MRI Evaluation of Extramural Venous Invasion (EMVI) with Rectal Carcinoma Using High Resolution T2 and Combination of High Resolution T2 and Contrast Enhanced T1 Weighted Imaging

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ABSTRACT

Background: EMVI is a direct invasion of a vein by a tumor. As a predictor of hematogenous metastasis, it is a poor prognostic factor in rectal cancer and can be accurately identified on MRI prior to surgical procedure. Objective: To evaluate the role of contrast-enhanced T1-weighted magnetic resonance imaging (CET1WI) in addition to high-resolution T2-weighted imaging (HRT2WI) in assessing extramural venous invasion (EMVI) of rectal cancer. Methods: In all 195 patients with rectal cancer, HRT2WI and CET1WI sequences were produced within pre-operative MRI for the purpose of assessing for the presence of EMVI (mrEMVI). CET1WI sequences were produced following administration of Gadolinium contrast medium. mrEMVI assessment results were classified into two groups. Group A consisted of mrEMVI assessment results obtained using HRT2WI sequences only. Group B consisted of mrEMVI assessment results obtained using a combination of HRT2WI + CET1WI sequences. Results obtained for each group (A and B) were correlated with a histopathological finding (pEMVI) as a reference standard. Results: Out of a total of 195 rectal cancer patients, mrEMVI was positive in 41 (21%) patients in group A, and in 45 (23%) patients in group B. Histopathological finding demonstrated pEMVI in 54 (27.7%) patients. A statistical analysis of group A (HRT2WI sequences) resulted in 75.9% sensitivity to mrEMVI and 96.4% specificity, Positive Predictive Value of 89.1% and Negative Predictive Value of 91.2% (95% confidence interval (CI), p< 0.05). Statistical analysis of group B (HRT2WI + CET1WI sequences) resulted in 83.3% sensitivity to mrEMVI and 98.5% specificity, Positive Predictive Value of 89.1% and Negative Predictive Value of 91.2% (CI 95%, p< 0.05). Conclusion: T1-weighted magnetic resonance imaging (CET1WI) in addition to high-resolution T2-weighted imaging (HRT2WI) increased evaluation of extramural venous invasion (EMVI) of rectal cancer. Keywords: extramural venous invasion, EMVI, rectal carcinoma, MRI.

1. BACKGROUND

From the viewpoint of surgical oncology, rectal cancers are considered a particular problem amongst the colorectal malignancies (1). MRI is an important tool in pre-operative assessment of rectal carcinoma (2). MRI finding of rectal carcinoma includes the estimation of tumor size and location, and its relationship to the mesorectal fascia (MRF) and anal sphincters. MRI assessment also implies insight into extramural spread (T stage), peritoneal reflection, lymph node involvement, presence of bone metastases and extramural venous invasion (EMVI) (3, 4).

As a direct invasion by tumor, EMVI ought to be an integral part of every histopathology report (pEMVI), even though it is not included in TNM staging. It is defined as tumor lying within an endothelium-lined space that is either surrounded by a rim of muscle or contains red blood cells. If tumor has obliterated the lumen of a vein, an elastic stain may highlight the wall, confirming a rounded structure as a vein (5) (Figure 1 and Figure 2).

As a predictor of hematogenous metastasis, EMVI is a poor prognostic factor in rectal cancer and can be accurately identified on MRI, pre-operatively (6–9). mrEMVI is seen as tubular or serpiginous projections of intermediate signal intensity, which follows a
course of a perirectal vein. It may be either directly contiguous with the tumor or non-contiguous. An initial mrEMVI is important in patient stratification for selection of an appropriate treatment, especially for administration of an adjuvant therapy (10). The presence of EMVI on pre-treatment MRI has been associated with a four-fold increase in risk of distant metastases, and a significant reduction in disease-free survival, from 74% to only 35% (11).

2. OBJECTIVE

The aim of this study was to evaluate the role of contrast-enhanced T1-weighted magnetic resonance imaging (CET1WI) in addition to high-resolution T2-weighted imaging (HRT2WI) in assessing extramural venous invasion (EMVI) of rectal cancer.

3. PATIENTS AND METHODS

Our study was designed as an analytical and comparative study involving 195 patients with rectal carcinoma verified on the basis of a histopathology biopsy specimen. The study was conducted from October 2012 to September 2020. All patients underwent pre-operative MRI for the purpose of surgical resection planning. Within this MRI protocol, HRT2WI and CET1WI sequences were produced in order to assess for the presence of mrEMVI. Contrast CET1WI sequences were produced following intravenous administration of a contrast medium, Magnevist® (gadopentetate dimeglumine), manufactured by Bayer. Examinations were carried out on 1.5 T MRI devices manufactured by General Electric and Siemens. Ultrasound gel was applied per rectum as a contrast medium for rectal lumen marking. Body matrix coil was used, placed on pelvis so that the lower edge of coil was below the pubic bone. The coil was attached with a belt, and the patient entered the machine head first. The protocol had the following sequences: T1FLAIR cor FS FOV400 slice thickness (sl.th.) 2 mm TR 3.25, TE 1.2, voxel size 1.7 x 1.6 x 2 mm; T2 TR/TE 3D cor FOV 450, sl.th.1 mm TR 4.09, TE 1.8 voxel size 1.6 x 1.4 x 1; T2TSE sag FOV 280 sl.th.4mm TR 3700, TE 101 voxel size 0.7 x 0.7 x 4; T2TSE tra FOV 210, sl.th. 4 mm TR 3730, Te101 voxel size 0.8 x 0.8 x 4; T2 cor FOV 500 sl.th. 4 mm, TR 5250, Te99, voxel size 0.7 x 0.7 x 4; VIBE T1 FS tra FOV 450, TR 4.99, TE 2.61, sl.th. 2.5 mm voxel size 2.7 x 1.8 x 2.5; T2TSE tra FOV 210, sl.th. 4mm, TR 666, Te10, voxel size 0.8 x 0.8 x 4.1p2d; DWI FOV 380, TR 4600, TE 76, sl.th. 4mm, B value 50, 300, and 600 with ADC map.

An agreement test between two independent radiologists in evaluation of mrEMVI was performed. Parameters of mrEMVI evaluation were: serpent-like tubular tumor extensions of veins, varicose veins with an irregular contour, presence of intermediate signal intensity along the veins in the vicinity of rectal carcinoma. The results of mrEMVI evaluation were classified into two groups. Group A consisted of results of mrEMVI evaluation using HRT2WI sequences alone. Group B consisted of results of mrEMVI evaluation using a combination of HRT2WI + CET1WI sequences. The pathological status of EMVI (pEMVI) was used as a standard reference. A sensitivity and specificity test was performed, and PPV and NPV for the results of both groups (A and B) were determined. Statistical package MedCalc Statistical Software version 15.2 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2015) was used.

4. RESULTS

Out of a total of 195 patients in our study with histopathologically verified rectal carcinoma, 98 (50.25%) were male and 97 (49.75%) were female. Average age was 62 years ±10.41.

An agreement test between two independent radiologists in mrEMVI detection resulted in a significant statistical concordance, Kappa coefficient (Measure of Agreement Kappa) was 0.864 (p<0.0005).

Out of all 195 patients with rectal carcinoma, mrEMVI was positive in 41 (21%) patients in group A, and 45 (23%) patients in group B. A histopathological finding demonstrated pEMVI in 54 (27.7%) patients. A statistical analysis of group A (HRT2WI sequences) revealed 75.9% sensitivity to mrEMVI and 96.4% specificity, Positive Predictive Value.
of 89.1% and Negative Predictive Value of 91.2% (CI 95%, p<0.05).

A statistical analysis of group B (HRT2WI + CET1WI sequences) revealed 83.3% sensitivity to mrEMVI and 98.5% specificity, Positive Predictive Value of 89.1% and Negative Predictive Value of 91.2% (CI 95%, p<0.05) (Table 1).

Stage II rectal carcinoma was present in 26.2% of the patients with EMVI, while stage III was present in 46.1%.

### 5. DISCUSSION

As a spread of rectal tumor to veins beyond muscularis propria, EMVI may be detected on MRI (mrEMVI). mrEMVI is present when veins in the vicinity of the tumor are noticeable and presented as obviously irregular, varicose and as having a modified tumor signal intensity. Thin section T2-weighted magnetic resonance imaging (MRI) can be used to demonstrate a number of adverse prognostic features for local rectal recurrence and survival in patients with rectal cancer. This implies an estimation of tumor extension to the lateral resection margin, the depth of extramural tumor extension and EMVI.

High-resolution T2-weighted imaging is the key sequence in the magnetic resonance (MR) imaging evaluation of primary rectal cancer. This sequence generally consists of thin-section (3-mm) axial images obtained orthogonal to the tumor plane, with an in-plane resolution of 0.5–0.8 mm. For a good assessment, HR T2-weighted images in three planes are used: sagittal plane, coronal plane and also in axial plane orthogonal to the tumor. This technique allows for a distinction between a T2 stage representing tumor restriction to the rectal wall only and a T3 stage when the tumor reaches beyond muscularis propria.

Most importantly, the depth of invasion beyond muscularis propria may be evaluated with a high degree of accuracy (12). In addition, T2-weighted high-resolution images allow for evaluation of morphological appearance of pelvic lymph nodes. Differentiating between a tumor invasion of minor lymph nodes and the blood vessels may be a problem with MRI. It is established that Gadolinium contrast sequences are not particularly helpful in diagnosing TN stage of rectal

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**Table 1.** HRT2WI in mrEMVI and HRT2WI + CET1WI in mrEMVI test results. MRI HRT2WI, Sensitivity =0.7592592592592593, Specificity =0.9645390070921985, Positive Predictive Value =0.8913043478260869, Negative Predictive Value=0.9391891891891891

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**Figure 3 a,b,c dilates veins have the intensity of tumor tissue a.t2sag, b. t2tra nativ, c. t2 + CE d,e,f serpentine appearance of vein f Ill with a tumor in d.t1tra nativ; e,f t1 tra+CE**
carcinoma. However, considering that administration of Gadolinium significantly enhances the visibility of blood vessels, it can be of great importance for EMVI demonstration (Figure 3).

Generally, small-vessel involvement is difficult to assess, and the involvement of larger vessels such as the midrectal or superior rectal arteries or veins is suggested by the visualization of tumor in the vessel lumen on contiguous sections (15). In 2008, Smith et al. highlighted the importance of future research in development of capabilities of recognizing EMVI in order to stratify patients for the purpose of administration of optimal neoadjuvant systemic chemotherapy so that emergence of remote relapses can be prevented (14). Chand et al. reported extramural venous invasion (EMVI) as a poor prognostic factor in rectal cancer (15). EMVI is associated with greater incidence of metastases, local relapse, poorer response to pre-operative chemoradiotherapy and an overall lower survival rate (16,17). Pre-operative chemoradiotherapy has no significant effect on the diagnostic performance of MRI. Currently, EMVI status does not directly influence the initial management of rectal carcinoma. This available and potentially prognostic feature could be used to guide treatment pathways to increase disease-free survival (18).

In our research, a histopathological finding confirmed pEMVI in 27.7% of the patients with rectal carcinoma. A study by Jhaiver et al. resulted in a somewhat bigger proportion–pEMVI was present in 31% of the pathology specimens (19). Our pEMVI result most closely approximates a comprehensive study published by McClelland et al., where EMVI presence was reported in 27.9% of colorectal cancer excision specimens. The same authors stressed the importance of EMVI and other pathological factors in colorectal carcinoma and confirmed that in an individual center study EMVI is being detected at an appropriate rate and is of prognostic significance (20). In a study by W.G. Bugg et al., 26.2% of rectal carcinoma patients had positive EMVI. Of the patients with EMVI, 24.5% developed metastases at 1 year follow-up, compared to 6.7% of those without. Those with EMVI have 3.7 times increased relative risk of developing metachronous metastases within 1 year of diagnosis (18). Smith et al. published in a retrospective analysis that mrEMVI was present in a quarter of patients with rectal carcinoma (13). In 2008, Smith et al. highlighted the importance of future research in development of capabilities of recognizing EMVI in order to stratify patients for the purpose of administration of optimal neoadjuvant systemic chemotherapy so that emergence of remote relapses can be prevented (14).

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6. CONCLUSION

T2-weighted magnetic resonance imaging (CET1WI) in addition to high-resolution T2-weighted imaging (HRT2WI) increased evaluation of extramural venous invasion (EMVI) of rectal cancer. A reliable mrEMVI evaluation is very beneficial for a safer selection of optimal oncologic treatment and a more reliable prediction of rectal carcinoma prognosis.

REFERENCES


