

Diagnostic Accuracy of Rectal Tumor Staging MRI in Evaluating Extramural Vascular Invasion

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ABSTRACT

AIM: To determine the diagnostic accuracy of baseline pre-operative MRI in detecting extramural vascular invasion in rectal tumors compared with histopathological reference standard.

MATERIALS AND METHODS: Patients presenting with rectal carcinoma at Salmaniya Medical Complex, Bahrain between 1st January 2017 and 31st December 2019 were retrospectively reviewed for the presence of extramural vascular invasion (EMVI) detected on pre-operative staging MRI and a 5-point EMVI score (0-4) was assigned. These findings were then correlated with histopathology reports that were labelled as either positive or negative for EMVI.

RESULTS: A total of 82 patients were included in this study. Out of these patients, 71 patients (86.5%) received pre-operative chemotherapy and radiotherapy. 11 patients (13.4%) did not receive any pre-operative chemotherapy or radiotherapy and proceeded directly to surgery. On MRI EMVI (mr-EMVI) was reported in 31 patients (37.8%) while on pathology it was seen in 26 patients

(31.7%). Sensitivity, specificity and accuracy of mr-EMVI were 81.2%, 90% and 86.6%, respectively. It was noted that upon staging the tumor, the stage most frequently associated with EMVI was Stage T3c with 18 out of the 31 cases (58%) showing EMVI on MRI. The predominant location of the tumors showing mr-EMVI was in tumors located in mid rectum (90.3%; 28/31).

CONCLUSION: Pre-operative baseline MRI for staging rectal tumors is a highly effective imaging modality to evaluate for the presence of EMVI which can have a significant effect on the management plan.

Key words: Rectal cancer; Colorectal cancer; Extramural invasion; Extramural vascular invasion; MRI

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INTRODUCTION

Tumor staging plays a vital role in patient management and evaluating the prognosis of the disease. Rectal tumor staging is hence very important in deciding the appropriate management. Magnetic Resonance Imaging (MRI) is increasingly being performed for the local tumor staging of rectal tumors as it can accurately depict the extent of the tumor and outline any local organ involvement as well as involvement of the neurovascular bundles^[1,2]. Extramural vascular invasion (EMVI) of rectal tumors is defined as malignant cells present within the blood vessels located beyond the muscularis propria^[3]. The presence of EMVI is a poor prognostic factor in rectal tumors. Talbot et al. reported 5-year survival rate of merely 33 % in patients with tumor invading the extramural veins^[3]. EMVI also predicts distant tumor metastasis, and response to chemoradiotherapy^[4]. The main purpose of this study was to determine the diagnostic accuracy of pre-operative rectal tumor staging MRI in the characterization of extramural vascular invasion in comparison with post-operative histopathological findings.

METHODS

Patients

The institutional review board of our hospital approved the retrospective study and waived the requirement for informed consent. The clinical data of all the patients presenting for rectal carcinoma to the surgical and oncology departments at Salmaniya Medical Complex between 1st January 2017 and 31st December 2019 were retrospectively assessed. The inclusion criteria were patients with pathologically proven rectal carcinoma who underwent pre-operative baseline MRI for staging purposes and then proceeded to either chemoradiotherapy or surgical resection in our institution. Patients who had received previous treatment in the form of either chemo or radiotherapy or surgery were excluded from the study. Hence, a total of 82 patients were included in our study.

MRI Protocols

All the MRI examinations were performed with a 1.5 Tesla system (MAGNETOM - Siemens), applying a phased-array body coil on the anterior and another phased-array spine coil on the posterior aspect of the patient. The MRI protocol included multiparametric MRI sequences including diffusion-weighted imaging (DWI) and contrast enhanced images. The standard dose of intravenous gadolinium-based contrast was given to the patients (0.1 mmol/kilogram of body weight).

Image Analysis

After image acquisition, the study was archived in the computerized radiological database for image analysis and reporting. The studies were retrospectively evaluated by two body-imaging consultant radiologists for the presence of EMVI. The two radiologists were blinded to any previous radiological and pathological reports and the surgical outcome. The features suggestive of EMVI were vascular irregularity or expansion, loss of the signal void with intermediate signal intensity tumor within the vessel and contrast enhancement. A 5-point scoring system devised by Smith et al was used and a score of 0-4 was assigned based on the radiological features, with the studies receiving a score of 0,1 and 2 being labelled as negative for EMVI and those with scores of 3 and 4 were considered positive for EMVI^[1].

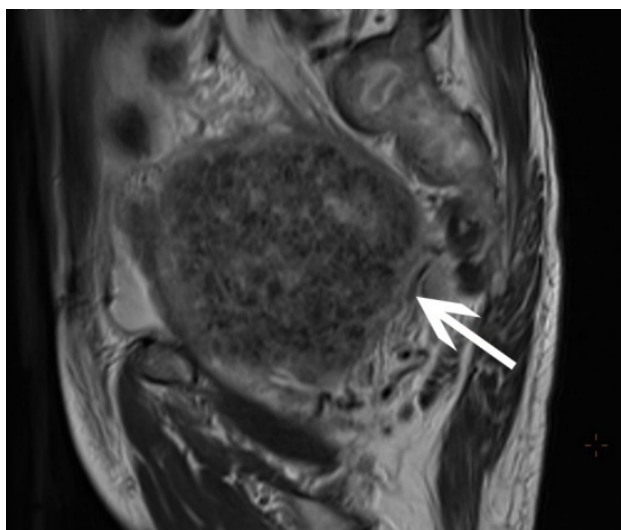


Figure 1 T2-weighted sagittal MRI image showing a large rectal tumor encasing a vessel (arrow) which shows loss of the normal flow void with no significant expansion or contour irregularity, representing MRI-EMVI score of 3.

Histopathological Analysis

Slides were prepared for histological examination according to the standard guidelines. They were evaluated by two consultant histopathologists with over 10 years of experience. They reported the presence or absence of EMVI according to the standard definition: the presence of tumor tissue within an endothelium lined space, which was either surrounded by a rim of smooth muscle or contained red blood cells^[1].

Statistical Analysis

The sensitivity, specificity, accuracy, positive and negative predictive values for the detection of EMVI by MRI were calculated by comparing the mr-EMVI score with the histopathological results. The correlation between mr-EMVI and other clinical factors were analyzed by Pears on Chi-Square and Fisher's Exact test where appropriate. All statistical analyses were performed using SPSS version 26.0.

RESULTS

A total of 82 patients with mean age of 61 years (38 - 81 years) were included in our study. 51 were male and 31 were female patients. 71 patients (86.5 %) received pre-operative chemotherapy and radiotherapy, while 11 patients (13.4%) did not receive any pre-operative neo-adjuvant therapy and proceeded directly to surgery. On histopathological evaluation, 48 patients were found to have moderately differentiated adenocarcinoma, 12 had adenocarcinoma with signet ring morphology, 9 were found to have well-differentiated adenocarcinoma, 7 patients had poorly differentiated adenocarcinoma and 6 patients had mucinous adenocarcinoma. On MRI EMVI (mr-EMVI) was reported in 31 (37.8%) patients, while on pathology it was noted in 26 patients (31.7%) (Figures 1 and 2).

The most likely explanation for this discrepancy might be related to tumor response to pre-operative chemoradiotherapy. Statistically, there was an insignificant impact of pre-operative therapy on EMVI meaning that downstaging the tumor by neo-adjuvant therapy also decreases the extramural vascular invasion on the pathological specimen. There was also a close association noted between the baseline mr-EMVI status and the extent of mesorectal invasion. It was noted that a statistically significant increase in mr-EMVI was observed in tumors of stage T3c (5-15 mm) with 18 out of the 31 cases (58%) showing EMVI on MRI, as compared to tumors with

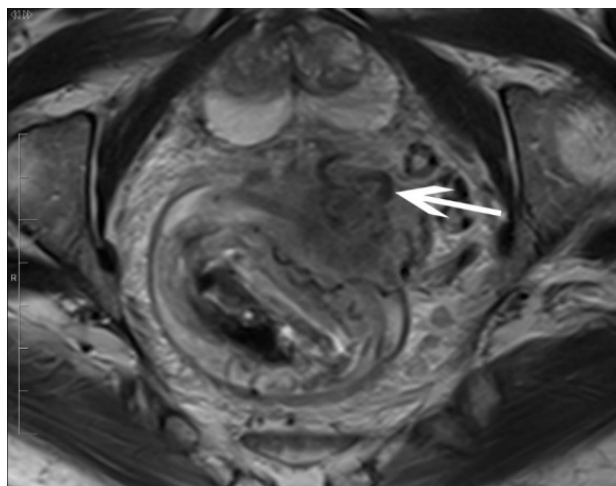


Figure 2 T2-weighted axial MRI image showing eccentrically located rectal tumor with adjacent vessel (arrow) which appears expanded with loss of normal flow void, representing MRI-EMVI score of 4.

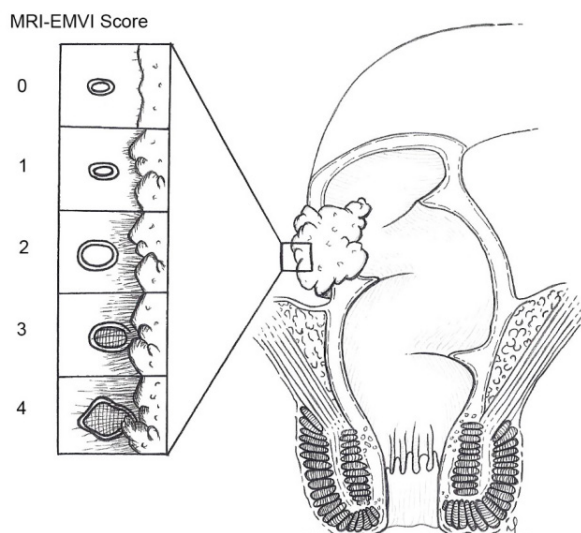


Figure 3 Illustration showing a summary of magnetic resonance imaging - extramural vascular invasion (EMVI) scoring system

less than 5mm depth of extramural invasion (19.3%; 6/31) and tumors with less than 1mm invasion (6.4%; 2/31) ($p = 0.000$). A strong correlation was also noted between the location of the tumor in the rectum and the EMVI status, with the tumors located in the mid rectum showing increased mr-EMVI (90.3%; 28/31) (Table 1).

The pathological extramural vascular invasion status by tumor grade, location and T-category was analyzed and can be seen in (Table 2). A total of 26 patients (31.7%) were EMVI-positive on pathology, out of which there were 24 patients (29.2%) who had received pre-operative therapy, while 2 patients (2.4 %) underwent surgery without chemoradiotherapy and showed presence of EMVI. We found that there was a statistically significant association between the pathological EMVI status and the grade of the tumor ($p = 0.000$). High grade tumors were observed to show an increased risk of EMVI 61.5% (16/26) while moderate and low-grade tumors showed EMVI in 11.5% (03/26) and 15.3% (04/26).

Overall, baseline pre-operative MRI revealed sensitivity, specificity and accuracy of 81.2%, 90% and 86.6%, respectively in detecting EMVI.

DISCUSSION

One of the most common gastrointestinal malignancies worldwide is rectal carcinoma with high mortality rates due to increased risk of local recurrence and distant metastasis^[5,6]. About 98% of the rectal tumors are adenocarcinoma on histopathology and they predominantly affect the elderly population (> 50 years) with a slight male predominance^[6]. Patients with rectal tumors usually present with symptoms of painful defecation, lower gastrointestinal and rectal bleeding as well as altered bowel habits^[7]. Imaging plays a vital role in the staging of rectal malignancy and aids in the assessment of other important prognostic features like extramural tumor invasion, extramural tumor vascular invasion (EMVI)^[4,8].

MRI is the modality of choice for staging rectal tumors along with computed tomography of the chest, abdomen and pelvis to screen for distant metastasis. This is then followed by surgery with or without prior chemoradiotherapy depending on the stage of disease and the extent of tumor infiltration. The higher-grade tumors are subjected to pre-operative chemoradiotherapy to downsize the tumor. Hence, accurate pre-operative staging is very vital as it would allow the surgeons to decide suitable management plan^[6]. MRI staging of

Table 1 Comparison of the imaging features of tumors on the staging MRI with MRI detected extramural vascular invasion (mr-EMVI).

Imaging Features	Number of Patients			P- value
	mr-EMVI Positive	mr-EMVI Negative	Total (percentage)	
Tumor Location				
Upper	2	17	19	0.005
Mid	28	29	57	
Lower	1	5	6	
Tumor Stage on MRI				
T2	0	5	5	0.01
T3	28	46	74	
T4	3	0	3	
Depth of Extramural Invasion				
T3a (<1mm)	2	17	19	0.03
T3b(1-5mm)	6	7	13	
T3c(5-15mm)	18	24	42	
T3d(>15mm)	5	3	8	
Mesorectal Fascia Involvement				
Yes	30	47	77	0.64
No	1	4	5	

Table 2 Comparison of the histopathological features of the tumors with pathology detected extramural vascular invasion (EMVI) status.

Histopathological EMVI Status	Number of Patients (percentage)			P- value
	EMVI Positive	EMVI Negative	Total	
Pre-operative Therapy				
Yes	24	47	71	0.48
No	2	9	11	
Tumor Grade				
No Residual Tumor	3	19	22	0
Low	4	27	31	
Moderate	3	6	9	
High	16	4	20	
Histological Tumor Stage				
No Residual Tumor	0	21	21	0
T1	3	2	5	
T2	2	24	26	
T3	21	5	26	
T4	0	4	4	

rectal tumors evaluated the tumor location, depth of invasion and its relationship with adjacent viscera, neurovascular bundles, peritoneal reflection, internal sphincter, nodal involvement and osseous metastasis. MRI also has high specificity in detecting extramural invasion into mesorectal fat and extramural vascular invasion^[9].

EMVI is defined as tumor extension along vessels in the mesorectal fat surrounding the tumor and can be contiguous or noncontiguous^[10]. Prior studies have shown that patients with positive EMVI are at an increased risk of developing local recurrence and distant metastasis^[3]. Another study by Smith et al in 2008 revealed that there is a 4-fold increased risk of distant metastasis in patients with positive EMVI and reduces 3-year survival rate to just 35% from 74% in comparison with EMVI negative patients^[11]. 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^[10]. EMVI is graded on the basis of 5-point scale in which the scores of 0-1 are considered as definitely negative; score of 2 is considered equivocal

and scores of 3-4 are considered definitely positive^[11]. Score 0 is defined as non-nodular tumor extension through the muscle coat with no vessels adjacent to areas of tumor penetration. Score 1 is minimal extramural stranding/nodular extension, but not in the vicinity of any vessels. Score 2 is characterized by stranding in the vicinity of extramural vessels, but the vessels maintain normal caliber with no definite tumor signal within. Score 3 is intermediate signal intensity within vessels, although the contour and caliber of the vessels is only slightly expanded. And finally score 4 is obvious irregular vessel contour or nodular expansion of vessel by definite tumor signal^[1] (Figure 3).

Surgical excision is the main treatment for rectal tumors with the main goal to achieve negative resection margins, this in turn reduces the risk of local recurrence. Therefore, rectal tumors are occasionally down staged before surgery with chemoradiotherapy in cases of advanced tumors^[12]. Additionally, in recent years total mesorectal excision (TME) is being used frequently for T2 and T3 tumors as it has been reported to have reduced the overall local recurrence rate and improved 5-year survival rate as compared to conventional surgery; but in cases of T3 tumors circumferential resection margin (CRM) is another significant parameter that need to be evaluated by MRI before surgery; as positive CRM is known to be associated with increased rates of postoperative local recurrence^[13,14]. Therefore, in such cases pre-operative neoadjuvant therapy is recommended to reduce the risk of post-operative local recurrence^[14].

The incidence of pathologically proven EMVI in our study (31.7%) is consistent with other reported values^[1]. The difference noted between the baseline mr-EMVI (37.8%) and the histopathological EMVI (31.7%) could be attributed to tumor downstaging due to chemoradiotherapy. We observed several limitations in our study. Firstly, the design of the study was retrospective and secondly, the number of patients was limited in our study. However, the results obtained reflect the effectiveness of pre-operative MRI in detecting EMVI.

In conclusion, pre-operative baseline MRI is a highly effective imaging modality to evaluate for EMVI in patients with rectal tumors, and this can have a significant independent impact on the management plan.

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