal cancer[(8)]. High-resolution T2-weighted images are the gold standard for evaluating rectal cancer. Proper planning of high-resolution T2 imaging sequences is essential in staging accuracy[(9)].

However, structural imaging techniques have shown clear limitations in tumor evaluation. Different functional and molecular imaging techniques such as DWI and dynamic contrast-enhanced (DCE) imaging are useful tools for providing insights into tumor phenotype and improving tumor response to treatment [(10,11)].

DW-MRI enables a noninvasive characterization of biologic tissues on the basis of their water diffusion properties [(12)].

Aim of the study was to discuss the accuracy of MRI at staging cancer rectum using high-resolution MRI sequences and to give a brief review about more emerging important aspects of rectal cancer staging, such as the circumferential resection margin, extramural vascular invasion, and the staging of low rectal cancers.

PATIENTS AND METHODS

A prospective study has been conducted on 24 patients; they were clinically suspected of having cancer rectum. The patients were referred from the Surgery Department to the Radiodiagnosis Department, Magnetic Resonance Imaging Unit, Zagazig University Hospitals over a period between October 2019 and October 2020.

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Ethical considerations:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee.

The nature and the aim of the study were explained to the patients, and informed written consents were obtained from all of them. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria:

Patients who were diagnosed with cancer rectum by CT study colonoscopy and rectal biopsy before MRI study.

Exclusion criteria:

Patients who received radiotherapy or chemotherapy. Patients had contraindications for MRI such as patients with; implanted electric and electronic devices, heart pacemakers, insulin pumps, implanted hearing aids, patients with ferromagnetic vascular clips or metallic spinal prosthesis, first-trimester pregnant females (relatively contraindicated), and patients who were unwilling to complete the study.

All patients were subjected to complete history taking, full clinical examination, MR Imaging.

MRI Technique:

All patients were asked to get rid of any metallic objects. They were also asked about any contraindication to MRI examination (artificial heart valve, cardiac pacemaker, metallic stent or joint prosthesis except that made of titanium). The patients were informed about the duration of the examination, the position of the patient, and the importance of being motionless.

All MR sequences were done using a 1.5 Tesla superconducting MR imager (Achieva-class IIa, Philips medical system), equipped with a phased array body coil. The patients were positioned on the MRI examination table in the supine position headfirst.

Coil positioning: The coil may need repositioning depending on the location of the tumor seen on sagittal sequences. The cranial border of the coil should not be higher than L5, and the caudal border of the coil should be 10 cm below the symphysis pubis in low rectal tumors.

IV contrast enhancement with gadolinium was not included for all of our patients.

All patients were subjected to the following MRI sequences:

I) Conventional MRI:

Initial localization images in the coronal and sagittal planes were needed to plan the high-resolution images. The first series was the sagittal T2-weighted, fast (turbo) spin-echo sequence from one pelvic sidewall to the other. The second series consisted of large-field-of-view axial sections of the whole pelvis.

The scan protocol was TR 3000–4000 ms, TE 70–90 ms, field of view (FOV) 28–32 cm×28–32 cm, matrix 276×384, slice thickness 5 mm, and gap 1 mm.

The third series consisted of the high-resolution images that were T2-weighted thin-section axial images through rectal cancer and adjacent tissues. These sequences must be performed perpendicular to the long axis of the rectum and at the level of the tumor.

The fourth series consisted of high-spatial-resolution coronal imaging parallel to the anal canal for patients with low rectal cancers.

High-resolution T2W protocol (TR 4200–5000 ms, TE 108 ms, slice 3 mm, 210–300s acquisition time, FOV 180–240 mm).

T1 weighted images.

T1 post-contrast-enhanced imaging.

II) DW imaging with ADC mapping:

Prior to contrast agent administration, breaths hold axial DWI was done with a single-shot spin-echo sequence. The scan protocol was TR 3200 ms, TE 74 ms, field of view (FOV) 300 mm×244 mm, matrix size 128×128, slice thickness 7 mm, interslice gap 2.1 mm, b factor 0 and 1000 s/mm^2. ADC maps were calculated and meant ADC values were measured from a sample of three round/oval-shaped regions of interest (ROIs) that were manually placed within solid tumor parts (as identified as focal masses showing intermediate signal intensity on the anatomical T2-weighted images) of three independent tumor-containing slices.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean ± SD (Standard deviation).

RESULTS

This table shows that the mean age of the studied participants was about 60 years. The female to male ratio was 2:1. The commonest presentation among the studied patients was bleeding per rectum followed by constipation **(Table 1)**.

Table (1): Demographic data and Clinical presentation of the studied group

		Studied group (n=24)	
Demographic data	**Age:**		
	Range	45- 75	
	Mean ± SD	60 ± 8.6	
		No	**%**
	Sex:		
	Female	16	66.6
	Male	8	33.3
Clinical presentation	**Findings:**		
	• Bleeding per rectum	18	75
	• Constipation	5	20.8
	• Cachexia	3	12.5
	• Intestinal obstruction	2	8.3

This table shows that the annular growth pattern was the commonest detected pattern among the studied patients. the majority of patients had tumors with a craniocaudal extension of less than 10 cm. most of our patients had tumors with less than 5 cm distance from the lower margin of the tumor to the anal verge (lower rectum) **(Table 2)**.

Table (2): Growth pattern of the tumor, craniocaudal extension of the tumor and distance of lower margin of the tumor from the anal verge among the studied group

		Studied group (n=24)	
		No	**%**
Growth pattern of the tumor	**Annular pattern:**	20	83.3
	Fungating pattern:	4	16.7
Craniocaudal extension of the tumor	**<5 cm:**	10	41.7
	5-10 cm:	10	41.7
	>10 cm:	4	16.7
Distance of lower margin of the tumor from the anal verge	**<5 cm:**	16	66.7
	5-10 cm:	6	25
	>10 cm:	2	8.3

This figure shows that most of our cases had intermediate signals at T2WI. On diffusion imaging, all of our patients had restricted diffusion depicted as high signal intensity on DWI and low SI at ADC map**.** ADC value of studied patients ranged between (0.94 and 1.69 x 10^{-3} mm^2/s) with a mean value of 1.29 x 10^{-3} mm^2/s **(Figure 1)**.

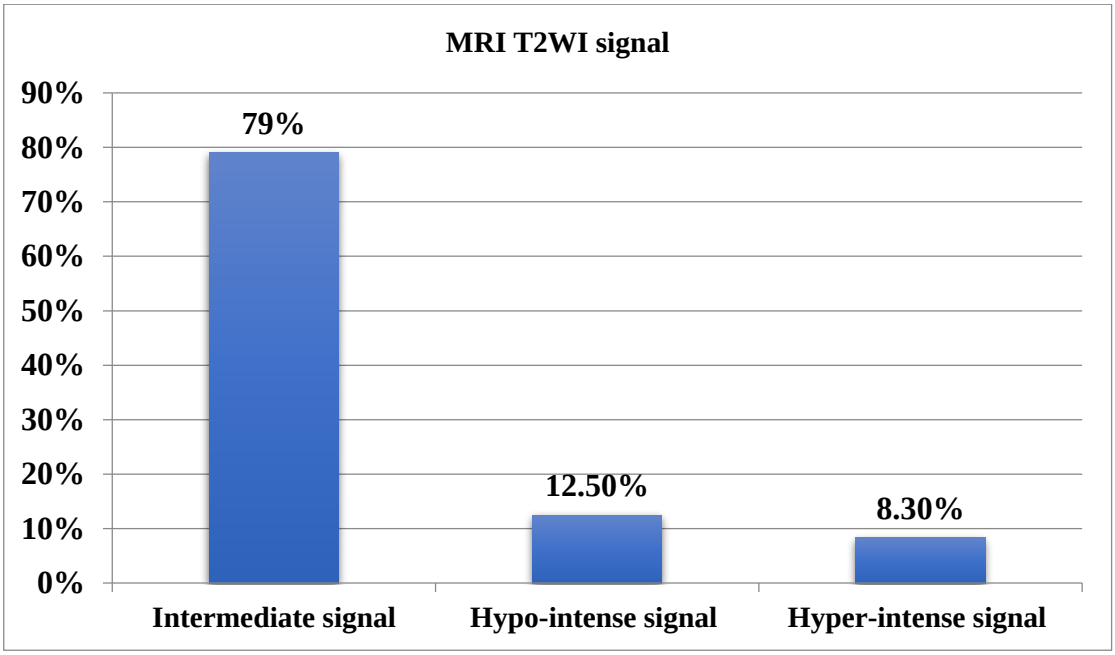

Figure (1): MRI T2WI findings among the studied group

This figure shows that most of our cases were of T3 stage by MRI study and histopathologic exam, and the least were staged as T2 patients **(Figure 2).**

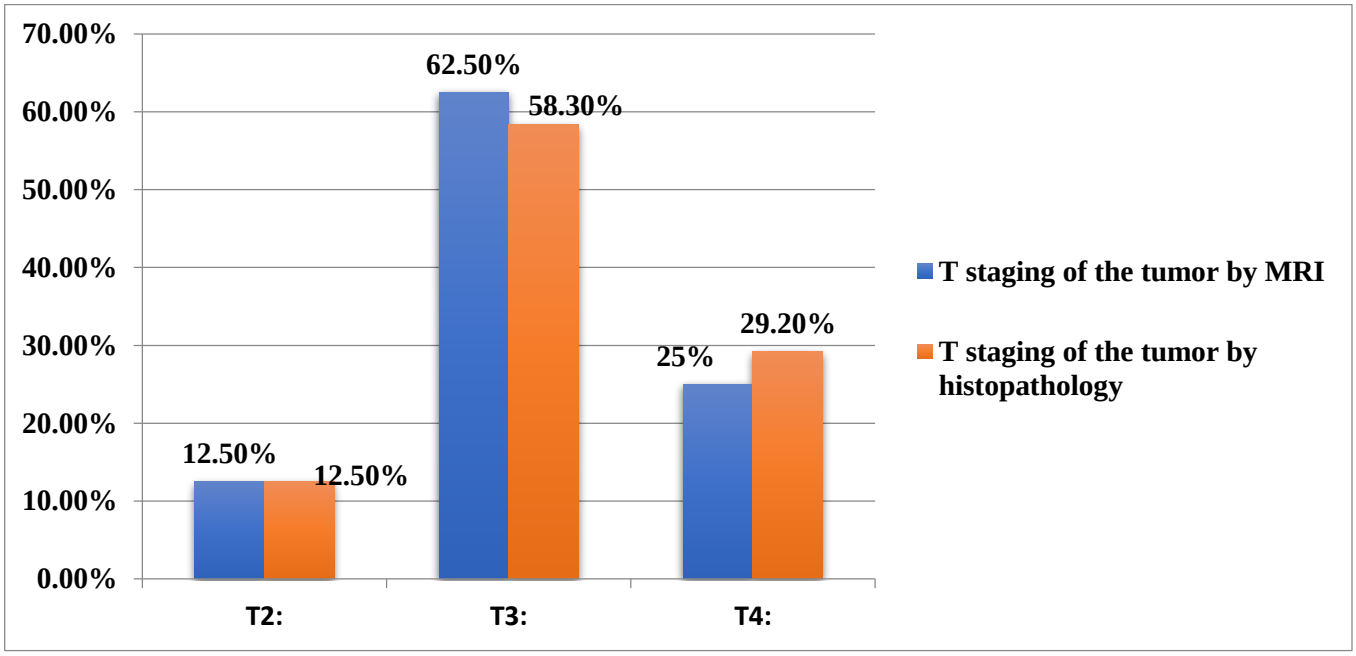

Figure (2): T staging of the tumor by MRI and histopathology among the studied group

This table shows that N1 stage was the most common stage among our cases detected by both MRI and histopathology **(Table 3)**.

Table (3): N staging of the tumor by MRI and histopathology among the studied group

N staging	N staging of the tumor by MRI (n=24)		N staging of the tumor by histopathology (n=24)	
	No	%	No	%
N0:	5	20.8	4	16.7
N1:	11	45.8	11	45.8
N2:	8	33.3	9	37.5

This table shows that MRI detected 12 patients with mesorectal fascia involvement out of 14 patients detected by histopathology. MRI detected 14 patients with positive circumferential resection margin status; however, only ten patients were detected by histopathology. MRI detected four patients with extramural vascular invasion were among our cases, however, only three patients were seen by histopathology**.** MRI detected 5 patients with pelvic sidewall invasion; only three patients were detected by histopathology **(Table 4)**.

Table (4): Extracolonic involvement among the studied group

Extracolonic involvement	MRI (n=24)		Histopathology (n=24)	
	No	%	No	%
Meso-rectal fascia involvement:				
• Involved:	12	50	14	58.3
• Free:	12	50	10	41.7
Circumferential Resection Margin:				
• Positive:	14	58.3	15	62.5
• Negative:	10	41.6	9	37.5
Extramural vascular invasion:				
• Positive:	4	16.7	3	12.5
• Negative:	20	83.3	21	87.5
Pelvic side wall involvement				
• Positive:	5	20.8	3	12.5
• Negative:	19	79.1	21	87.5

This table shows that the commonest detected tumor was adenocarcinoma (83.3%) **(Table 5).**

Table (5): Type of the tumor detected by histopathology among the studied group

Type of the tumor by histopathology	Studied group (n=24)	
	No	%
Adenocarcinoma:	20	83.3
Mucinous adenocarcinoma:	2	8.3
SCC:	2	8.3

This table shows that the accuracy of MRI was best at detecting stage T2 (91%) **(Table 6).**

Table (6): Validity of MRI in the diagnosis of T staging of tumors compared to histopathology

T stage	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Accuracy
T2	66.7 %	95.2 %	66.7 %	95.2 %	91 %
T3	85 %	70 %	80 %	87.5 %	79%
T4	71.4%	88.9%	83.3%	88.9%	87%

This table shows that the accuracy of MRI was best at detecting stage N2 (79.1%) with higher sensitivity 66.7%. At the same time, it was the least for stage N1 58.3% **(Table 7)**.

Table (7): Validity of MRI in the diagnosis of N staging of tumors in comparison to histopathology

N stage	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Accuracy
N0	50 %	85 %	40 %	89 %	79.1 %
N1	54.5 %	61.5 %	54.5 %	61.5 %	58.3 %
N2	66.7%	86.7%	75%	81.3%	79.1%

MRI has better accuracy in detection of mesorectal fascia invasion 83.3% while it was less accurate at assessing circumferential resection margin 79.1%. MRI shows high accuracy in detection of extramural vascular invasion 87.5%. MRI accuracy at detecting pelvic sidewall involvement was 83.3% **(Table 8).**

Table (8): Validity of MRI in the diagnosis of extracolonic involvement compared to histopathology

Extracolonic involvement	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Accuracy
Mesorectal fascia invasion	78.6 **%**	90 %	91.7 %	75 %	**83.3 %**
Circumferential resection margin	80 **%**	77.8 %	85.7 %	70 %	**79.1 %**
Extramural vascular invasion	66.7%	90.5 %	50 %	95%	**87.5 %**
Pelvic side wall involvement	66.7%	85.7%	40%	94.7%	**83.3%**

DISCUSSION

Our study enrolled 24 patients who fulfilled the inclusion criteria. Their ages ranged from 45 to 75 years with a mean ± SD age of 60 years±8.6. A similar finding was reached by **Sun *et al.*[13],** who reported that cancer rectum is often diagnosed in the 6th decade of life.

According to the clinical history, the main clinical presentation of cancer rectum was bleeding per rectum, followed by changing of bowel habits (75 % and 20.8%, respectively). In our study, we had 18/24 patients presented with bleeding per rectum, 5/24 patients presented with constipation, 3/24 patients presented with vomiting and cachexia. Some patients had more than one presenting finding; these results correlate with **Abdelhamid [14],** who found the predominant presenting symptom was bleeding per rectum in 57.9% of his patients.

Our study showed that the commonest site detected among the studied patients was the lower rectum (lower margin < 5 cm from the anal verge) in 66% of our patients, followed by the middle part of the rectum (5-10 cm from the anal verge) in 25% of our patients, 8% of our patients had rectal cancer at the upper rectum (lower margin >10 mm from the anal verge). These results were close to **Xu *et al.* [15],** who reported that the commonest site of rectal cancer was the lower rectum, followed by the mid-rectum (54% and 45.9 %, respectively). However, our results were different from **Hassan *et al.* [16],** who reported that the upper rectum was the commonest site for rectal cancer in 62% of cases.

Concerning the growth pattern of the tumor, our study showed that the annular pattern of growth was the commonest detected pattern among the studied patients, followed by fungating one (83.3% and 16.6%, respectively).

Our study showed that the majority of the patients had a craniocaudal tumor extension of less than 10 cm; about 10/24 patients had craniocaudal extension less than 5 cm, and 10/24 of patients had craniocaudal extension (5-10 cm), and only four patients had extension more than 10 cm.

By conventional MRI, on T2WI, we found 20/24 tumors with intermediate signal intensity, 3/24 of low signal intensity, 2/24 were of focal or diffuse high signal intensity due to their mucinous nature. This was in agreement with **Rao *et al.* [17],** who found that rectal masses are more common to have an iso-intense signal to the rectal wall or skeletal muscle on T2WI.

On diffusion imaging, all of our patients had restricted diffusion depicted as high signal intensity on DWI and low SI at ADC map. The ADC values measured on the ADC map, ranged from (0.94 -1.69) x 10^{-3} mm^2/s with a mean ADC of 1.29 ± 0.24 x 10^{-3} mm^2/s. This was coordinated with the mean value of **Sun *et al.* [18]**, who reported that the mean ADC value for the cancer rectum was 1.3 ± 0.21 x 10^{-3} mm^2/s.

On pathologic study: the commonest detected tumor was adenocarcinoma (83.3%); this was in agreement with **Xu *et al.* [15]**, who reported that adenocarcinoma was the commonest type of rectal cancer.

As regards T staging of rectal cancer by MRI: of all of our patients, 3/24 patients were staged as T2 (in our study T1, T2 stages were combined in one T stage T2 stage; because of limitation of MRI in distinguishing T1 and T2), 15 /24 were staged as T3 and 6/24 patients as T4 with MRI staging, after histopathological examinations of the 24 neoplasms, 3/24 were staged as T2, 14/24 were staged as T3, 7/24 were staged as T4. The difference between MRI and pathologic results was due to the desmoplastic response of some tumors that might lead T2 tumors to be misdiagnosed as T3 tumors. Also, it mightbe led to the loss of fat planes between the rectum and other organs and the overestimation of T3 as T4.

The accuracy of each T stage was; stage T2 accuracy was 91%, with a sensitivity of 66.7%; these results were consistent with **Rao *et al.* [17]**, who reported that the accuracy of MRI was 89% for tumors T2 stage. T3 stage accuracy was 83%, with a sensitivity of 93.3 %, specificity of 66.7%. This was in agreement with the results of **Xu *et al.* [15],** who reported that T3 stage accuracy was about 83%, with a sensitivity of 91%. Regarding the T4 stage, the accuracy was 87%, with a sensitivity of 71.4%, specificity of 88.9%; there was some sort of agreement with **Rao *et al.* [17],** who reported the accuracy of T4 stage was 95%.

Regarding the N stage: MRI detected (5/24) of patients with N0 stage of the tumor, (11/24) of them were of N1 stage, and the remaining (8/24) were of N2 stage, compared to pathological exam (4/24) patients had N0 stage, (11/24) had N1 stage, (9/24) % had N2 stage.

The accuracy of MRI at N0 was 79.1 % with sensitivity of 50% and specificity of 85%, while for N1 stage the accuracy was 58.3 %, sensitivity 54%, and specificity 61%; and for the N2 stage, the accuracy was 79.1 %, with sensitivity 66.7 %, specificity 86.7%. **Xu *et al.* [15]** reported that the MRI accuracy for each N stage 63% for stage N0, 63.9 % for stage N1, and 82.4 % for N2 stage. The difference between MRI and pathologic results was that perirectal LNs might be too small to be depicted by MRI; also reactive LN swelling might be difficult to differentiate from involved nodes.

In our study, mesorectal fascia was involved in 12/24 patients; on pathology, 14/24 patients were found to have MRF involvement.

The diagnostic accuracy of MRI for determining mesorectal fascia invasion was 83%, sensitivity 78.6%; these findings were in partial agreement with **Hassan *et al.* [16]**, who reported MRI accuracy at MRF invasion detection about 88%, sensitivity 90%.

Concerning the circumferential resection margin status, using a cut-off distance of about 1 mm

between the tumor and mesorectal fascia, we found 14/24 cases to be CRM positive, 10/24 of patients had negative CRM, on the pathological exam, we found 15 /24 cases to be CRM positive, MRI accuracy was 79.1% with sensitivity 80%, specificity 77.8%, this showed lower results than the previous study of **Hassan *et al.*** [16] who reported MRI sensitivity about 95%, and specificity 87%.

As an important prognostic factor, the extramural vascular invasion was found in 4/24 patients, while on the pathological study, we found 3/24 with positive extramural vascular invasion. Our study demonstrated higher sensitivity and specificity of MRI at extramural vascular invasion detection with 87.5% accuracy, 66.7 % sensitivity, 90.5 % specificity, compared to the previous study made by **Sohn *et al.*** [19], who found the sensitivity and specificity Of MRI at extramural vascular invasion detection were about 28%, 94% respectively.

Regarding pelvic sidewall invasion, 5/24 were involved by MRI. However, only three were proven by histopathology; the accuracy of MRI was 83.3%, sensitivity was 66.7%, and specificity was 85.7%.

CONCLUSION

Preoperative MRI utilizing high-resolution sequences is an accurate modality for preoperative grading of rectal carcinoma, delineation of mesorectal fascia, circumferential resection margin, and extramural vascular invasion, so categorize patients who can go directly for surgery from patients who may go for neoadjuvant therapy. DWI that correlated with ADC value helps for more accurate definition of the tumors.

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