

RECTAL TUMOR STAGING MRI. HOW EFFECTIVE IS IT IN CHARACTERIZATION OF DEPTH OF EXTRAMURAL INVASION AND EXTRAMURAL VASCULAR INVASION?

Javaria Aleem,¹ Pir Abdul Ahad Aziz,¹ Muhammad Talha Yaseen,¹ Kashif Siddique,¹ Amna Babar²

¹Department of Radiology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan.

²Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan.

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ABSTRACT

INTRODUCTION: Rectal cancer is amongst the most common gastrointestinal tumors. MRI is required at diagnosis followed by with or without neoadjuvant therapy and surgery. Accurate staging is not only important for predicting prognosis but also determine the risk of recurrence. Independent prognostic factors like extramural invasion (EMI) into mesorectal fat, extramural vascular invasion (EMVI) and circumferential resection margins are also very important and needs to be addressed in MRI reports as presence of any of these factors may change the management plan entirely. **OBJECTIVE:** The purpose of this study is to determine accuracy of baseline MRI in detecting extramural tumor extension and extramural vascular invasion in rectal tumors taking pathological staging as gold standard. **MATERIALS AND METHODS:** The study was approved by our institutional review board which waived the requirement for informed consent. The clinical data of all the patients treated for rectal carcinoma at Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore between 1st December 2015 and 30th November 2017 were retrospectively evaluated for the presence of EMI and EMVI by rectal carcinoma on MRI. EMVI was then graded over 5 point scale. Findings of MRI were then correlated with histological findings and were labelled as positive or negative on the basis of per-operative presence or absence of EMI and EMVI. **RESULTS:** 117 patients were included in this study. Out of these 117; 111 patients (94.9 %) received pre-operative chemoradiotherapy. 6 patients (5.1%) did not receive pre-operative chemotherapy and underwent upfront surgery. On MRI EMVI (mr-EMVI) was present in 22 (18.8%) patients while on pathology it was present in 19 (16.2%) patients. A close association was observed between the baseline mr-EMVI status and the extent of mesorectal invasion. Stage T3c tumors were the most frequent to present EMVI i.e. 54.5% (12/22). On baseline MRI mr-EMVI was predominantly present in tumors located in mid rectum (86.4%; 19/22). EMI was also seen frequently in stage T3c patients (i-e 45/117;38.5%). Overall MRI accuracy in T3 disease was found to be 76.14%. **CONCLUSION:** Baseline MRI is highly effective imaging modality to evaluate pre-operative EMI and EMVI in rectal cancers which have a significant independent impact on the management plan.

Keywords: Rectal cancer, Extramural invasion, Extramural vascular invasion, MRI.

Introduction

Staging of tumor plays an important role in deciding the appropriate management plan and predicting the

outcome of the disease. Similarly, appropriate tumor staging in cases of rectal tumor is vital. Magnetic

Correspondence : Dr. Pir Abdul Ahad Aziz
Department of Radiology,
Shaukat Khanum Memorial Cancer Hospital
and Research Center, Lahore, Pakistan
Email: abdulahad.q@gmail.com

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Resonance Imaging (MRI) is usually performed for the local tumor staging of rectal carcinoma due to its high resolution in depicting the characteristics and extent of the tumor and its relationship with adjacent viscera and neurovascular bundles.^{1,2} Extramural tumor invasion (EMI) and Extramural vascular invasion (EMVI) are two very important prognostic factors which independently predicts the local or distant tumor metastasis,³ response to chemoradiotherapy (CRT) and overall survival.^{4,5}

The purpose of our study is to identify the effectiveness of rectal tumor staging MRI in the characterization of extramural invasion and extramural vascular invasion as no such local data is available in the literature.

Material and Methods

The study was approved by our institutional review board which waived the requirement for informed consent. The clinical data of all the patients treated for rectal carcinoma at Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore between 1st December 2015 and 30th November 2017 were retrospectively evaluated. Only those patients fulfilling the inclusion criteria were included in the study. Inclusion criteria were: patients of rectal carcinoma who have (1) preoperative baseline MRI examination, (2) surgery in our hospital with or without pre-operative chemo-radiotherapy, (3) availability of surgical pathology results of EMVI, (4) histopathology evaluation in our hospital. 117 patients who fulfilled the inclusion criteria were inducted in the study.

MRI imaging was performed at 1.5 Tesla (Philips Ingenia) and 3.0 Tesla (Siemens Magnetom Vida) systems. The MRI protocol included the multiparametric MRI sequences included DWI and contrast enhanced images. The standard dose of intravenous contrast gadobutrol (Gadovist®) was given to all patients (i.e 0.1 mmol per kilogram of body weight).

MRI images of these 117 patients were then retrospectively evaluated by 3 Radiology fellows independently; supervised by 1 Consultant Radiologist for the presence of EMI and EMVI by rectal carcinoma on MRI. All three fellows were blinded to previous MRI reports and surgical outcome. The MRI features suggesting EMVI were: 1) vascular irregularity or vascular expansion 2) intermediate signal intensity

tumor within the vessel lumen 3) loss of vascular flow void or contrast enhancement. EMVI was then graded over 5 point scale suggested by Smith et al. Findings of MRI were then correlated with histological findings and were labelled as positive or negative on the basis of per-operative presence or absence of EMI and EMVI. The correlation between mr-EMVI, depth of extramural invasion and other clinical factors were analysed by Pearson Chi-Square and Fisher's Exact test where appropriate. All statistical analyses were performed using SPSS version 25.0.

Results

A total of 117 patients with mean age of 62 years (19-81 years) were included in study. Out of these 117 patients 82 were males and 35 were females. On histopathological evaluation 70 patients had moderately differentiated adenocarcinoma, 16 patients had adenocarcinoma with signet ring morphology, 13 patients had well differentiated adenocarcinoma, 13 patients had poorly differentiated adenocarcinoma and 5 patients had mucinous adenocarcinoma. 111 patients (94.9%) received pre-operative chemoradiotherapy. 6 patients (5.1%) did not receive pre-operative neo-adjuvant therapy and underwent upfront surgery.

On MRI EMVI (mr-EMVI) was present in 22 (18.8%) patients while on pathology it was present in 19 (16.2%) patients (Fig.1a, b). This discrepancy may be explained due to tumor shrinkage in response to pre-operative therapy. Statistically there is insignificant impact of pre-operative therapy on EMVI which means downstaging the tumor by neo-adjuvant therapy also reduces the extramural vascular invasion on pathological specimen. A close association was observed between the baseline mr-EMVI status and the extent of mesorectal invasion. Statistically significantly more mr-EMVI was seen in tumors of stage T3c (5-15 mm) i.e. 54.5% (12/22) as compared with those with the depth of extramural penetration less than 5 mm (18.2%; 4/22) and those which are less penetrative tumors i.e. < 1mm (4.5%; 1/22) ($p = 0.000$). The location of circumferential tumor within rectal wall was also found to be strongly related to the presence of EMVI. On baseline MRI mr-EMVI was predominantly present in tumors located in mid rectum (86.4%; 19/22). All MRI features are summarized seen in (Tab.1).

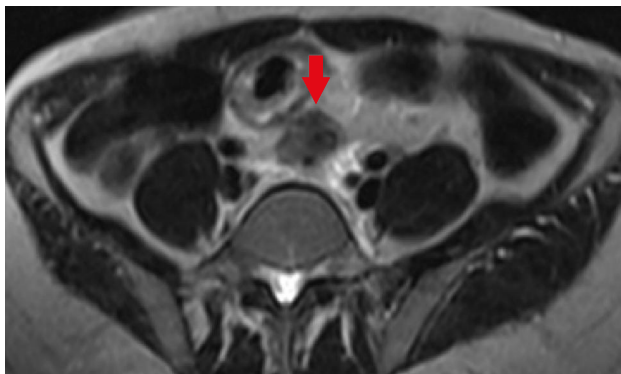


Figure 1a: MRI T2 weighted axial image showing extramural vascular invasion depicted by loss of vascular flow void with intermediate signal soft tissue surrounding vessel lumen (red arrow).



Figure 1b: MRI T2 weighted sagittal image showing circumferential rectal tumor with tubular structure in pre-sacral space representing involved vessel; note the involved mesorectal node (red arrow).

The pathological extramural vascular invasion (pEMVI) status by tumor location, grade and T category analyzed and can be seen in (Tab. 2). The total of 19 patients (16.2%) were pEMVI-positive, of whom 18 (15.4%) had received preoperative CRT while in 1 (0.9%) underwent upfront surgery and showed presence of EMVI (Fig. 2a, b). We found that there was statistically significant association between the pEMVI status and the grade of the tumor ($p = 0.000$). The pEMVI was more frequent in pT3 tumors that included 16 (13.7%). High grade tumor shows greater risk of EMVI 63.2% (12/19) while in moderate and low grade tumors EMVI was seen in 5.3% (01/19) and 31.6%

Imaging Features	No. (%) of Patients			P
	mr-EMVI Negative	mr-EMVI Positive	Total	
Tumor Location				
Distal	39 (33.3%)	02 (1.7%)	41 (35.0%)	0.010
Mid	49 (41.9%)	19 (16.2%)	68 (58.1%)	
Upper	07 (6.0%)	01 (0.9%)	08 (6.8%)	
MRI Tumor Stage				
T2	04 (3.4%)	00 (0.0%)	04 (3.4%)	0.073
T3	91 (77.8%)	21 (17.9%)	112 (95.7%)	
T4	00 (0.0%)	01 (0.9%)	01 (0.9%)	
Extramural depth of invasion in T3 & T4 tumor				
T3a (<1mm)	29 (24.8%)	04 (3.4%)	33 (28.2%)	0.000
T3b (1-5 mm)	31 (26.5%)	01 (0.9%)	32 (27.4%)	
T3c (5-15 mm)	33 (28.2%)	12 (10.3%)	45 (38.5%)	
T3d (> 15 mm)	02 (1.7%)	05 (4.3%)	07 (6.0%)	
Mesorectal fascia involvement by tumor				
No	14 (12.0%)	01 (0.9%)	15 (12.8%)	0.279 ^a
Yes	81 (69.2%)	21 (17.9%)	102 (87.2%)	

^aAssociations were examined using the one-sided Fisher exact test.

Table 1: Comparison of Imaging features of the Tumors on Baseline MRI With MRI detected Extramural Venous Invasion (mr-EMVI) Status

Pathology-Detected EMVI Status	No. (%) of Patients			P
	pEMVI Negative	pEMVI Positive	Total	
Preoperative therapy				
No	05 (4.3%)	01 (0.9%)	06 (5.1%)	1.000 ^a
Yes	93 (79.5%)	18 (15.4%)	111 (94.9%)	
Tumor grade				
No residual tumor	30 (25.6%)	00 (0.0%)	30 (25.6%)	0.000
Low	46 (39.3%)	06 (5.1%)	52 (44.4%)	
Moderate	12 (10.3%)	01 (0.9%)	13 (11.1%)	
High	10 (8.5%)	12 (10.3%)	22 (18.8%)	
Histologic tumor stage				
No residual	30 (25.6%)	00 (0.0%)	30 (25.6%)	0.000
pT1	03 (2.6%)	03 (2.6%)	06 (5.1%)	
pT2	20 (17.1%)	0 (0.0%)	20 (17.1%)	
pT3	43 (36.8%)	16 (13.7%)	59 (50.4%)	
pT4	02 (1.7%)	0 (0.0%)	02 (1.7%)	

^aAssociations were examined using the one-sided Fisher exact test.

Table 2: Comparison of Histopathologic Features of the Tumors With Pathology-Detected Extramural Venous Invasion (pEMVI) Status

(06/19). In 30 patients (25.6%) cases no residual tumor was detected on histopathology after pre-operative chemo-radiotherapy.

The other factor focused in study is to determine accuracy of baseline MRI in depicting extramural mesorectal fat invasion of rectal tumor. Out of 117

patients, 33 were having depth < 1mm (T3a), 32 within 1-5 mm (T3b), 45 above 5mm but below 15 mm (T3c) and only 7 patients were having advanced disease with depth above 15 mm (T3d) (Fig. 1c). Overall MRI showed sensitivity of 75.86%, specificity of 100% and diagnostic accuracy of 76.14% in T3 disease.

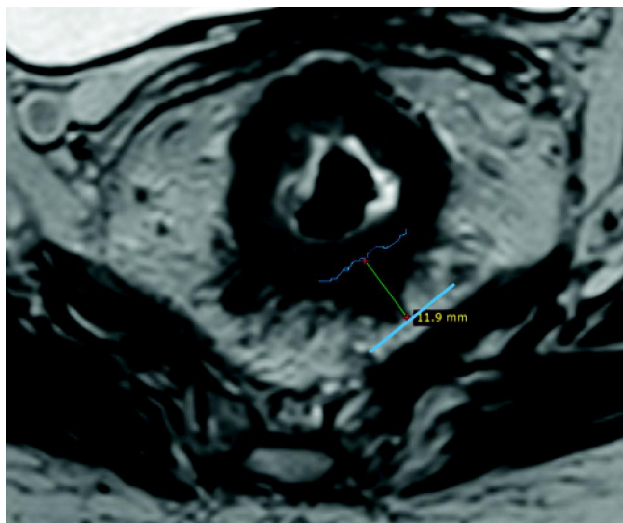


Figure 1c: Oblique axial thin-section T2-weighted MR images showing extramural tumor invasion. Note the nodular intermediate signal intensity tumor invading the mesorectal fat with the depth of invasion measuring 11.9 mm (T3c).

Discussion

Rectal carcinoma is amongst the most common gastrointestinal malignancies worldwide⁶ with high mortality rates due to increased risk of local recurrence and metastasis.⁷ About 98% of the rectal tumors are adenocarcinoma on the histopathology which usually affects elder population i-e > 50 years with slight male predominance;⁷ therefore the focus of this article is on rectal adenocarcinoma being the most common rectal malignancy. Patients with rectal cancer usually present with symptoms of painful defecation, rectal bleeding and altered bowel habits.⁸

Radiological imaging not only plays a vital role in the staging of rectal carcinoma but also plays a key role in the assessment of other important prognostic features like extramural tumor invasion (EMI), extramural tumor vascular invasion (EMVI).^{4,9} Usually, rectal tumors are staged with MRI followed by surgery with or without prior CRT which depends on the stage of disease and extent of tumor infiltration and later

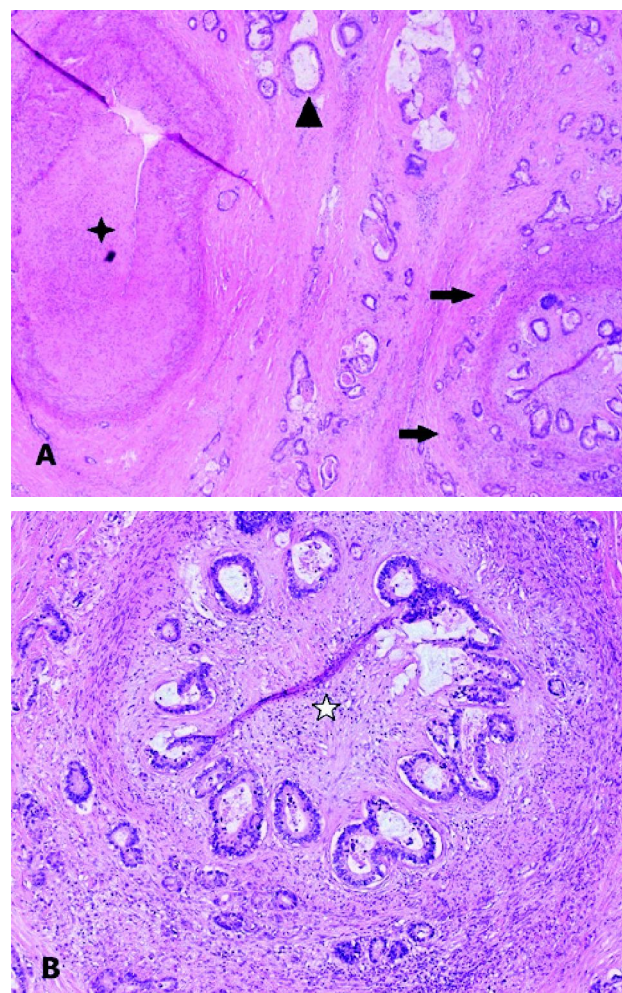


Figure 2: A) Histopathological image showing thick walled artery (asterisk) adjacent to vein. EMVI is present in vein (black arrows), perineural invasion is also present (black arrow head). **B)** Magnified high resolution view showing extramural venous invasion by tumor cells (white star).

for post-operative follow-up or surveillance in cases of non-operative approach. Therefore, accurate pre-operative tumor staging is very important as it would allow surgeons to decide appropriate management plan i-e surgical technique or pre-surgery tumor bulk reduction by chemoradiotherapy.⁷ MRI staging of rectal cancer comprises of assessment of tumor location and its depth of invasion and its relationship with adjacent viscera, neurovascular bundles, levator sling, peritoneal reflection and internal sphincter, nodal involvement, evaluation of mesorectum and osseous metastasis. MRI is also very specific in the detection of extramural invasion into mesorectal fat and extramural vascular invasion.¹⁰ EMI is defined as an extension of tumor beyond muscularis propria

into the mesorectal fat; whereas, EMVI is defined as tumor extension along vessels in mesorectal fat away from tumor itself¹¹ and can be contiguous or non-contiguous. Prior studies have shown that patients with positive EMVI are associated with increased risk of developing metastases and local recurrence.³ Another study conducted by Smith et al. in 2008 showed that positive EMVI increases the risk of distant metastasis up to 4 times and reduces 3-year survival to 35% from 74% in comparison to EMVI negative patients.¹ It is important to mention here that pre-operative CRT to downsize the tumor is also significantly associated with changing the patient's EMVI positive status on baseline MRI to negative on histopathology.¹¹ EMVI is graded on the basis of 5 point scale in which score of 0-1 is considered as definitely negative; score of 2 is considered equivocal and score of 3-4 is considered definitely positive.¹²

Surgical excision is the mainstay of treatment for rectal cancers with the prime goal to achieve negative resection margins and to reduce risk of local recurrence. Therefore, tumors are usually down-staged prior to the surgery with CRT in cases of advance tumor.¹³ Additionally, in recent years total mesorectal excision (TME) is being used frequently for T2 and T3 cancers as it has been reported to have reduced the local recurrence and improve 5 years survival rate as compared to conventional surgery;¹⁴ but in cases of T3 tumors circumferential resection margin (CRM) is another important parameter to be evaluated prior to surgery by MRI; as positive CRM is highly associated with increased rates of postoperative recurrence;¹⁵ therefore, in such cases pre-operative neoadjuvant treatment is recommended to reduce risk of post-operative recurrence.¹⁶ The criteria for predicting CRM infiltration on MRI was first established by Beets-Tan et al in 2001;¹⁷ they suggested that distance between tumor and mesorectal fascia of at least 5mm helps in predicting negative CRM of 1mm on histologic evaluation with the confidence of 97%.⁷ Nevertheless, evaluation of CRM by MRI may be limited by few factors like in tumors of the anterior rectal wall due to poor visualization of mesorectal fat and skinny patients with very little perirectal fat.⁷ On the other hand, patients with T1 cancers are usually treated by local transanal excision or transanal endoscopic microsurgery;¹⁸ whereas, those with T4 cancer requires a long course of pre-operative CRT

to downsize tumor prior to surgery and increase chances of getting negative resection margins and negative EMVI status.¹⁹

We observed several limitations in our study which needs to be considered. Firstly, the design of the study we conducted was retrospective and secondly, the number of patients was limited in our study.

Conclusion

In conclusion, baseline MRI is highly effective imaging modality to evaluate pre-operative EMI and EMVI in rectal cancers which have a significant independent impact on the management plan.

Conflict of Interest: None

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