Section: Radiology

Original Research Article

STUDY TO ASSESS SENSITIVITY AND SPECIFICITY OF 3 TESLA MR IN PREDICTION OF BOWEL WALL INVASION AND METASTATIC ADENOPATHY

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Abstract

Background: Primary rectal cancer is a common malignancy that has a variable prognosis, with local recurrence after surgical resection often leading to incurable disease. Phased-array MR imaging best fulfills the requirements for preoperative staging of rectal cancer. Present study was to assess the accuracy of 3-T high-field MRI in prediction of bowel wall invasion and metastatic adenopathy in patients of rectal cancer. **Material and Methods:** Present study was prospective, observational study, conducted in patients referred to department of radiology (MRI), with a diagnosis of rectal carcinoma, based on manual palpation and proctoscopic results and confirmed by means of endoluminal biopsy. **Results:** In presents study, 30 patients were studied, average age being 53.07 ± 14.36 years & 76.7% cases were males. In present study, 86.7% cases had Circumferential or Annular followed by 13.3% had Polypoidal tumor. 13.3% cases had sphincter involvement; 14.3% cases had CRM involvement & 90.0% cases were on CRT. In present study, 96.7% of pre CRT cases had tumor stage T3 which was more as compared to 81.5% of post CRT cases but the difference was not significant. Parameters for comparison between MRI & histopathology for CRM involvement were Sensitivity: 33.33%, Specificity: 100%, PPV: 100% & NPV: 66.67%. On comparison between MRI & histopathology for bowel wall invasion pre-CRT parameters were Sensitivity: 100%, Specificity: 100%, PPV: 100% & NPV: 100% In post CRT patients MRI tends to overstage the lesions as compared to the histopathological results. Parameters were Sensitivity: 100%, Specificity: 33.33%, PPV: 54.55% & NPV: 100%. Parameters were Sensitivity: 75%, Specificity: 86.36%, PPV 66.67% & NPV 90.48%. Parameters on comparing nodal staging on MRI and histopathology were Sensitivity: 88.89%, Specificity: 95.45%, PPV: 88.89% & NPV: 95.45%. **Conclusion:** MR imaging is in the forefront as a problem-solving technique for treatment planning in patients with rectal carcinoma.

INTRODUCTION

Primary rectal cancer is a common malignancy that has a variable prognosis, with local recurrence after surgical resection often leading to incurable disease. Early detection and treatment of the tumor are important determinants of prognosis, but prediction of clinical outcome depends chiefly on the stage of the tumor at the time of clinical presentation.[1]

Rectal cancer has a male predilection, and its prevalence increases steadily after the age of 50 years. The diagnosis is usually made based on a digital rectal examination, sigmoidoscopy, a double contrast enema, and confirmatory histological findings. These do not show the depth of tumor spread or the extent of lymph node involvement, both of which are important prognostic factors.

MR imaging has an undeniable role in the management of rectal cancer. Furthermore, the results of recent surgical trials indicate that evaluation of the involvement of the mesorectal fat and mesorectal fascia is more important than T staging for treatment planning.[2,3] At present, phased-array MR imaging best fulfills the requirements for preoperative staging of rectal cancer. It also accurately delineates sphincter involvement by tumor.[4] The purpose of present study was to assess the accuracy of 3-T high-field

MRI in prediction of bowel wall invasion and metastatic adenopathy in patients of rectal cancer.

MATERIAL AND METHODS

Present study was prospective, observational study, conducted in department of radiodiagnosis, at RCSM Govt Medical College Kolhapur, India. Study duration was of 1 year (December 2020 to December 2021). Study was approved by institutional ethical committee.

Inclusion Criteria

- All patients referred to department of radiology (MRI), with a diagnosis of rectal carcinoma, based on manual palpation and proctoscopic results and confirmed by means of endoluminal biopsy.

Exclusion Criteria

- Patients who did not have surgery
- Patients whose surgical specimens did not have complete pathological data.
- Suboptimal imaging due to movement artifacts and suboptimal perfusion study.

Study was explained to patients in local language & written consent was taken for participation

MR Imaging Examination:

i) Coils- phased array external coils (body coil)

ii) Sequence protocols

A preliminary pilot study was performed on 5 patients. Various imaging sequences were performed, before and after administration of Gadolinium which included T1, T2 and fat suppressed images and the optimum sequences were selected for application in the final study.

High-resolution T2-weighted imaging was used in this study. This sequence uses a high-resolution matrix, thin-section (3–5 mm) imaging, and a small field of view. Images were acquired in the axial, coronal, and sagittal planes to depict the length and extent of the tumor in all three dimensions. MR imaging was performed at our institution at 3 T (Ingenia; Quasar Dual, Philips Medical Systems, the Netherlands). Subjects were positioned supine and in the head first position.

Sequences Used Were

1. PRECONTRAST T1-WEIGHTED two-dimensional turbo spin echo (656/10 msec; echo train length, five; section thickness, 8 mm; intersection gap, 0.8 mm; number of signals acquired, four; matrix, 166 x 256; field of view, 25 cm; and T2-weighted two-dimensional turbo spin echo high resolution images (3,427/150; echo train length, 25; section thickness, 4 mm; intersection gap, 0.8 mm; number of signals acquired, eight; matrix, 175 x 256; field of view, 20 cm; voxel size, 2.43 mm^3).
2. The precontrast T1-weighted sequence was performed in the transverse plane, and the images serve as a reference for accurate planning of the sagittal T2-weighted turbo spin-echo sequence.
3. 3 PLANE T2-WEIGHTED turbo spin-echo images: The sagittal images were used to plan thin-slice axial and coronal imaging. The axial and coronal T2-weighted TSE sequence was angled perpendicular to the long axis of the rectal cancer.
4. T2 SPAIR (FAT SATURATED). This sequence is especially useful foe detection of the lymph nodes.
5. M-DIXON SEQUENCE: This sequence gives in phase and out of phase imaging by suppressing water and fat.
6. DIFFUSION WEIGHTED IMAGING was performed at the B values of 0, 400 and 800.
7. DYNAMIC CONTRAST ENHANCED PERFUSION SEQUENCE (E-THRIVE): was performed after injection of 10-12 ml of intravenous gadolinium contrast agent. 8 acquisitions were taken in the region of interest.

The total imaging time was approximately 40 minutes. The different image series were evaluated by using the consensus of an experienced radiologist. The reviewer knew only that the patients had been referred for the preoperative staging of rectal cancer and was unaware of the final surgical and histologic results. Radiologic staging was performed according to the TNM staging and evaluated.

The patients were subjected to pre op RT and/or chemotherapy depending on clinical assessment and MR staging and subsequently taken up for surgery. The extent of local tumor spread in each histopathologic slice was then assessed according to the tumor component of the TNM system.[5] An overall histopathologic tumor stage for the whole tumor was also assigned, according to the maximal degree of local spread in any slice.[6]

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

In presents study, 30 patients were studied. Age of the patients were ranging from 26 - 77 years with average age being 53.07 ± 14.36 years. Majority of cases were from age group of 50- 70 years (60 %) followed by age group of 30-50 years (23.3%). 76.7% cases were males followed by 23.3% cases were females.

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Table 1: Age & gender distribution

	No. of Cases (N=30)	Percentage (%)
Age (in years)		
< 30	03	10.0
30 - 50	07	23.3
50 - 70	18	60.0
> 70	02	06.7
Gender		
Male	23	76.7
Female	07	23.3

46.7% cases had tumor in the middle third followed by 30.0% cases had tumor in the upper third and 23.3% cases had tumor in the lower third rectum.

Table 2: Location of tumor

Location	No. of Cases (N=30)	Percentage (%)
Upper third	09	30.0
Middle third	14	46.7
Lower third	07	23.3

In present study, 86.7% cases had Circumferential or Annular followed by 13.3% had Polypoidal tumor. 13.3% cases had sphincter involvement., 14.3% cases had CRM involvement & 90.0% cases were on CRT.

Table 3: Tumor morphology on MRI

Tumor morphology	No. of Cases (N=30)	Percentage (%)
Circumferential / Annular	26	86.7
Polypoidal	04	13.3
Other		
Sphincter involvement	04	13.3
CRM Involved (n=21)	03	14.3
Receiving CRT	27	90

In present study, 80.0% cases had moderately differentiated tumor followed by 20.0% cases had poorly differentiated tumor. 3.3% cases had distant metastasis.

Table 4: Histopathology findings

Grade on pathology	No. of Cases (N=30)	Percentage (%)
• Poorly differentiated	06	20.0
• Moderately differentiated	24	80.0
Distant metastasis	01	03.3

In present study, 96.7% of pre CRT cases had tumor stage T3 which was more as compared to 81.5% of post CRT cases but the difference was not significant. On HPE, 46.7% cases had tumor stage T3 followed by 33.3% cases had T2.

Table 5: Profile of tumor staging (PRE AND POST CRT)

Stage	On MRI (Pre CRT)	on MRI (Post CRT)	On HPE
Tis	0	0	2 (6.7 %)
T1	0	0	0
T2	01 (3.3 %)	05 (18.5 %)	10 (33.3 %)
T3	29 (96.7 %)	22 (81.5 %)	14 (46.7 %)
T4	0	0	0
Undetermined	0	0	4 (13.3 %)

In present study, average size of lymph nodes, average thickness of LN & average length of the segment involved was more in pre-CRT cases which were significantly low among post CRT cases & difference was statistically significant.

Table 6: Pre and post CRT measurements

	Pre CRT	Post CRT	P value
Average size of lymph nodes (MM)	8.00 $\pm$ 3.7	*6.00 $\pm$ 2.9	0.008
Average thickness	14.50 $\pm$ 4.95	10.33 $\pm$ 3.88	0.018
Average length of the segment involved (cm)	5.10 $\pm$ 4.95	4.06 $\pm$ 4.95	0.035

88.9% cases were Responders. 45.8% cases had near complete response followed by 29.2% cases had partial response and 25.0% cases had complete response to CRT.

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Table 7: Response to CRT

Response to CRT	No. of Cases (N=27)	Percentage (%)
Responders	24	88.9
• Complete response	06	25.0
• Near complete response	11	45.8
• Partial response	07	29.2
Non-responders	03	11.1

Parameters for comparison of residual disease on MRI (POST CRT) & histopathology were Sensitivity: 33.33%, Specificity: 100%, PPV: 100% & NPV: 27.27%.

Table 8: Comparison between residual disease on MRI (POST CRT) & histopathology

Residual disease	MR positive	MR negative	
HP positive	08	16	24
HP negative	0	06	06

Parameters for comparison between MRI & histopathology for CRM involvement were Sensitivity: 33.33%, Specificity: 100%, PPV: 100% & NPV: 66.67%.

Table 9: Comparison between MRI & histopathology for CRM involvement

CRM on MRI	CRM on histopathology		
	Involved	Not involved	Total
Involved	3	0	3
Not involved	6	12	18

On comparison between MRI & histopathology for bowel wall invasion pre-CRT parameters were Sensitivity: 100%, Specificity: 100%, PPV: 100% & NPV: 100%.

Table 10: Comparison between MRI & histopathology for bowel wall invasion pre-CRT

Stage on MRI	Stage on histopathology		
	T1/T2	T3/T4	TOTAL
T1/T2	1	0	1
T3/T4	0	2	2
TOTAL	1	2	3

In post CRT patients MRI tends to overstage the lesions as compared to the histopathological results. Parameters were Sensitivity: 100%, Specificity: 33.33%, PPV: 54.55% & NPV: 100%.

Table 11: Comparison between MRI & histopathology for bowel wall invasion post CRT

Stage on MRI	Stage on histopathology		
	T1/T2/Tis	T3/T4	TOTAL
T1/T2	5	0	5
T3/T4	10	12	22

Out of 8 patients who showed metastatic lymphadenopathy MRI correctly identified 6, MRI falsely showed metastatic disease in 3 patients when there was no evidence of metastatic adenopathy on histopathology. Parameters were Sensitivity: 75%, Specificity: 86.36%, PPV 66.67% & NPV 90.48%.

Table 12: Comparison between MR & HPE in predicting metastatic adenopathy

	HP POSITIVE	HP NEGATIVE	TOTAL
MRI POSITIVE	6	3	9
MRI NEGATIVE	2	19	21

A correct diagnosis was made with MR imaging in metastatic nodal staging (N0, N1, 2, 3) in 24 patients which correlated with histopathology staging. 3 patients were over staged as compared to histopathology and 3 patients were under staged. Parameters on comparing nodal staging on MRI and histopathology were Sensitivity: 88.89%, Specificity: 95.45%, PPV: 88.89% & NPV: 95.45%.

Table 13: Comparison between nodal staging on MRI and histopathology

	N0	N1/2/3	Total
MR	21	09	30
PATH	22	08	30

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DISCUSSION

In recent years, MRI with external body coils has been increasingly advocated in diagnosing and staging rectal cancer. The UK cancer research statistics reveal that the age group with the highest prevalence is 60 to 80 years, whereas most of our patients were in the 50-70 age group (60%). The Mercury group.[7] showed a mean age of 68 years, while the mean age in our study was 53.07 years. In the Indian scenario, also rectal cancer is commoner as patient age increases, but Pal et al.,[8] noted that the distribution was 42% in patients less than 40 years and 57% in patients more than 40 years.

There were more males than females affected in our study [76.6%] as seen in Table 2, in keeping with studies by Lafrate et al.,[2] and Chun et al.,[9] The UK cancer research statistics reveal a higher prevalence in males and this predominance was also noted in the large multicenter trial by the Mercury Group[7], 60% of whose patients were males.

In present study, most tumors were in the upper and middle third of the rectum. This was also seen in a study by the Mercury group.[7] The predominant tumor stage at presentation, was T3 (tumor breaching the low signal intensity line of the muscularis and extending into the perirectal fat), on MR imaging and pathology, which was also supported by review of literature.[1,5,10,11] A correct diagnosis was made with MR imaging in T staging of bowel wall invasion in all 3 patients who had evidence of invasion on histopathology. Our study showed an overall sensitivity of 100% and specificity of 100% in predicting bowel wall invasion in pre-CRT patients.

MR can cause overstaging or understaging borderline T3-T2 tumors due to the presence of tumour spicules extending into the mesorectal fat – these can be due to radiation fibrosis or desmoplasia or due to tumour masses. Making this distinction is often difficult and has been encountered in several previous studies.[12] Hence the poor specificity in distinguishing T2 and T3 lesions. However, differentiating between minimal T3 infiltration and T2 lesions is often of relatively little consequence, as patients with minimal infiltration into perirectal fat are at low risk of surgical failure from circumferential excision margin involvement, as shown in the study by Brown et al.[12]

Our study showed a sensitivity of 33.33 % and specificity of 100% for Circumferential resection margin [CRM] involvement on MRI. We also found that it is particularly difficult to stage in patients with a paucity of fat. Measurement of CRM was also difficult anteriorly as most patients had annular tumors, this area needed to be assessed in most patients. Other studies have also reported similar difficulties.[13]

In a study of 26 specimens obtained after total mesorectal excision, Blomqvist et al.,[14] showed a sensitivity and specificity of 100% and 61%, respectively, for the prediction of involvement of the circumferential resection margin. In a study of 43 patients with rectal cancer, Bissett et al.,[13] found an accuracy, sensitivity, and specificity of 95%, 67%, and 100%, respectively, for prediction of the circumferential resection margin. In a study of 98 patients, Brown et al showed agreement in 95% of cases between MR imaging and histologic findings for the prediction of circumferential resection margin.

While determining CRM involvement in post CRT patients it is necessary to differentiate between fat stranding in mesorectal tissue which is due to post therapy fibrosis and inflammatory changes from that due to tumor infiltration. This is very difficult and needs very detail analysis. Dynamic contrast enhanced MRI could play a role in this situation and help in differentiating fibrosis from tumor infiltration.

CRM infiltration was found in 3 tumours on MR with a mean of 3.97 mm but on pathology only 9 had CRM involvement with a mean of 4.3 mm. In a large study assessing the use of CRM, the risk of recurrence in CRM positive patients was higher than CRM negative patients, and the risk of death was three times. Also, CRM positive patients have only a 15% 5-year survival.[8]

A valid criterion on MR for predicting CRM infiltration is 6 mm between tumor and the mesorectal fascia. This was established by Beets-Tan et al.[15] In their experience, at 5 mm between tumor and the mesorectal fascia at MR imaging predicted an uninvolved CRM of 1 mm at histologic analysis with 97% confidence.

In our study comparison between MRI & histopathology for CRM involvement, demonstrated sensitivity 33.33%, specificity 100%, PPV 100% & NPV 66.67%. The Mercury Group showed an accuracy for prediction of clear CRM as 91% and a NPV of 93% in patients who had undergone short course RT or no RT. In those who had received long course RT, the accuracy was 77 % and NPV was 98%.

For nodal [N] staging, a correct diagnosis was made with MR imaging in 24 patients which correlated with histopathology staging. 3 patients were overstaged as compared to histopathology and 3 patients were understaged. For comparison between MR & pathology in predicting metastatic adenopathy, our study showed 75% Sensitivity, 86.36% specificity, Positive predictive value 66.67%, and Negative predictive value 90.48%.

There are widely varying results in the various studies reviewed with no observed trend or correlation in prediction of metastatic adenopathy, but the consensus is that MR fares poorly in this aspect.[2,12] Predicting metastatic adenopathy is a challenge due to the multifactorial determinants involved considering size, signal and contour and the high prevalence of tumour in normal sized nodes and enlarged nodes with just benign reactive change.[12]

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Only 1 of 30 (3.3 %) of patients had distant metastases. Most other studies also had a low prevalence of distant metastasis except, O'Connell et al report a significant drop in 5-year survival from 44 % in those with nodal disease without metastases, to a dismal 8% in those with metastases. [16] 80% of the tumors in our study were moderately differentiated adenocarcinomas, as observed in other reports. [7]

27 patients out of 30 received preoperative CRT therapy because suspected extensive rectal cancer & to make potentially curable tumours amenable to surgery. According to a study by Vliegen et al.,[3] short course radiotherapy resulted in no discernible histopathologic difference or effect on the tumors. There was no evidence of florid inflammation or fibrosis. Accordingly, they consider that this treatment had no effect on results.

Gagliardi et al.,[17] reported a sensitivity of MRI in detecting invasion through the bowel wall as 89% (16/18), specificity as 80% (8/10), and accuracy as 86% (24/28). Sensitivity for malignant lymphadenopathy was 67% (8/12), specificity was 71% (10/14), and accuracy 69% (18/26). [11]

Blomqvist et al.,[14] reported a near complete visualisation of the various layers of the rectal wall on pelvic phased-array images. The sensitivity of MR in correctly staging T3 tumours compared with histopathology was 81% with a specificity of 82%. Penetration of the rectal wall was predicted with a sensitivity of 82% and a specificity of 87%. Sensitivity and specificity in predicting lymph node metastases was 83% and 74% respectively.[10]

In summary, in our study sensitivity, specificity, PPV and NPV of 3 Tesla MR for prediction of metastatic adenopathy were 75%, 86.36%, 66.67% and 90.48 % respectively. Sensitivity, specificity, PPV and NPV of 3 Tesla MR for prediction of bowel wall invasion pre CRT were 100% and 100%, 89.7% and 100 % respectively. Sensitivity, specificity, PPV and NPV of 3 Tesla MR for prediction of bowel wall invasion post CRT were 100%, 33.33%, 54.55% and 100% respectively. Sensitivity, specificity, PPV and NPV of 3 Tesla MR for prediction of CRM involvement = 33.33%, 100%, 100% and 66.67 % respectively.

High resolution T2 weighted images proved to be the best imaging sequence for prediction of rectal wall anatomy as well as determination of tumour stage. Review of literature revealed comparable results of imaging with 3 Tesla MR when compared to 1.5 Tesla MR with no added benefit due to higher field strength.

IMAGES

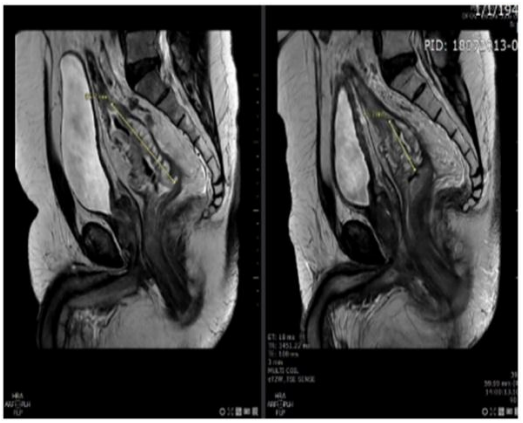

Figure 1

Pre and post CRT comparison of the length of the lesion. As shown in the image on the right side the length of the affected segment has decreased significantly as compared to the pre CRT image on the left side.

Figure 2

Pre and post CRT images of a patient showing significant decrease in the thickness of the lesion. Also seen is decrease in the size of the lymphnode in the posterior perirectal space.

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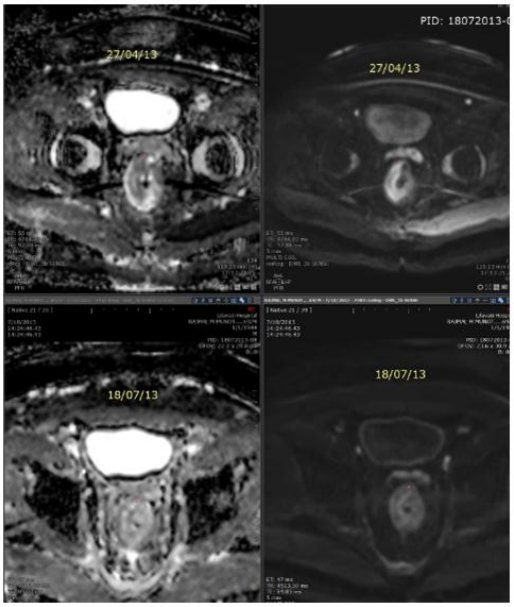

Figure 3

Pre and post CRT images of a patient showing changes in diffusion restriction. The images in the upper half (pre CRT) show restricted diffusion in the rectal lesion. Images in the lower half (post CRT) show no evidence of restricted diffusion indicating response to CRT.

Figure 4

Pre and post CRT changes in the length and thickness of the rectal lesion. As compared to the pre treatment images on left side there is significant decrease in length and thickness of the lesion in post CRT images(right side). Also note decrease in the perirectal fat stranding and disappearance of a small lymph node. This indicates downstaging of the lesion from T3 to T2 and N1 to N0

CONCLUSION

MR imaging is in the forefront as a problem-solving technique for treatment planning in patients with rectal carcinoma. Initial results in older studies were disappointing due to technical limitations. However, advances in terms of imaging equipment, coils, and sequences have consistently improved the technique, with a progressive increase in accuracy. Because most tumours are T3 at presentation and due to its excellent contrast and spatial resolution and large field of view, MR imaging has fulfilled the requirements for becoming the imaging technique of choice for the preoperative staging of rectal cancer.

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