Chapter 6

Evaluation of MR diffusion-weighted imaging in differentiating endometriosis infiltrating the bowel from colorectal carcinoma

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Abstract

Objective: Endometriosis infiltrating the bowel may be difficult to differentiate from colorectal carcinoma in cases that present with non-specific clinical and imaging features. The aim of this study is to assess the value of MR diffusion-weighted imaging (DWI) in differentiating endometriosis infiltrating the bowel from colorectal carcinoma.

Methods: In 66 patients, MR DWI was added to the standard imaging protocol in patients visiting our outdoor MR clinic for the analysis of suspected or known deep infiltrating endometriosis (DIE). In patients diagnosed with DIE infiltrating the bowel on MR imaging, high b-value diffusion-weighted images were qualitatively assessed by two readers in consensus and compared to high b-value diffusion weighted images in 15 patients evaluated for colorectal carcinoma. In addition, ADC values of lesions were calculated, using b-values of 50, 400 and 800 s/mm².

Results: A total of 15 patients were diagnosed with DIE infiltrating the bowel on MR imaging. Endometriosis infiltrating the bowel showed low signal intensity on high b-value diffusion-weighted images in all patients, whereas colorectal carcinoma showed high signal intensity on high b-value diffusion-weighted images in all patients. Mean ADC value in endometriosis infiltrating the bowel (0.80 ± 0.06 x 10⁻³ mm²/s) was significantly lower compared to mean ADC value in colorectal carcinoma (0.86 ± 0.06 x 10⁻³ mm²/s), but with considerable overlap between ADC values.

Conclusion: Only qualitative assessment of MR DWI may be valuable to facilitate differentiation between endometriosis infiltrating the bowel and colorectal carcinoma.
Introduction

The bowel is a common location of deep infiltrating endometriosis (DIE) [1]. Patients with DIE infiltrating the bowel present with a broad spectrum of symptoms, including dysmenorrhea, dyschezia, (cyclic) hematochezia, obstipation and pencil-like stool. Endometriosis infiltrating the bowel may be difficult to diagnose and may mimic clinically and pathologically a wide spectrum of diseases, including: neoplasms [2-6], infectious etiologies and inflammatory bowel disease. Patients may present with rectal bleeding, change in bowel habits and bowel obstruction, as do patients with colorectal cancer.

In most patients, differentiation between DIE infiltrating the bowel and colorectal carcinoma is facilitated by clinical and imaging features. Colorectal carcinoma is more frequently diagnosed in male patients, whereas DIE is only diagnosed in female patients. Moreover DIE is found predominantly in premenopausal patients, whereas prevalence of colorectal carcinoma increases with age. Characteristic imaging features may also be valuable in differentiating DIE infiltrating the bowel and colorectal carcinoma. DIE infiltrating the bowel is an extrinsic lesion that is serosal or intramural in most cases [7,8], whereas in colorectal carcinoma mucosal lesions are characteristic. Colonoscopy with biopsies, used to diagnose colorectal carcinoma, therefore has limited value for diagnosis of endometriosis infiltrating the bowel [9]. MR imaging has demonstrated high accuracy in diagnosis of DIE [1,7]. However, in medical centers that have less experience in the evaluation of endometriosis patients, the diagnostic accuracy of DIE may be lower [10]. Occasionally, clinical features are not specific and imaging techniques performed may not show characteristic signs [5,6,11].

Also, bowel wall thickening may be found incidentally on MR imaging. In these cases, MR DWI in addition to conventional MR imaging, may be valuable to facilitate differentiation between DIE and colorectal carcinoma.

In the present study we assess the value of MR DWI to facilitate differentiation between endometriosis infiltrating the bowel and colorectal carcinoma.
Materials and methods

Patient population
This study was performed in a tertiary referral center for the evaluation of endometriosis and colorectal malignancy. The institutional review board (IRB) granted permission for this study and the requirement for informed consent was waived. Between July 2008 and April 2010, MR DWI was added to the standard MR imaging protocol in all patients suspected of DIE (n=66). Clinical features and surgical history were retrospectively studied in all patients diagnosed with colorectal DIE. The standard of reference for diagnosis of DIE was defined as a combination of histopathology (if available), clinical features, and consensus opinion in an expert panel formed by a senior gynaecologist and radiologist. In our center, DWI is part of the routine MR imaging work-up in patients with colorectal cancer. To compare MR DWI in DIE infiltrating the bowel and colorectal carcinoma, 15 randomly chosen patients, who were evaluated for colorectal carcinoma, were studied (12 men and 3 women; mean age: 70 years; range 55-96 years). Patients who were diagnosed with colorectal carcinoma and underwent chemo or chemoradiation therapy prior to MR imaging evaluation were excluded from the analysis (5 out of 20). In all patients with colorectal carcinoma, diagnosis was confirmed by histopathology.

MR Imaging technique
MR imaging in patients with DIE infiltrating the bowel or colorectal carcinoma was performed at 1.5 Tesla (Avanto, Siemens, Erlangen, Germany) using a six-channel pelvic phased-array coil. Scan sequences included high resolution turbospin echo (TSE) T2-weighted imaging in the axial, coronal and sagittal planes (repetition-time (TR) msec/echo-time (TE) mc 6000-10,000/136, echo-train length (ETL) 61, number of acquisitions 3) and fat suppressed spin-echo T1-weighted imaging in the axial and sagittal planes (540/12; number of acquisitions 2) using a multislice technique. Slice thickness varied from 4 to 6 mm with a 0.8 to 1.2 mm interslice gap. Matrix size varied from 512x435 to 256x144 (the latter for T1-weighted images), and the field of view (FOV) ranged from 350 to 400 (depending on the size of the patient). In addition, the (standard) imaging protocol in patients evaluated for colorectal carcinoma included contrast enhanced imaging, which was not used in the analysis.
of this study. DWI was performed in the axial plane, using a single-shot echo-planner imaging (EPI) sequence (4100/82, number of acquisitions: 4), FOV 350 cm, matrix 192x192, slice thickness/inter-slice gap 4/0 mm, and b-values of 50, 400 and 800 s/mm². In patients evaluated for colorectal carcinoma b-values of 50, 400 and 800 s/mm² were used. The total imaging time per patient was approximately 24 minutes. The added examination time for DWI was approximately 4 minutes.

Image analysis
Exams were analysed on a picture archiving and communication system (Sectra RIS/PACS) viewing station (Sectra Imtec AB, Linköping, Sweden) using standardized data scoring sheets. All MR images were evaluated by two readers in consensus, with experience in the evaluation of endometriosis and colorectal carcinoma. The joint presence of signal intensity abnormalities as well as morphologic abnormalities as reported previously by Bazot et al [1] was used for the diagnosis of DIE infiltrating the bowel. High b-value (b-800) diffusion-weighted images were qualitatively assessed in all patients (hyperintense/hypointense signal). For the quantitative analysis of DWI images, ADC values were calculated using b-values of 50, 400 and 800 s/mm². Operator-defined regions-of-interest (ROIs) of at least 30mm² were placed on part of the tumor that showed highest signal intensity on diffusion-weighted images (b-800), taking care not to include major vessels or borders of lesions. For accurate (identical) anatomical placement of the ROIs, they were copied from each respective image.

Histopathology
In 7 out of 15 patients diagnosed with colorectal carcinoma on MR imaging total mesorectal excision (TME) was performed. In 8 patients diagnosis was based on biopsies. All pathologic specimens were examined by one pathologist. Histopathologic examination included tumor type and differentiation grade. Colorectal carcinoma was diagnosed as mucinous adenocarcinoma when a content of 50% or more consisted of extracellular mucin [12]. In 3 out of 15 patients diagnosed with endometriosis infiltrating the bowel on MR imaging, histopathology was obtained. Diagnosis of endometriosis infiltrating the bowel was made when endometrial glands and stroma were found infiltrating the muscular layer of the bowel wall [13].
Statistical evaluation

Statistical parameters (mean and range) were calculated using the Statistical Package for Social Sciences (SPSS 15.0, Chicago Ill) program. Mann-Whitney U test was used to compare ADC values of DIE infiltrating the bowel and colorectal carcinoma. A p-value of less than 0.05 was considered statistically significant.

Results

Patient characteristics in DIE infiltrating the bowel
In all patients MR imaging was performed because of suspected DIE, which was based on clinical symptoms (e.g. dysmenorrhoea, dyspareunia, dysuria, dyschezia, (cyclic) hematochezia, rectal bleeding and pencil-like stool). A total of 15 out of 66 patients were diagnosed with DIE infiltrating the bowel on MR imaging (mean age 33 years: range 22-44 years). Patients presented with dyschezia in 4 cases and dyschezia with (cyclic) hematochezia in 5 cases.

Conventional MR findings in endometriosis infiltrating the bowel
DIE lesions were localized in the rectum and rectosigmoid in 9 and 5 patients, respectively and in the sigmoid in another patient. Mean distance from the anal verge was 99.3 ± 41mm (range: 60-200 mm). On T2-weighted MR imaging lesions showed a “fan shaped” configuration with homogeneous (n=12) or inhomogeneous (n=3) isointense signal intensity compared to muscle, due to foci of high signal intensity. On T1-weighted (fat suppressed) imaging 14 lesions showed homogeneous isointense signal intensity compared to muscle and one lesion inhomogeneous isointensity, due to foci of high signal intensity, indicating hemorrhage.

Conventional MR findings in colorectal carcinoma
A total of 15 out of 20 patients diagnosed with colorectal carcinoma were analysed (5 patients were excluded because of prior chemo or chemoradiation therapy). Mean distance from the tumors to the anal verge was 70.7 ± 18 mm (range: 42-102 mm). Most lesions showed isointense to slightly hyperintense signal compared to muscle on T2-weighted and T1-weighted fat suppressed imaging. One tumor diagnosed as mucinous carcinoma on MR imaging, showing
predominantly high signal intensity compared to muscle on T2-weighted imaging and slightly high signal intensity compared to muscle on T1-weighted fat suppressed imaging.

**Histopathology**

In all patients diagnosed with colorectal carcinoma histopathology revealed adenocarcinoma. Analysis of biopsies (n=8) and resection specimens (n=7) showed 14 tumors were poorly differentiated and one was a mucinous adenocarcinoma.

In three patients diagnosed with endometriosis infiltrating the bowel on MR imaging histopathology was obtained. In one patient biopsy showed endometriosis infiltrating the bowel wall and in two patients analysis of the resection specimen (low-anterior resection) confirmed endometriosis infiltrating the bowel wall.

**Diffusion-weighted MR imaging and ADC values**

Mean ADC value in DIE infiltrating the bowel was $0.80 \pm 0.06 \times 10^{-3} \text{ mm}^2/\text{s}$ (range: $0.65-0.89 \times 10^{-3} \text{ mm}^2/\text{s}$) and was significantly lower compared to mean ADC value in colorectal carcinoma ($0.86 \pm 0.06 \times 10^{-3} \text{ mm}^2/\text{s}$; range: $0.74-0.98$; $p=0.02$). Calculated ADC value in one mucinous adenocarcinoma was highly variable, ranging from $0.98 \times 10^{-3} \text{ mm}^2/\text{s}$ in part of the tumor that showed isointense signal intensity compared to muscle on T2-weighted imaging to $1.58 \times 10^{-3} \text{ mm}^2/\text{s}$ in part of the tumor that showed high signal intensity compared to muscle on T2-weighted imaging (mucin).

The distribution of ADC values in DIE infiltrating the bowel and colorectal carcinoma is shown in Figure 1. All DIE lesions showed low signal intensity on diffusion-weighted images with high $b$-values ($b$-800: Fig 2). All colorectal carcinomas showed high signal intensity on diffusion-weighted images with high $b$-values ($b$-800: Fig 3).
**Discussion**

This study demonstrates that endometriosis with deep infiltration of the bowel shows low signal intensity on DWI with high $b$-values, whereas colorectal carcinoma shows high signal intensity on DWI with high $b$-values. The high signal intensity on high $b$-value diffusion-weighted images in colorectal carcinoma might be predominantly due to a higher cellularity and number of cell membranes per unit volume in colorectal carcinomas compared to endometriosis infiltrating the bowel. Previously it was demonstrated, qualitative assessment of DW MR imaging is useful for detecting colorectal cancers [14]. Furthermore, it has been known previously that a number of benign lesions can exhibit hyperintensity on images with high $b$-values, [15] and that ADC values in benign and malignant lesions may overlap, which makes it difficult to distinguish lesions using MR DWI alone.

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**Fig 1.** Distribution of ADC values ($x \times 10^{-3}$ mm$^2$/s) in endometriosis infiltrating the bowel and colorectal carcinoma.
The value of MR diffusion-weighted imaging in differentiating DIE infiltrating the bowel wall from colorectal carcinoma

Fig 2. A 34 year old woman who was referred to us from another hospital with dyschezia and pencil-like stool. A and B: Sagittal and Axial T2-weighted images show lesion infiltrating the rectum and rectosigmoid, demonstrating isointense signal intensity compared to muscle (white arrows). C: Axial diffusion-weighted image (b-800) shows low signal intensity of the lesion (white arrow). D: Corresponding ADC map: the calculated ADC value of the lesion (white arrow) was 0.85 x 10^-3 mm^2/s, indicating restricted diffusion.

However, DIE lesions infiltrating the bowel show hypointense signal intensity on high b-value DWI with corresponding low ADC values. Previously, it was demonstrated that hematomas [16], ordinary leiomyomas [17] and certain benign tumours of the ovaries (cystadenofibroma, ovarian fibromas, Brenner tumours) [18] with low ADC values did not exhibit a high b-1000 signal on DWI [14]. The low signal intensity of DIE lesions on high b-value DWI may be partly explained by the “T2-blackout effect”, since DIE lesions are (very) hypointense on T2-weighted imaging,
Fig 3. A 82 year old man diagnosed with rectal carcinoma. A and B: Axial and sagittal T2-weighted images shows iso- to slightly hyperintense lesion compared to muscle in the rectal wall (white arrow) with invasion of the perirectal fat. C: Axial diffusion-weighted image (b-800) shows high signal intensity of the lesion (white arrow). D: Corresponding ADC map: the calculated ADC value of the lesion (black arrow) was 0.90 x 10^{-3} \text{mm}^2/\text{s}, indicating restricted diffusion due to a high cellularity of the lesion.

as a consequence of smooth muscle hyperplasia, smooth muscle proliferation and fibrous tissue. In these lesions, restricted diffusion might be explained by fibres blocking diffusion and also by low water content. High $b$-value DWI in addition to conventional MR imaging may therefore be used to facilitate differentiation
between endometriosis and malignant lesions of the bowel in cases of incidental bowel wall thickening on MR imaging or patients with non-specific symptoms.

The calculated mean ADC value in endometriosis infiltrating the bowel was significantly lower compared to the mean ADC value in colorectal carcinoma. However, there was a considerable overlap in ADC values. Therefore quantitative DWI alone may not be valuable for differentiation between endometriosis and colorectal carcinoma. ADC values of colorectal carcinoma in our study are lower compared to ADC values previously reported in these tumors [19-21]. This may be due to the method used to calculate ADC values, as we selected part of the tumor that showed highest signal intensity on high b-value images, to be certain not to include borders of the lesion, whereas in previous literature the entire lesion was included in the measurement.

Previously, mucinous adenocarcinoma of the rectum showed higher ADC values compared to well-differentiated adenocarcinoma as a result of low cellularity, due to extracellular mucin [19]. Our study supports this finding, as the ADC value of mucinous adenocarcinoma was variable within the tumor. In part of the tumor that demonstrated high signal intensity on T2-weighted imaging, the ADC value was higher compared to the ADC value in part of the tumor that showed hypointense signal.

Although in patients diagnosed with endometriosis infiltrating the bowel on MR imaging, histopathological confirmation was only obtained in three patients, which is a limitation of this study, MR imaging previously demonstrated high accuracy in diagnosis of endometriosis infiltrating the bowel [1,7]. Another limitation may be that we included male patients diagnosed with colorectal carcinoma, whereas endometriosis should only be included in the differential diagnosis of female patients, and we were not able to match patients according to age. This can be explained by the fact that endometriosis may only occasionally be found in postmenopausal women and colorectal carcinoma occurs in younger female patients less frequently. However, we believe these factors will not substantially influence results of our study.
In conclusion, MR DWI, with the use of a qualitative assessment of high $b$-value images, may be a valuable, non-invasive tool, to facilitate differentiation between endometriosis infiltrating the bowel and colorectal carcinoma when bowel wall thickening is found on MR imaging incidentally, or in patients with non-specific symptoms.
References


