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Extramural venous invasion in rectal cancer: overview of imaging, histopathology, and clinical implications

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Abstract

Objective: Extramural venous invasion (EMVI) is an independent prognostic factor for prediction of overall unfavorable outcomes in rectal cancer. While EMVI has traditionally been detected in postoperative pathologic specimens, MRI can provide this important piece of information preoperatively. This article reviews the methods of EMVI detection and their clinical implications for treatment and outcomes of rectal cancer.
Conclusion: EMVI has fundamental implications for rectal cancer prognosis and long-term outcomes. Since MRI has the advantage of preoperative detection of EMVI, it has been suggested that MRI-detected EMVI be incorporated for preoperative chemoradiotherapy (CRT) treatment stratification of rectal cancer for better patient triage and outcomes.

Key words: Extramural venous invasion (EMVI)—Histopathology—MRI—Rectal cancer—Cancer staging—Chemoradiation therapy

Rectal cancer accounts for about one-third of colorectal cancer which is the third most commonly diagnosed cancer among both men and women in North America [1, 2]. More than forty thousand new cases of rectal cancer are estimated to be detected in the United States during 2018 [3]. While the overall incidence of rectal cancer has been declined in recent years, there has been an increase of incidence in the population younger than 50 years old [4]. The survival rate from rectal cancer has been increased from 48% in 1975–77 to 68% in 2006–2012; still, the mortality rate is among the highest in malignancies. Although this improvement in survival is partly related to introduction and dissemination of colorectal cancer screening techniques, new approaches for rectal cancer treatment, especially in early stages, also play a substantial role [1].

Based on large-scale randomized trials, current treatment guidelines recommend preoperative chemoradiotherapy (CRT) followed by TME (total mesorectal excision) for all Stage II and Stage III rectal cancer patients. This treatment approach is recommended since it has been shown to decrease the risk of local recurrence [5]. Unfortunately, however, CRT leads to poorer bowel and sexual functions compared with surgery alone. Therefore, strategies to appropriately select patients for CRT are important and need to focus on node-negative T3 tumors, because this is the most heterogeneous and controversial group of patients with respect to clinical

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management [6–8]. Apart from T stage, several additional adverse prognostic factors have been identified and include tumor perforation, high tumor grade, lymphatic (LI) or blood vessel invasion (BVI), and perineural invasion [7–11]. In particular, there is a large body of evidence that EMVI, defined as involvement of the veins beyond the muscularis propria, is an independent predictor of local tumor recurrence, metachronous nodal and distant metastases, and overall mortality [12–19]. Traditionally, EMVI is diagnosed in the postsurgical pathology specimen (pEMVI); however, since pEMVI is identified after surgery, it does not play a role in preoperative treatment planning for patients with rectal cancer. MRI is a highly accurate and reproducible modality for the preoperative identification of EMVI (mrEMVI) as well as other adverse local prognostic features, which can assist in treatment planning [20–27]. Some authors have proposed local T staging and mrEMVI as only selection criteria for neoadjuvant therapy [8].

In this review article, we present an overview of EMVI, its methods of detection by imaging (specifically MRI), and histopathology and its clinical significance.

Imaging assessment of EMVI

Magnetic resonance imaging (MRI) is routinely used as the standard of care in the preoperative local staging of rectal cancer and considered a superior imaging modality for the detection of local adverse prognostic factor of rectal cancer. Since the seminal study by Brown et al in 2002, high-resolution MRI has been recognized as a promising and reproducible technique to identify EMVI. Several studies have since confirmed comparability of MRI-detected EMVI (mrEMVI) with that detected on subsequent pathological assessment (pEMVI), with moderate-to-high sensitivity and specificity [5, 6, 12, 13, 15, 16, 20, 21, 24, 25]. Due to sampling issues and under-recognition of pEMVI, some have suggested that MRI findings might be used as a guide to improve detection of EMVI in pathology specimens [28]. Moreover, MRI has the advantage of detecting EMVI in vivo, before the disruption of the tumor bed by surgery and its potential dissemination.

Rectal MRI technique

If imaging parameters are optimized, both 1.5T and 3T field strengths can be used for evaluation of rectal cancer with comparable results. Although performing MRI in a 3T scanner can decrease acquisition time and increase the signal-to-noise ratio, no significant improvement is reported in local staging accuracy compared with a 1.5 Tesla field [29].

MRI for staging of rectal cancer is best performed using high resolution multichannel phased-array pelvic surface coils which give a larger field of view for better evaluation of peripheral structures and lymph nodes, higher signal-to-noise ratio and spatial resolution. Endorectal coil can improve image quality regards to the rectal wall, but there is not enough evidence to support its routine application considering their additive costs and patient's discomfort [30]. In addition, currently, no consensus has been reached in endorectal filling with gel [31]. Although rectal distension with gel or other intraluminal agents can improve detection of small primary tumors and reducing susceptibility artifact from endoluminal gas [12, 31, 32], in local staging of a known rectal cancer, over distension of the rectal wall may decrease the tumor distance from mesorectal fascia or obscure suspicious lymph nodes. Therefore, it can potentially over-stage or under-stage a tumor resulting in critical changes in individual patient's tumor management [33]. Bowel preparation is not mandatory; however, antispasmodics reduce peristalsis and resultant motion artifact, and recommended on a routine basis unless contraindicated [12, 34]. The rectal MRI protocol at our institution includes four fast spin-echo multiplanar T2-weighted conventional sequences and high-resolution oblique T2-weighted sequence plus axial T1-weighted sequence and multiparametric MRI sequences including diffusion-weighted imaging (DWI) and contrast-enhanced MRI [22, 34]. Table 1 summarizes sample parameters for all required T2 sequences and other supplementary sequences for an optimal rectal MRI.

High-resolution oblique T2 images are the main images in which EMVI is identified and scored. The image acquisition protocols must be strictly followed, and appropriate interpretation method should be applied to optimize EMVI identification. Image acquisition should be perpendicular to a rectal tumor long axis to enhance detection of the vessels. Oblique coronal images parallel to the long axis of the tumor may also be beneficial in detecting EMVI. Furthermore, proper selection of the field of view will maximize spatial resolution and accuracy of the tumors' signal detection in smaller vessels.

MRI criteria and scoring system

By definition, EMVI is tumor invasion into veins beyond muscularis propria; therefore, these tumors should be considered as T3 [12, 17]. The veins are visualized either as signal void linear structures or as smaller serpiginous structures lying in mesorectal fat and can be recognized because of tortuosity and branching. Very small vessels may be seen radiating outward from the edge of the muscularis propria into the mesorectal fat, while the larger named veins, such as middle rectal vein, are recognizable considering their consistent anatomical positions [20, 35].

MRI-detected EMVI was initially described by Brown et al as a serpiginous extension of tumor signal within a vascular structure [21]. Smith et al subsequently

Table 1. Sample 3-T MRI parameters for staging rectal cancer

MRI parameter	TSE T2-weighted imaging				DWI	3D T1-weighted GRE
	Sagittal	Axial	Coronal	High-resolution oblique		
TR/TE	4000/91	4000/91	4000/91	3300/80	6317/69.4	3.51/1.44
No. of slices	46	48	36	20	36	30-60
Bandwidth(HZ/pixel)	391	391	391	391	1628	520
FOV (mm)	220	220	220	200	340	240
Slice thickness (mm)	3	4	4	3	4	3
Distance factor (%)	18	18	25	0	25	20
Phase FOV (%)	100	100	100	100	100	100
No. of acquisitions	2	2	1	4	4	4
Matrix	350 × 263	350 × 263	350x263	350 × 263	250 × 250	240 × 240
Phase encode direction	Anteroposterior	Transverse (right to left)	Transverse (right to left)	Transverse (right to left)	Anteroposterior	Anteroposterior
Saturation band	Anterior	NA	NA	Superior and inferior	NA	NA
Acquisition time (min)	4.5	6.5	2.5	5.5	5.5	5
Voxel size (mm)	0.7 × 0.7 × 3.0	0.6 × 0.6 × 4.0	0.7 × 0.7 × 4.0	0.6 × 0.6 × 3.0	1.8 × 1.8 × 4.0	0.8 × 0.8 × 4.0

provided a meticulous 5-point scoring system [15, 20]. Accurate assessment of four components is essential to assign the probability of EMVI. These criteria include the pattern of tumor margin, location of the tumor relative to major vessels, caliber of the vessel, and vessel border, and signal intensity changes in a vein. The tumor pattern can be smooth or nodular, the latter of which increases probability of EMVI. This nodularity should be distinguished from desmoplasia as fine low signal stranding in mesorectal fat. Tumor proximity to vessels should also be determined. Moreover, the vein caliber (normal or slightly expanded or grossly expanded), border (smooth or irregular) and any changes in the normal signal void appearance of larger vessels should be precisely identified. Based on these criteria, radiologists will be able to categorize probability of EMVI based on

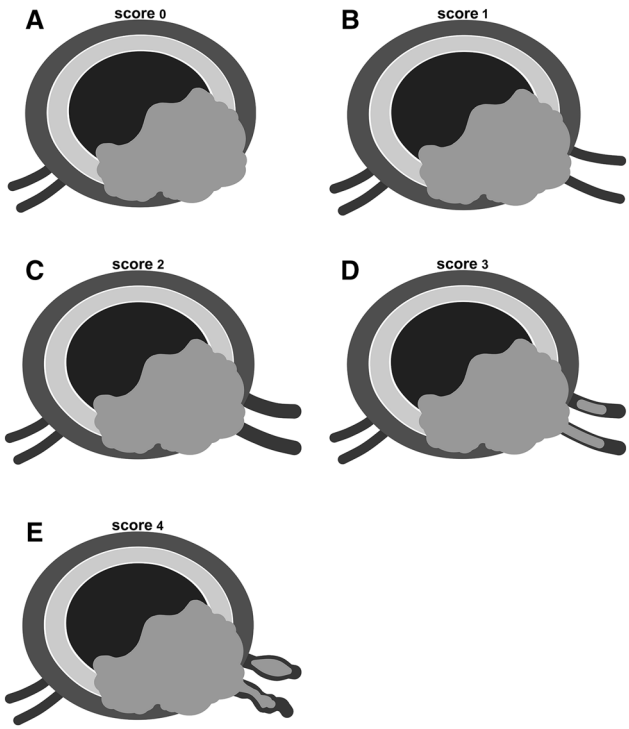

Fig. 1. MRI-based EMVI scoring system. EMVI will be reported as negative for score 0–1, equivocal for score 2, and positive for scores 3–4. **A** Score 0 demonstrates no vessel in vicinity of extramural tumor penetration. **B** Score 1 demonstrates vessel with normal caliber and with no obvious tumor signal intensity. **C** Score 2 demonstrates slightly expanded vessel with no obvious tumor signal intensity. **D** Score 3 demonstrates intermediate tumor signal intensity inside an expanded vessel. **E** Score 4 demonstrates evident irregular vessel contour or nodular expansion of the vessel by tumor signal. Reprinted with permission from the American Journal of Roentgenology, Jhaveri K S, Hosseini-Nik H, Thipphavong S, et al. MRI Detection of Extramural Venous Invasion in Rectal Cancer: Correlation With Histopathology Using Elastin Stain, AJR Am J Roentgenol 206: 747–755.

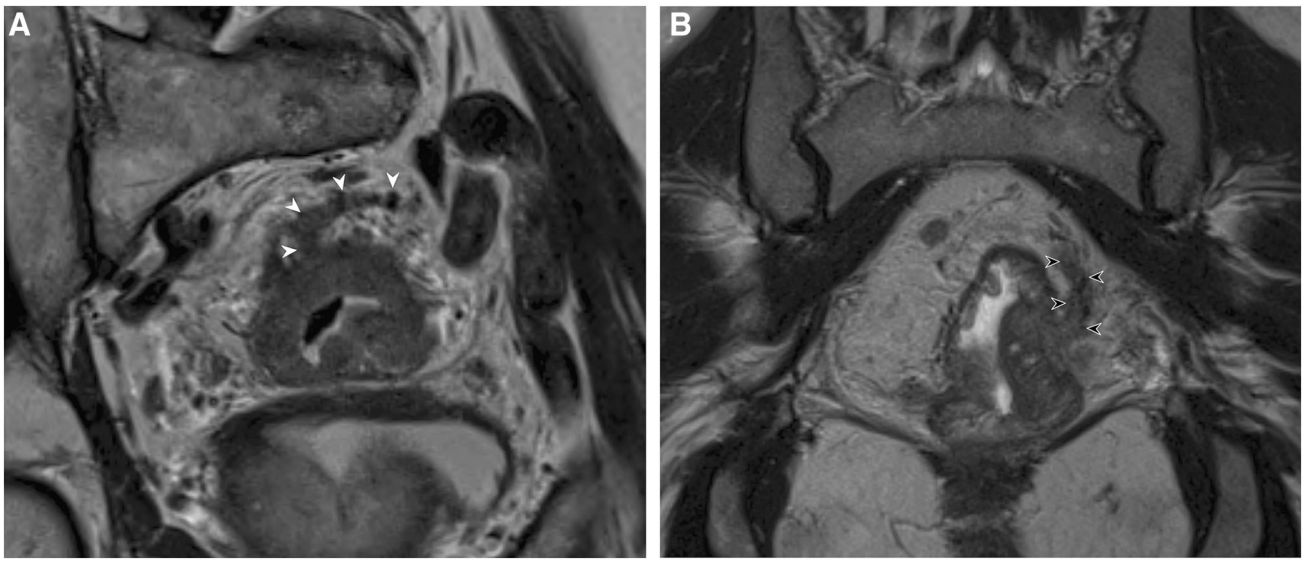

Fig. 2. **A** 74-year-old man with Score 3 histologically proven EMVI depicted in high-resolution oblique T2-weighted image (white arrowheads). **B** 50-year-old woman with Score 3 histologically proven EMVI in coronal T2-weighted image (black arrowheads).

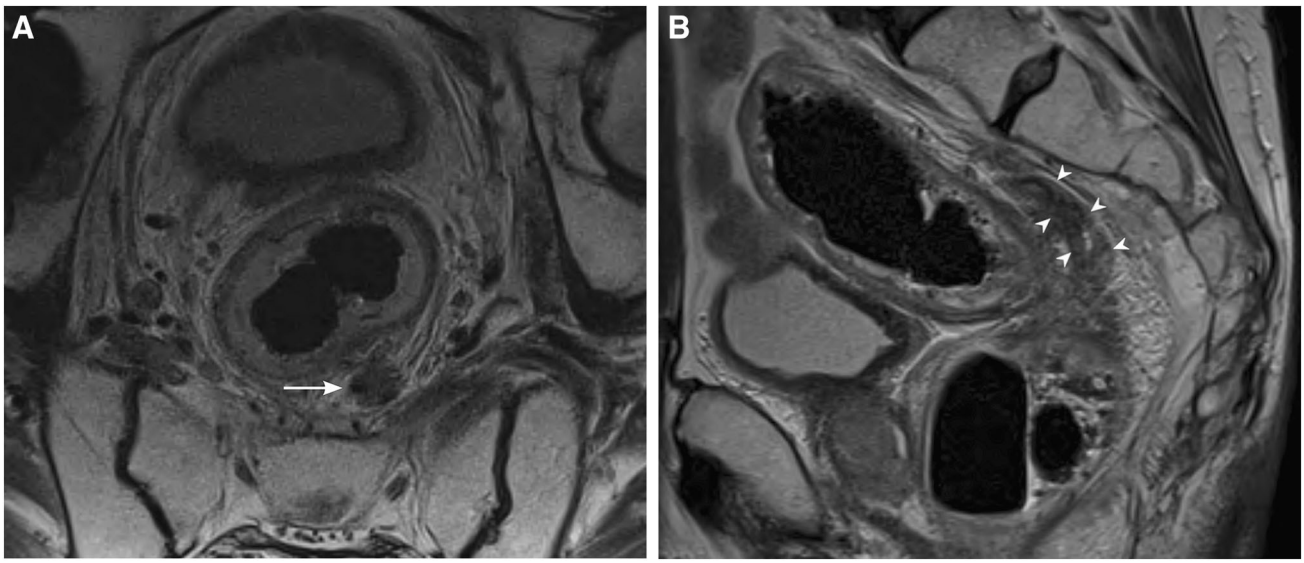

Fig. 3. 85-year-old man with histologically proven EMVI (score 4 on MRI). High-resolution oblique T2-weighted MR image (**A**) and Sagittal T2- image (**B**) obtained after preoperative CRT demonstrate persistent EMVI as tumor signal intensity inside considerably expanded vein (arrow in image **A** and arrowheads in image **B**) which can be misinterpreted as invaded lymph node in this axial image alone.

the Smith's 5-point scoring system. Jhaveri et al used a modified version of this scoring system, which is better described in Fig. 1 [22]. Lower scores (0 and 1) are not associated with histologically proven EMVI and considered negative in MRI, whereas a score of 3 (Fig. 2) or 4 (Fig. 3) is classified as definite EMVI. Following tubular structures of the vessels will provide a better understanding of three-dimensional vascular anatomies and avoiding misinterpretation of nodal involvement as EMVI [22, 35] (Fig. 3).

A Score 2 or mild expansion of the vein with no obvious tumor signal is considered equivocal and is not indicative of overt EMVI [5, 15, 20, 22, 23, 32, 36]. Jhaveri et al found that contrast-enhanced images may increase reader's confidence in the better stratification of these equivocal cases [22]. These sequences are of particular importance in post-CRT images where image distortion may further affect accurate diagnosis. In fact, positive clues such as filling defects in postcontrast-enhanced vessels will reclassify a score 2 equivocal case as

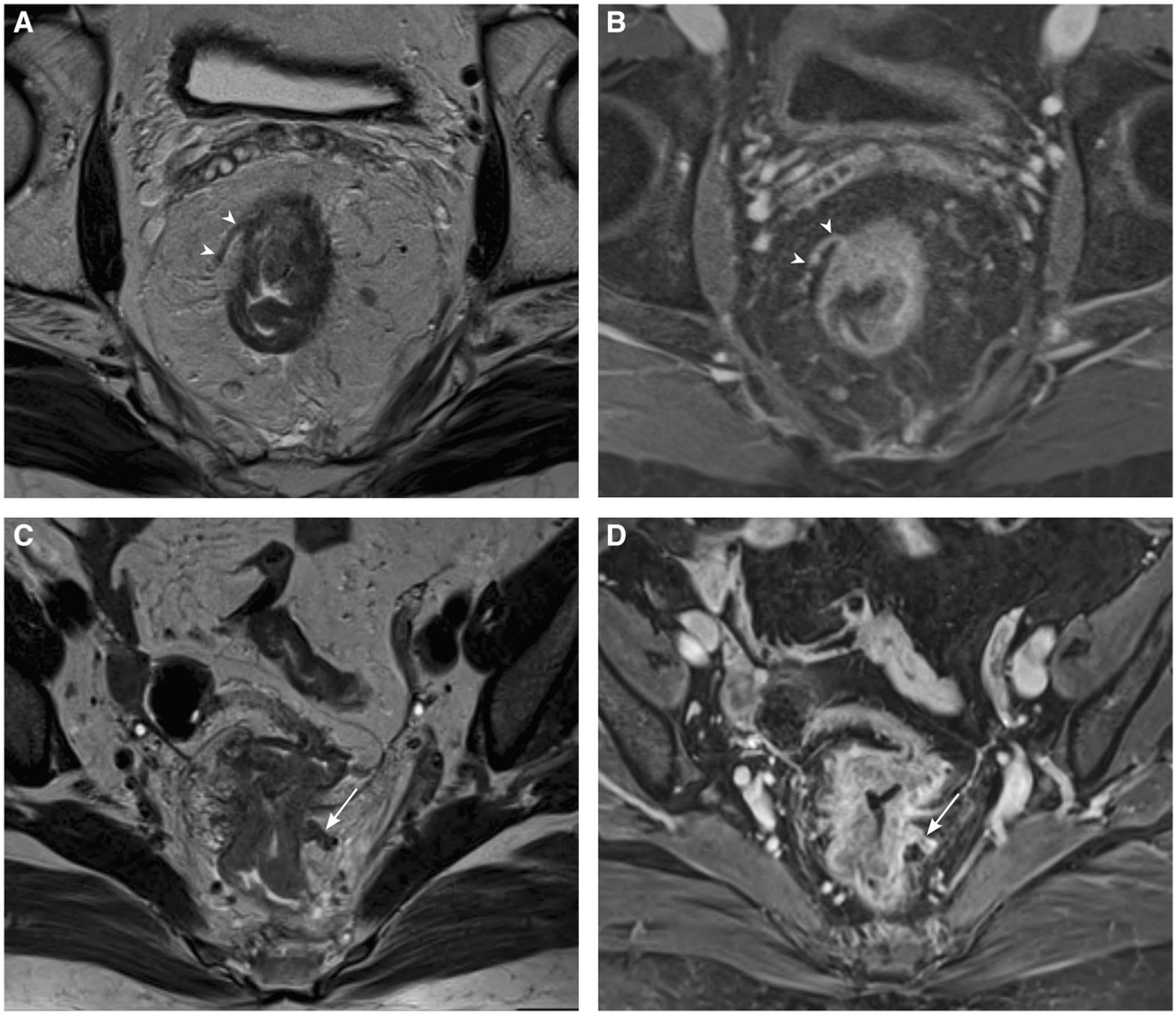

Fig. 4. Added value of contrast-enhanced MRI to T2WI for EMVI scoring. **A** and **B** 39-year-old male with slightly prominent vein (score 2) depicted in axial T2-weighted image which after contrast administration demonstrates normal enhancement and reclassified as score 1 (arrowheads). **C** and **D** In this 50-year-old woman, axial T2-weighted image shows mildly expanded vein which cannot be classified as definite EMVI based on this image alone; while, postcontrast image reveals obvious filling defect which categorizes this tumor as EMVI positive (arrows).

score 3 definite EMVI; whereas, normal enhancement of a suspicious vessel will be rescored as negative for EMVI which will eventually improve MRI sensitivity in identification of EMVI [22] (Fig. 4)

DWI sequences are especially useful in post-CRT evaluation of a tumor; still, they may have some value in the detection of EMVI as well [12]. Since a relationship has been shown between the mesorectal extension of a tumor and mrEMVI, extra attention should be directed for detection of EMVI in tumors within 5 mm from mesorectal fascia or more than 5 mm protrusion to mesorectal fat [22]. Smaller vessels normally exhibit low-to-intermediate signal; therefore, they need to be expanded or demonstrate irregular border to be classified as positive for EMVI [35]. Finally, after identification of positive EMVI, the 2015 template of the Synoptic MRI Report for Pre-Operative Staging of Rectal Cancer requires determination of the clock-face position and distance from mesorectal fascia; since if it is less than 1 mm of the fascia, it can potentially threaten postoperative clear margin, and surgeons need to be aware of this ahead of surgery [32].

MRI accuracy

Brown et al reported 85 percent agreement between mrEMVI and pEMVI. They were able to correctly identify 15 out of 18 of EMVI-positive vessels larger than 3 mm

size, with 62% sensitivity and 88% specificity [21]. Several subsequent studies have demonstrated a moderate-to-strong correlation between mrEMVI and pEMVI based on routine H&E slides (sensitivity 28% to 100% and specificity 88% to 94% when scores 3 and 4 considered positive in vessels larger than 3 mm in MRI) [5, 6, 15]. This wide range of sensitivity may be related, at least in part, to heterogeneity with respect to histopathologic definitions, methods, and diagnostic accuracy [13]. In fact, MRI's ability to detect EMVI is at least comparable with routine histopathology analysis of specimens in identifying EMVI with added benefit of being preoperative [28]. In a recent study [22], MRI revealed a high specificity (96%) and a moderate sensitivity (54%) in the detection of EMVI in vessels of size equal to or more than 3 mm using pEMVI detected on elastin-stained slides by an experienced gastrointestinal pathologist as the "gold standard". Despite the increased sensitivity of pEMVI detection when an elastin stain is used, the sensitivity and specificity of mrEMVI in this study remained comparable to that of previous studies in which pathology assessment was based on H&E alone. EMVI identification in an intact rectal tumor or its persistence after preoperative CRT may necessitate preoperative CRT or intensifying previous treatment, respectively. As a result, to avoid false-positive results, EMVI should be reported only when tumor signal intensity is clearly visualized in a vessel lumen, which is equal to score three to four of MRI scoring system [22]. Smith et al detected mrEMVI in 39.4 percent compared to 26.8 percent in postsurgical pathology. They suggested that this difference could be related to post-CRT downstaging of a tumor, yet MRI might be more successful in detecting vessels which were destructed by a tumor with small remaining endothelial lining beyond pathological recognition while they may be more readily appreciated on serial MR images [15, 16]. A meta-analysis by Siddiqui et al has shown that mrEMVI detection prevalence was 34.6% (23.7% to 47.6%) which is more consistent finding comparing pEMVI (9% to 90%) [23].

MRI has also demonstrated high accuracy in detection of EMVI following CRT (ymrEMVI) using the same criteria mentioned before [37]. Chand et al investigated agreement between ymrEMVI- and histopathologic-detected EMVI after CRT (ypEMVI) and their results showed a striking difference. Of the 99 patients who remained EMVI positive after CRT, 63 (63.6%) were only identifiable by MRI rather than standard methods of histopathology [36]. Indeed, preoperative CRT does not seem to affect the diagnostic performance of MRI for detection of EMVI [22] (Fig. 3). Some authors argue that MRI capabilities are limited to detection of EMVI larger than 3 mm and invasion to smaller extramural and intramural vessels cannot be identified by MRI. However, as we discussed before, small vessel vascular invasion may be more difficult to identify both radiologically and histopathologically.

Other imaging techniques

Other imaging modalities have not been successful in the detection of EMVI. Currently, there is no role for positron emission tomography (PET) scans in the local preoperative staging of rectal cancer.

A study with multidetector CT scan in which, the preoperative diameters of the inferior mesenteric vein and the superior hemorrhoidal vein (with a cut off value of 3.7 mm) have been used for prediction of VI with high sensitivity and specificity [38]. Role of CT scan in the identification of EMVI needs more investigation and is probably limited to situation where MRI is not accessible.

Histopathologic assessment

VI was defined by Talbot et al as the presence of tumor within an endothelium-lined space that is either surrounded by a rim of smooth muscle or contains fibrin or red blood cells [39]. More recently, this definition has been expanded to include the demonstration of convincing elastin staining around rounded or elongated tumor profiles, usually adjacent to an artery [8, 28, 40]. VI includes intramural venous invasion (IMVI; involvement of vessels confined to the submucosa or muscularis propria) and extramural VI (EMVI; involvement of larger vessels beyond the muscularis propria). EMVI in particular, is a strong predictor of adverse outcome [7, 8, 11, 14, 41], but there is accumulating evidence to suggest that IMVI may also be prognostic [7, 14, 40, 42]. The superior prognostic significance of EMVI, is recognized in both the College of American Pathologists (CAP) colorectal cancer Protocol and the United Kingdom Royal College of Pathologists (RCPathUK) Colorectal Cancer Dataset [2, 43].

The RCPath(UK) colorectal cancer guideline recommends that VI should be detected in at least 30% of colorectal cancer resection specimens. However, this is a minimum standard, and several centers in the United Kingdom and Canada with expertise in CRC pathology report VI-detection rates of more than 40% [43, 44]. Nonetheless, population based studies suggest that VI remains widely under reported [41, 45].

The detection of VI can be challenging on H&E slides, particularly when the muscular wall of the vein is effaced by tumor or altered by the effects of neoadjuvant CRT. In such circumstances, VI can be easily missed if key morphologic clues are not appreciated. These include the 'orphaned arteriole' sign (a circumscribed tumor nodule adjacent to a muscularized artery without an obvious accompanying vein, and the 'protruding tongue' sign (a smooth bordered protrusion of tumor into pericolic fat). The finding of either of these morphologic clues should prompt the use of an elastin stain (Fig. 5), which will resolve the vast majority of equivocal cases

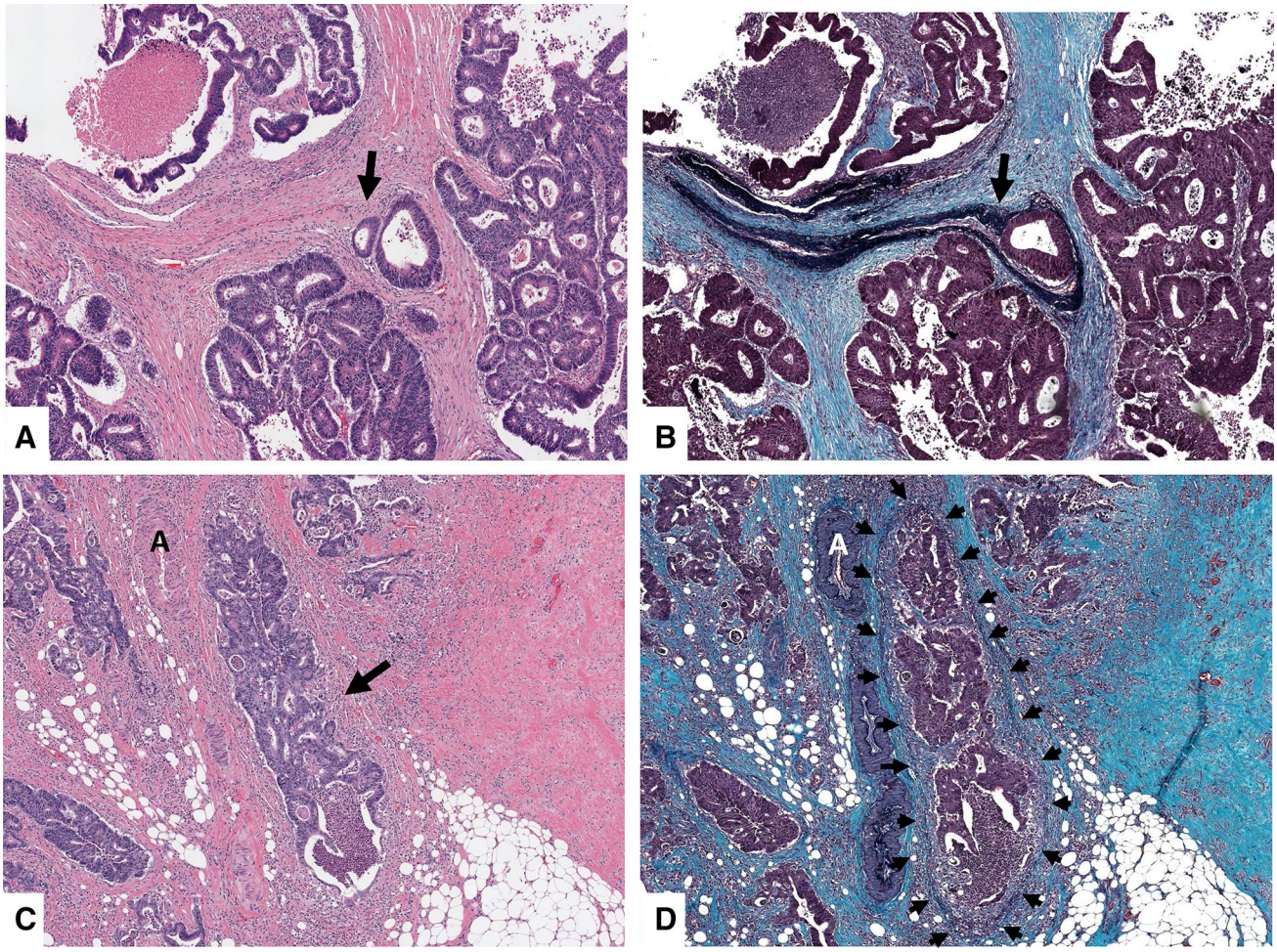

Fig. 5. Utility of elastin stains in the detection of venous invasion. H&E (**A**, **C**) and corresponding elastin trichrome stains (**B**, **D**) illustrating the utility of elastin stains in the detection of VI. Note the ease with which VI is detected on elastin trichrome stains (**B** and **D**), with residual black-staining elastic fibers of the vessel wall (arrows) surrounding malignant glands. The intravascular location of these tumor nodules (arrows) is less easy to appreciate on corresponding H&E-stained sections (**A** and **C**). Note also the adjacent paired artery (labeled **A**) in figures **C** and **D** (the so-called "orphaned artery" sign).

[18, 46]. Superiority of elastin staining over traditional H&E stains has been confirmed in several studies. Most studies report a two to threefold increase in VI-detection rates when an elastin stain is used [19, 40, 46, 47]; a modest improvement in interobserver agreement has also been reported [46]. The routine use of elastin staining is advocated by several authors, who cited the low cost of such stains and their minimal impact on turnaround time and workload [8, 19, 28, 46–50]. The RCPath(UK) CRC dataset recognizes the utility of elastin stains in both increasing the sensitivity of VI detection and improving its ability to stratify risk in CRC.

Post CRT diagnosis of EMVI

A growing use of preoperative neoadjuvant CRT has led to new challenges in identifying EMVI in histopathologic specimens. Radiation induced fibrosis and destruction of the veins' endothelium after radiotherapy is responsible for high false negative results up to 30%. In fact, radiotherapy destroys most of the landmarks which aid pathologists for accurate diagnosis. Utilization of elastin stains will enhance residual venous wall and increases accurate diagnosis of persistent VI [28, 46]. Examining a greater number of blocks with more concentration on area of fibrosis in irradiated region might also be helpful [35]; still, the worst results in pEMVI detection came from preoperatively treated rectal cancers [28, 45, 51]. MRI, on the other hand, has the advantage of mutiplanar sectioning which allows radiologists to follow a lesion in different planes to determine their continuity with vessels. In addition, not only could normal anatomical location of the vessels be advantageous in MRI detection of the post-CRT vessels, but MRI also has the advantage of visualizing the entire rectum rather than relatively small sample of specimen, and these reasons explain why

post-CRT MRI can detect more patients with persistent EMVI than histopathology (53% vs. 19%) [36].

Prognostic significance of EMVI

Although it seems quite logical that access of cancer cells to draining vessels is considered as a prerequisite for visceral metastases, this fact was largely ignored until the work of Brown and Warren in the late 1930s based on this assumption that a tumor distant spread results from lymphatic permeation and embolism [39, 52]. For the first time, at autopsy, they revealed that visceral metastases especially liver was present in 71% of patients with VI, but no metastasis in cases without VI [53]. Talbot et al have reported almost fourfold risk of developing liver metastases and 5-year survival rates of only 33% in patients with invasion of extramural veins. Many subsequent studies have demonstrated pEMVI, whether it is detected by routine H&E or by additive elastic stains, as a strong independent predictor of poor outcomes such as local recurrence, lymph node metastasis, synchronous and metachronous distant metastases, and overall poor survival. This is of particular importance in patients in stage II where more detailed prognostic determinants are required to decide for treatment [7, 8, 14, 18, 39, 40, 46, 47]. Indeed, Roxburgh et al have suggested a combination of T Stage and VI as a new staging method (TVI) that they found it particularly useful in node-negative patients in predicting outcome after curative resection. Furthermore, it has been shown that the prognostic value of this combination in predicting cancer-specific survival is at least equivalent to T stage and nodal status [8].

New advances in MRI as an accurate and reproducible method for preoperative staging made radiologists capable of determining EMVI before surgery with high accuracy, and it seems reasonable to think it has the same prognostic significance. In fact, it has been confirmed in many studies since 2002 that mrEMVI has equal prognostic value as pEMVI for predicting lymph node and visceral metastasis and patient's survival [6, 13, 15, 20, 27]. In a recent meta-analysis, mrEMVI's poor prognostic significance was evidenced by the fivefold increased rate of synchronous metastases and almost fourfold ongoing risk of developing postoperative metachronous metastases [23]. In another study, the 3-year disease-free survival (DFS) for EMVI-positive stage II was similar to those that had stage III disease [5]. In addition, the severity of MR imaging–depicted EMVI and size of the involved vessels have been found to be correlated with metachronous metastasis, response to postoperative CRT and disease-free survival [5, 6, 15, 25, 27].

MRI, in particular, is important in detection of the post-CRT EMVI (ymrEMVI) regression. Chand et al defined a regression scoring system based on the degree of MRI evidence of fibrosis and applied it for predicting patients' outcome. They found that demonstration of more than 50 percent fibrosis in previously detected EMVI is associated with better prognosis (87.9% 3-year disease-free survival compared to 45.8% in patients with less than 50 percent fibrosis. Moreover, the recurrence rates were 9% for good mrEMVI vs. 44% for poor mrEMVI responders. They suggested that this scoring system can be used as an imaging biomarker to measure the effectiveness of such a treatment [25]. In another study, they showed that those regressed ymrEMVI-negative tumors after CRT had similar low rates of metastatic disease compared to those who were mrEMVI-negative on baseline MRIs, while DFS was significantly reduced in those who remained yEMVI positive either in pathology or MRI [36].

Implications for treatment

In their recent practice guidance, most national guidelines recommend preoperative CRT for high-risk patients to improve their outcome [54]. As described earlier, EMVI either it is identified in postoperative pathology or an MRI before surgery is a strong and independent prognostic factor for patients' overall outcome; however, there is no consensus for stratification of these patients as high risk and following decision on preoperative or postoperative CRT [23]. In a recent survey, only 55% of surgeons and 57% of oncologists considered it when deciding on postoperative treatment [55]. This may lead to underestimation of patient's risk for subsequent metastasis and consequent undertreatment of these high-risk groups.

Strong evidence from a large number of studies emphasize that a positive EMVI (whether it is determined before any intervention or persists in the patients' follow up) must be a fundamental part of risk stratification and decision making for stage II rectal cancers. As a result, EMVI detection before any surgical intervention mandates consideration of preoperative CRT, and persistence of residual tumor in involved vessels may be an indication for more intense additional courses of treatment. [14–16, 19–21, 23–27, 48, 49]. Patients need to be informed about this high-risk feature of their cancers to make better decision regard to preoperative or postoperative CRT. This might also affect their surveillance in terms of requirement for closer follow-up [5, 23, 25, 36].

MRI, as we discussed earlier has the advantage of more consistent and reproducible results and it makes radiologists capable of comparing results before and after CRT. Furthermore, MRI gives the patient and their healthcare provider the opportunity of determining this high-risk feature and modifying it before any surgical intervention which potentially may disseminate already ready-to-travel malignant cells. Some authors even argue that performing CRT might not be the optimal approach

for these mrEMVI patients. They believe that presence of mrEMVI is an indicator of micrometastases beyond the CT scan recognition capabilities, and necessitate preoperative full dose chemotherapy [5, 23, 25, 36]. Furthermore, although it is not verified through enough trials, Chand's post-CRT scoring system might be a great predictor for patients' call for further courses of pre or postoperative adjuvant therapy in those who there has been less than 50% regression [25].

Conclusion

EMVI is a strong poor prognosis predictor of stage II rectal cancers, the most heterogenous stage with regard to outcomes. EMVI identification must be included in preoperative staging, after neoadjuvant treatment and postoperative evaluations. Moreover, adding this essential finding in rectal cancer therapeutic decision stratification will help towards a standardized decision making for offering neoadjuvant or adjuvant treatment particularly for patients with node-negative rectal cancers.

Compliance with Ethical Standards

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Research involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent N/A

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