Abdominal Imaging / Imagerie abdominale

Evaluation of Extramural Venous Invasion by Diffusion-Weighted Magnetic Resonance Imaging and Computed Tomography in Rectal Adenocarcinoma

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Abstract

Purpose: The aim of this study is to evaluate the diagnostic contribution of diffusion-weighted magnetic resonance imaging (MRI) and computed tomography (CT) to distinguish extramural venous invasion (EMVI) in rectal adenocarcinoma.

Materials and Methods: Fifty-eight patients who had been diagnosed with rectal adenocarcinoma (30 patients with EMVI and 28 patients without EMVI) were enrolled in the study. Apparent diffusion coefficient (ADC) values of the tumour and the EMVI (+) vein, the lengths of the tumours were measured on MRI. The diameters of the superior rectal vein (SRV)-inferior mesenteric vein (IMV) and distant metastatic spread were evaluated on CT. The ability of these findings to detect EMVI was assessed using receiver operating characteristic (ROC) analysis. Pathology was accepted as the reference test for EMVI.

Results: Mean diameters of the SRV (4.9 ± 0.9 mm vs 3.7 ± 0.8 mm) and IMV (6.9 ± 0.8 mm vs 5.4 ± 0.9 mm) were significantly larger (P < .001) and tumour ADC values were significantly lower (0.926 ± 0.281 × 10^{-3} mm²/s vs 1.026 ± 0.246 × 10^{-3} mm²/s; P = .032) in EMVI (+) patients. Diameters of 3.95 mm for the SRV (area under the curve [AUC] ± standard error [SE]: 0.851 ± 0.051, P < .001, sensitivity: 93.3%, specificity: 67.9%) and 5.95 mm for the IMV (AUC ± SE: 0.893 ± 0.040, P < .001, sensitivity: 93.3%, specificity: 71.4%) and an ADC value of 0.929 × 10^{-3} mm²/s (AUC ± SE: 0.664 ± 0.072, P = .032 sensitivity: 76.7%, specificity: 57.1%) were found to be cutoff values, determined by ROC analysis, for detection of EMVI. Distant metastases were significantly more prevalent in EMVI (+) patients (P < .001).

Conclusion: The measurement of ADC values and SRV-IMV diameters seems to have contribution for diagnosis of EMVI in rectal adenocarcinoma. EMVI (+) patients appear to have higher risks of distant metastases at diagnosis.

Résumé

Objectif : L’objectif de cette étude est d’évaluer la contribution diagnostique de l’imagerie par résonance magnétique (IRM) pondérée en diffusion et la tomodensitométrie (TDM) pour distinguer les invasions veineuses extra pariétales (IVEP) au niveau des adénocarcinomes rectaux.

Matériel et méthodes : Cinquante-huit patients porteurs d’un diagnostic d’adénocarcinome rectal (30 patients avec IVEP et 28 patients sans) ont été inclus dans l’étude. Le coefficient de diffusion apparent (CDA) des tumeurs, les veines IVEP positives et la longueur des tumeurs ont été mesurés sur les clichés d’IRM. Le diamètre de la veine rectale supérieure (VRS) et de la veine méssentérique inférieure (VMI), ainsi que la diffusion métastatique à distance ont été mesurés sur les clichés de TDM. La capacité de détection des IVEP grâce à ces données a été déterminée en utilisant une analyse des caractéristiques de performance (ROC). La pathologie a été acceptée en tant que test de référence pour l’IVEP.

Résultats : Les diamètres moyens de la VRS (4.9 ± 0.9 mm contre 3.7 ± 0.8 mm) et de la VMI (6.9 ± 0.8 mm contre 5.4 ± 0.9 mm) étaient significativement supérieurs (P < .001) et les CDA de tumeur (0.926 ± 0.281 × 10^{-3} mm²/s contre 1.026 ± 0.246 × 10^{-3} mm²/s) étaient significativement inférieurs (P = .032) chez les patients IVEP positifs. Les valeurs seuils déterminées par analyse ROC pour la détection
d’IVEP étaient un diamètre de 3,95 mm pour la VRS (aire sous la courbe [ASC] ± écart type [EC]: 0,851 ± 0,051; P < .001; sensibilité: 93,3 %; spécificité: 67,9 %) et de 5,95 mm pour la VMI (ASC ± ET: 0,893 ± 0,040; P < .001; sensibilité: 93,3 %; spécificité: 71,4 %), et un CDA de 0,929 × 10⁻³ mm²/s (ASC ± SE: 0,664 ± 0,072; P = .032; sensibilité: 76,7 %; spécificité: 57,1 %). La fréquence des métastases était significativement supérieure chez les patients IVEP positifs (P < .001).

Conclusion : La mesure du coefficient de diffusion apparent (CDA) et du diamètre de la veine rectale supérieure (VRS) et de la veine mésentérique inférieure (VMI) semble contribuer au diagnostic d’une invasion veineuse extra pariétale (IVEP) pour les adénocarcinomes rectaux. Les patients IVEP positifs semblent présenter des risques supérieurs de métastases à distance, lors du diagnostic.

Key Words: Computed tomography; Magnetic resonance diffusion-weighted imaging; Extramural venous invasion; Rectal cancer; Superior rectal vein; Inferior mesenteric vein

Colorectal carcinoma is one of the most common gastrointestinal tract cancers and one of the leading causes of cancer-related death [1]. Currently, surgical resection is considered to be a curative treatment for rectal cancers. In locally advanced rectal cancers, neoadjuvant chemoradiotherapy has been increasingly used to preoperative downsizing of primary tumours [2,3]. Therefore, preoperative staging (identification of whether or not the tumour is in the advanced stage) is critical in determining treatment strategies for newly diagnosed patients [2]. Computed tomography (CT) and magnetic resonance imaging (MRI) are widely used for the preoperative staging of rectal cancers. MRI is the recommended imaging modality for locally staging rectal cancers, while CT exhibits some advantages in identifying distant metastatic spread and tumour-related complications [2].

Some factors affect patients’ outcomes in rectal cancers. Lymph node metastasis and tumour invasion depth beyond the muscularis propria, for instance, have been recognized as important factors that affect prognoses in colorectal cancers [3–6]. Extramural venous invasion (EMVI) has been established as an adverse prognostic feature in rectal cancers, independent of the stage [2–6]. EMVI is defined as the presence of cancer cells in blood vessels beyond the muscularis propria and can be evaluated on MRI [6,7]. Upholding histopathological results as the gold standard, it has been shown that MRI has a specificity as high as 96% in the discrimination of EMVI and an accuracy rate of 70%–80% [8,9] particularly in using T2-weighted images. Vessel expansion, disruption of vessel borders, an irregular or nodular configuration of the vessel, and tumour signal intensity within the vein all constitute convincing evidence of EMVI on MRI. In addition to focal amendments in the invaded perirectal veins present in MRI, changes in diameters of superior rectal vein (SRV) and inferior mesenteric vein (IMV) might be manifestations of EMVI on CT. It has been suggested in literature that in EMVI (+) patients, thrombosed veins and increased venous drainage may affect the diameters of the SRV and IMV, which are the major venous drainage pathways of the rectum [2].

The diffusion-weighted imaging (DWI) sequence is routinely performed in daily MRI scanning due to its superiority in tumour detection, characterization, and monitoring of tumour response in rectal cancers [9,10]. Some authors indicate that the DWI sequence does not have a major contribution in the detection of EMVI due to its low signal-to-noise ratio and suppression of signals, which lead to difficulty in detecting intermediate or high signal intensities of the tumour within the invaded venous structure on DWI [9,11]. However, limited literature has been published on the diffusion characteristics of rectal adenocarcinoma and the modification of the rectum’s major drainage veins in patients with EMVI. Therefore, this study aims to demonstrate the diagnostic contribution of the DWI-MRI and CT in detecting the presence of EMVI in rectal adenocarcinoma by measuring the apparent diffusion coefficient (ADC) values on preoperative MRI and the diameters of the SRV and IMV upon preoperative CT as a quantitative analysis.

Materials and Methods

Patient Selection

This retrospective study was approved by the Clinical Research Ethical Committee of the institution (ref no.: 04-218-18). Informed consent was obtained from all patients. The study was conducted in accordance with the principles of the Declaration of Helsinki. The institution’s radiology information system/picture archiving and communication system (Centricity 5.0 RIS-i, GE Healthcare, Milwaukee, WI) was utilized to identify patients with rectal adenocarcinoma. The picture archiving and communication system was searched using the key words “rectal cancer,” “rectal carcinoma,” and “rectal adenocarcinoma” to identify candidates for the study population. CT and MRI images of 208 patients, who were examined between April 2014-March 2017 and were reviewed by a consultant radiologist with a special interest in gastrointestinal imaging (A.E.) for the presence of EMVI.

The inclusion criteria in the study are as follows: the performance of both preoperative MRI and CT examinations, the definite presence of EMVI on the MRI (mrEMVI +), and the availability of pathology results. Therefore, 137 patients with rectal adenocarcinoma who did not undergo CT analysis at diagnosis, did not receive surgery or did not have available pathology results were excluded from the study. In the final
analysis, 43 patients were identified to have mrEMVI on T2-weighted images with available pathology results. Hospital records and CT images of those 43 patients were reviewed for the simultaneous presence of pelvic tumours or pelvic surgery, portal hypertension, cirrhosis, intra-abdominal venous thrombosis, and cardiac failure. These situations were considered exclusion criteria to avoid any of their potential effects on the diameter of the SRV or IMV. Furthermore, patients with mucinous rectal adenocarcinoma (appearing as completely hyperintense on T2-weighted images without a solid component or having only a small solid component) were not included in this study because mucinous cancers have low cellular density and result in higher ADC values [12]. Thus, 4 patients with mucinous rectal cancer, 6 patients who presented with motion artefacts, and 3 patients with laboratory, clinical, or imaging findings consistent with cirrhosis and cardiac failure were excluded from this study. Ultimately, 30 EMVI (+) patients were included. The control group consisted of 28 patients who were diagnosed with rectal adenocarcinoma during the same time period and did not present with EMVI (EMVI scores of 0, defined later in the image analysis subsection) upon MRI scanning with pathologic confirmation. Figure 1 shows the flowchart of the study population.

**CT and MRI**

Bowel cleansing preparation was not performed prior the studies. Patients were not given anti-spasmodic medication before the examinations. No rectal gel was used for the MRI. CT examination were performed on 16-slice (Siemens Somatom Sensation 16; Siemens, Forcheim, Germany) and 64-slice CT (Toshiba Aquilion 64, Japan) machines. Three hours prior to scanning, patients drank 50 mL of Urografin (Urografin 76%; Schering AG, Berlin, Germany) diluted in 1500 mL of water. CT images were acquired using the following parameters: 120 kvp, collimations of $16 \times 1.2$ and $64 \times 0.5$, axial reconstructions with 1.2 and 1 mm slice thickness, and 1 mm slice intervals. An automatic exposure control system was used (max 350 mAs, standard deviation: 12.5 [noise index]). In the present study, 1–1.5 mL/kg of contrast agent (350/100 Omnipaque, GE Healthcare, Oslo, Norway) was injected at a rate of 2.5 mL/s, and the scan was performed 70 seconds after injection began. Axial source data images and multiplanar reformatted images were analysed on a workstation (Advantage Workstation 4.3; GE Healthcare, Waukesha, WI).

Magnetic resonance (MR) images were obtained on a 3-T MRI scanner (Magnetom Verio; Siemens, Erlangen, Germany) using an 8-channel torso phased-array body coil. DWI images with 3 different b values (50, 400, and 1000 s/mm²) were obtained in the axial plane using a single-shot multi-slice echoplanar imaging sequence with spectral adiabatic inversion recovery fat suppression and with the following parameters: repetition time/echo time of 646/11 ms, field of view of $300 \times 300$ mm, matrix size of $160 \times 109$, slice thickness of 5.0 mm, distance factor of 30%, averages of 2, reduction factor of 2, and receiver bandwidth of 260 Hz/Px. The MRI pulse sequence parameters used in this study are shown in Table 1.

![Flowchart of the study population. This figure is available in colour online at http://carjonline.org/](http://carjonline.org/)
Veins around the rectum appeared as black serpiginous or tubular structures on the T2-weighted images due to the signal void of blood. The presence of mrEMVI was accepted when we observed the loss of signal void and intermediate tumour signal in the perirectal vein disrupting the normal configuration of the vessel, resulting in an irregular expansion of the vein. Sagittal and orthogonal high-resolution T2-weighted MR images were specifically analysed to determine the presence of EMVI. In this study, based on the mrEMVI scoring system of Chand et al [6], the EMVI (+) group was consisted of patients with mrEMVI scores of 3 and 4 (Figure 2). Lymphatic invasion was distinguished from venous invasion by the visualization of the course of the vein in mesorectal fat tissue on T2-weighted images [13]. A n EMVI score of 0 was accepted as the absence of tumoural extension through the extramural tissue/adjacent vessel. Table 2 shows the MRI scoring system for EMVI, which is based on the classification established by Chand et al [6].

Quantitative analysis was performed by 2 radiologists at different times separately (different from the consultant radiologist, A.G.C. and E.P.) with more than 5 years of experience in pelvic imaging. The anterior-posterior and transverse diameters of the SRV and IMV were measured on the true axial reformatted CT images, which were obtained perpendicular to the long axis of the vessel lumen using coronal and sagittal images. The diameters were measured from one outside wall of the vein to the other using a zoom function. Mean values were calculated. The diameter of SRV was measured at the level of S1 vertebrae, where the vessel was horizontal and could be easily detected due to the high contrast provided by fat tissue (Figure 3). The measurements of the IMV were obtained before its confluence with the superior mesenteric vein (SMV)-portal vein, slightly beyond the point where the IMV was joined with its last middle-left colic vein branch. The craniocaudal length of the tumour was measured, and distant metastases were recorded.

The presence of EMVI was accepted when intermediate or high tumour-signal intensity was observed within the peritumoural vein on DWI. After initializing DWI, DWI and T2-weighted images were evaluated side-by-side by the same radiologist on the monitor to compare and verify the tumour and the tumoural component within the vein and to clarify vein boundaries to have more accurate quantitative results. Then, the ADC values were measured. A freehand region of interest (ROI) was drawn around the borders of the tumour on the section with the largest cross-sectional area and the transverse diameters of the SRV and IMV were measured on the true axial reformatted CT images, which were obtained perpendicular to the long axis of the vessel lumen using coronal and sagittal images. The diameters were measured from one outside wall of the vein to the other using a zoom function. Mean values were calculated. The diameter of SRV was measured at the level of S1 vertebrae, where the vessel was horizontal and could be easily detected due to the high contrast provided by fat tissue (Figure 3). The measurements of the IMV were obtained before its confluence with the superior mesenteric vein (SMV)-portal vein, slightly beyond the point where the IMV was joined with its last middle-left colic vein branch. The craniocaudal length of the tumour was measured, and distant metastases were recorded.

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lowest signal intensity. The ADC value of the invaded vein was measured manually by tracing along its margins in the area, where the ADC map exhibited the lowest signal intensity. Figure 4 represents the measurement of ADC value of the tumour and the invaded vein in EMVI (+) patients. In the control group, ADC measurements of the vessels were performed on the section of ADC map that contained the largest tumour cross-section. The vein adjacent to the wall of the tumour with the largest volume was selected, and a freehand ROI was traced along the boundaries of this vein.

The tumour borders were traced manually on ADC map with freehand ROI, which gave information about the sectional area of the lesion. Then, tumour volume was calculated multiplying this area by the section thickness.

Histopathological Evaluation of EMVI

The histopathology result was accepted as the reference test for identification of EMVI. After surgery, the specimens were evaluated for the presence of EMVI by a single pathologist with more than 10 years of experience in gastrointestinal pathology. When tumour was observed within the endothelial-lined space beyond the muscularis propria, it was defined as pEMVI. In addition, venous invasion was diagnosed when sufficient elastin staining was observed surrounding rounded or elongated tumour cells adjacent to the vessel even if an endothelial-lined space was not obvious. All pathologic specimens were stained routinely with hematoxylin and eosin. For indeterminate patients,
especially those who underwent neoadjuvant chemoradiotherapy, the elastin stain was used to diagnose EMVI. In cases, to differentiate EMVI from lymphatic invasion a special immunohistochemical staining known as “D2-40,” which is specific for lymphatic endothelium, was utilized. Transvers dissection was performed for the pathologic specimen in which sections were taken perpendicular to the area of the tumour with maximal invasion. All hematoxylin and eosin and elastin-stained slices were evaluated under a light microscope.

Statistical Analysis

Descriptive statistics are summarized as counts and percentages for categorical variables and as means and standard deviations for continuous variables. Nominal variables were tested via a chi-square test. For continuous variables, the difference between two groups was evaluated via a Student’s t test or Mann-Whitney U test when applicable. Differences between paired measurements were evaluated via a Wilcoxon signed-ranks test. Receiver operating characteristic (ROC) curves were used to describe the diagnostic performance of vein diameters and tumour ADC values. Ninety-five percent confidence intervals (CI) for the areas under the ROC curves were calculated. Cutoff values were obtained by using Youden index. Sensitivity, specificity, positive predictive value, and negative predictive value, as well as their 95% CI, were also used to evaluate the diagnostic performance of vein diameters and tumour ADC values. The intraclass correlation coefficient (ICC) was used for evaluating the agreement between both observers. A P value of less than .05 was considered statistically significant.

Results

Demographics of Case and Control Population

A total of 58 patients (30 patients with EMVI and 28 patients without EMVI) met the inclusion criteria. The control group consisted of 13 male patients (46.4%) and 15 female patients (53.6%), with a mean age of 58.9 ± 11.9 (min-max, 34–81). The EMVI (+) group, consisted of 25 male patients and 5 female patients with a mean age of 61.2 ± 14.6 (min-max, 24–85). There were no statistical differences between the groups in terms of age (P = .517). Male predominance was present in the EMVI (+) group (P = .003). Of the 30 (+) patients, 8 received neoadjuvant chemoradiotherapy before the surgery. In these patients who had neoadjuvant chemoradiotherapy the mean time interval between surgery and preoperative MRI scans was 8–10 weeks, and in patients who did not receive preoperative chemoradiotherapy the mean time interval between surgery and diagnostic imaging was 7 days (min-max, 3–14). For chemoradiotherapy, 45 Gy/25 fractions (1.8 Gy/day) was delivered to the pelvis over the course of 5 weeks (excluding weekends), and after 25 days, 3-fraction boost radiotherapy was administered to the primary tumour. During all radiation therapy sessions, the patients concurrently received capecitabine (825 mg/m2 twice daily) via oral administration. After the end of chemoradiotherapy the patients who tolerated it well continued capecitabine in a scheme of 14 days on and 1 week off with doses of 1000–1250 mg/m2 twice daily until surgery. Patients therefore waited 8–10 weeks before surgery after preoperative MRI scans. The demographics of the study population are shown in Table 3.

Assessment of Metastatic Disease Status

Of the 30 patients with EMVI, 15 patients (50%) exhibited liver metastases at diagnosis and underwent metastasectomy surgery. No metastases were observed in the control group. Metastases at diagnosis were significantly more frequent in EMVI (+) patients compared to EMVI (−) patients (P < .001).

Quantitative Analysis and Initial Performance Estimates

The mean tumour length was 68.5 ± 20.6 mm (min-max, 35–118 mm) in EMVI (+) patients and 44.0 ± 17.4 mm (min-max, 10–81 mm) in EMVI (−) patients. Mean tumour length was significantly larger in the EMVI (+) groups than that of the EMVI (−) group (P < .001).
The mean diameters of the SRV and IMV were found to be 4.9 ± 0.9 mm (min-max, 2.3–6.6 mm) and 6.9 ± 0.8 (min-max, 5.5–8.5 mm) in EMVI (+) patients, respectively. The mean diameters of the SRV and IMV for EMVI (−) patients were 3.7 ± 0.8 mm (min-max, 2.1–5.4 mm) and 5.4 ± 0.9 mm (min-max, 3–6.7 mm), respectively. The mean diameters of the SRV and IMV were significantly larger in EMVI (+) patients as compared to the control group (P < .001). Table 4 summarizes the SRV and IMV diameters. Patients with SRV diameters of ≥3.95 mm (area under the curve [AUC] ± standard error [SE]: 0.851 ± 0.051, P < .001) appear much more likely to have EMVI. Using this cutoff value (≥3.95), the sensitivity, specificity, and positive (PPV) and negative predictive values (NPV), as well as their 95% CIs, were found to be 93.3% (78.7%–98.2%), 67.9% (49.3%–82.1%), 75.7% (95% CI: 62.3%–85.6%), and 90.5% (95% CI: 79.2%–96.2%), respectively. For the IMV, a diameter of 5.95 mm was identified as a cutoff value via ROC analysis (AUC ± SE: 0.893 ± 0.040, P < .001). This cutoff value had a sensitivity of 93.3% (78.7%–98.2%), a specificity of 71.4% (52.9%–84.7%), a PPV of 77.8% (64.6%–87.2%), and a NPV of 90.9% (79.7%–96.5%) in discriminating between the EMVI (+) and EMVI (−) groups.

The mean ADC values for the tumours and EMVI (+) veins were 0.926 ± 0.281 × 10⁻³ mm²/s and 1.028 ± 0.355 × 10⁻³ mm²/s, respectively. There was no significantly difference between the ADC values of tumour and its invaded vein (P = .075) in the EMVI (+) group, whereas in the EMVI (−) group, the difference between the tumour and vessel ADC values was statistically significant (1.026 ± 0.246 × 10⁻³ mm²/s vs 1.325 ± 0.573 × 10⁻³ mm²/s, respectively; P = .024). Tumour ADC values were significantly lower in the EMVI (+) patients than in the EMVI (−) patients (P = .032). Using ROC curve analysis, a cut-off value of 0.929 × 10⁻³ mm²/s for the tumour ADC was found to allow the appropriate combination of sensitivity (96.7% (95% CI: 83.3%–99.4%), specificity of 64.3% (95% CI: 45.8%–79.3%), PPV of 74.4% (95% CI: 60.9%–84.5%) and NPV of 94.7% (95% CI: 84.6%–98.6%) in detection of EMVI.

The mean sampled tumour volume was calculated as 6.06 ± 3.63 cm³ (min-max: 0.52–11.75) and tumour volume in the invaded vein was 0.17 ± 0.1 cm³ (min-max: 0.07–0.69).

The agreement between 2 observers in terms of SRV and IMV diameter measurements, and ADC measurements were excellent (ICC for the SRV = 0.942, P < .001; ICC for the IMV = 0.948, P < .001; ICC for the tumour ADC = 0.984, P < .001, ICC for the vein ADC = 0.981, P < .001).

Discussion

Tumour invasion beyond the rectum wall, lymph node metastasis, and the mesorectal fascia involvement are factors that affect prognosis and can be evaluated preoperatively on MRI [14]. EMVI has been identified as an important independent prognostic factor that affects the risk profile of local and distant recurrence [2–6,15,16]. Consistent with these findings, this study showed that EMVI is an adverse prognostic factor that tends to increase the risk of metastasis. In this study, half of the patients with EMVI had metastatic disease at diagnosis. This may be explained by Stephen Paget’s “seed and soil” hypothesis, which identifies metastatic spread as a multistep process [17]. First, the cancer cells must enter into the blood circulation, either directly via the vascular system or indirectly via the lymphatic system, in order to escape from the primary tumour. After intravasation, tumour cells must survive in the circulation. Therefore, cancer cells cover themselves with platelets as a form of protection against the shear stress and the immune response. If they survive in the blood circulation, the next step is to avoid host defense mechanisms (eg, Kupffer cells and Pit cells in the liver) and arrest in the host parenchyma (eg, in the liver) [17–19]. Based on this review, we concluded that EMVI facilitates escape from the primary site of the tumour.
which may explain the statistically increased frequency of metastasis in the EMVI (+) group.

Besides the intermediate tumour-signal intensity within slightly or irregularly expanded veins, EMVI may also be identified in some circumstances on contrast-enhanced CT by the irregular serpiginous expansion of perirectal veins and the absence of luminal enhancement in the peritumoral veins due to tumour tissue invasion. In addition to this, in our study, we observed that EMVI (+) patients had significantly larger SRVs and IMVs, which are the major drainage pathways of the rectum. This could be linked with the presence of arteriovenous shunts, which cause the arterIALIZATION of the SRV. Additionally, increased venous drainage due to tumour neoangiogenesis and elevated local venous pressure caused by tumour thrombosis in small non-muscularized blood vessels constitute potential causes of enlargement [2]. Khan et al [20] also claimed that patients with right colon cancer had increased mean SMV mean diameters because of the increased venous return as a result of neoangiogenesis. Dilatation of the IMV and SRV can occur in cases of portal venous hypertension, intra-abdominal venous obstruction, and cardiac failure. Further, in pelvic tumours, because of neoangiogenesis and increased venous drainage, increases in IMV diameter may be observed. For this reason, patients with portal hypertension, cardiac failure, and other co-occurring pelvic neoplasms were excluded from this study.

DWI-MRI may be used as a noninvasive biomarker to determine patients’ treatment strategies and prognoses. This hypothesis has been confirmed by other studies demonstrating a significant relationship between ADC values and tumour aggressiveness in rectal cancers [12,21—24]. According to research conducted by Curvo-Semedo et al [14], mesorectal fascia involvement and node-positive disease were observed more often in patients with lower ADC values, and a significant relationship was noted between ADC values and tumour differentiation. In line with these studies, Gu et al [24] observed a significant negative correlation between ADC and standard uptake value in rectal cancer. The present study demonstrates that mean ADC values acquired from the primary tumours were significantly lower in EMVI (+) patients than in those without EMVI. Lower ADC values are expected in poorly differentiated tumours, and these tumours with low ADC values represent more aggressive behaviour [10,25]. Therefore, ADC has been shown to be an indirect indicator of microvascular circulation [10,26]. In a study conducted by Sun et al [10] showed that the tumours with lower ADC values and lower perfusion-related parameters such as the pseudo-diffusion coefficient and perfusion fraction shows more aggressive behaviour. Taking these findings into consideration, we suggest that the poorly differentiated tumours, which show lower ADC values and lower perfusion-related parameters, had poor structures of lumened vessels due to unorganized neoangiogenesis, which might create easier pathways for extramural venous invasion.

In the current study, a ADC value of $0.929 \times 10^{-3}$ mm$^2$/s was identified as a cutoff value via ROC analysis with a sensitivity of 76.7% and specificity of 57.1%. Previous studies indicated different ADC values with different settings for rectal adenocarcinomas [10,27]. We assume that this incompatibility between ADC values is due to utilization of different scanners from different vendors [10] and this value may not be reproducible. However, from results of our study we emphasize reliably that EMVI (+) patients had lower ADC values compared to EMVI (−).

It is assumed in other studies that tumour size has a significant impact on the patient survival [28—30]. Li et al [31] found a significant positive correlation between tumour size and stage. According to research conducted by Hotta et al [32], tumour size (>5 cm) has a significant association with the presence of urinary tract invasion. In the present study, the craniocaudal lengths of the tumours in the EMVI (+) group were significantly longer than those in the EMVI (−) group. Furthermore, in the metastatic group, the tumour lengths were longer than those in the non-metastatic group. Larger tumour volume could indicate that more tumour cells are able to invade the blood circulation; and as the surface area of a tumour increases, contact with the veins increases. Therefore, tumour size might be an acceptable prognostic variable in rectal cancers.

Evaluating EMVI on MRI is challenging and most false positive diagnoses are related to tumour in lymphatics [9,10,33]. This is probably due to limited resolution of MRI scanners. Lymph node involvement is usually in nodular configuration and EMVI can be distinguished by the visualization course of the vein, which proximally continues with the signal void tubular structure. Furthermore, the subserosal extension of tumour without perirectal vein invasion, desmoplastic reaction, or obliteration of signal void in perirectal veins on T2-weighted images are all other potential sources of false positive results on the MRI imaging [9,33]. In this study, patients enrolled in the EMVI (+) group had intermediate or definite tumour signal intensity within slightly or obviously enlarged veins and they were determined to be definitely positive mrEMVI patients according to the classification established by Chand et al. Although prior literature has emphasized that, the addition of DWI to T2-weighted images contributes no further value in the diagnosis of EMVI, we think that lower ADC values may contribute to the diagnosis of EMVI evaluated with T2-weighted images. In support to this claim, Ahn et al demonstrate that when DWI and T2-weighted images are evaluated together, DWI decreases false negative results and increases reliability of EMVI diagnosed on T2-weighted images [9].

Nonetheless, this study has some limitations. Primarily, the number of patients included in this study is limited, and it employs a retrospective design. Although pathology results are accepted as the gold standard, complete radiologic-pathologic matching is not feasible due to its retrospective design. Further prospective studies could be required to conduct exact one-to-one matching. While this study evaluated a large number of rectal adenocarcinoma patients, the study cohort was small because only EMVI patients, in
which the extramural venous component was considerable enough to allow much more precise measurements were included. Further, the number of patients who underwent CT examinations was somewhat limited, as most of the patients underwent positron emission tomography CT scanning for staging. This led to a considerable number of patients being excluded from the study. With a larger prospective study cohort, these results would be strengthened. An additional limitation arises from the knowledge of the presence of EMVI on MRI and DWI, which could have led to bias in measuring the SRV-IMV diameters and ADC values.

Conclusion

EMVI is an adverse prognostic factor in rectal cancers. Our study suggests that enlargement of the SRV and IMV diameters and low ADC values seem to be reliable in identifying EMVI. The cutoff values of 3.95 mm and 5.95 mm for the SRV and IMV, respectively, exhibited high sensitivity and specificity values in the identification of EMVI. This study also supports the notion that tumours with lower ADC values are more aggressive and tend to more frequently exhibit EMVI. Finally, EMVI (+) patients appear to have higher risks of exhibiting distant metastasis at diagnosis.

References