

Deep infiltrating endometriosis of the bowel: MR imaging as a method to predict muscular invasion

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Abstract

Purpose: To evaluate magnetic resonance (MR) imaging morphologic- and signal intensity abnormalities of deep infiltrating endometriosis (DIE) of the bowel wall and to assess its value in predicting depth and extent of bowel wall infiltration.

Materials and methods: This single-center study was performed in a tertiary referral center for endometriosis. All patients ($n = 28$) who underwent segmental bowel resection (2004–2010) were retrospectively studied. MR images were analyzed by two experienced readers independently (number of lesions, location, size, signal intensity, and depth of bowel wall infiltration) and this was correlated with histopathology.

Results: The sensitivity, specificity, positive and negative predictive values, and accuracy for diagnosis of endometriosis infiltrating the muscular layer of the bowel were 100%, 75%, 96%, 100%, and 96%, respectively. The inter-rater agreement was 0.84. “Fan shaped” configurations with hypointensity on T2- and T1-weighted imaging were characteristic for thickening of indigenous smooth muscle and smooth muscle hyperplasia at histopathology, as a consequence of infiltration by endometriosis. Thickening of the (sub)mucosa corresponded to edema with or without infiltration of endometriosis.

Conclusion: MR imaging at 1.5 Tesla is useful to predict muscular infiltration of the bowel in endometriosis,

whereas it is of limited value in diagnosis of (sub)mucosal infiltration.

Key words: Magnetic resonance imaging—Deep infiltrating endometriosis—Bowel involvement—Segmental bowel resection—Endometriosis

Deep infiltrating endometriosis (DIE) infiltrating the bowel is estimated to be found in 31% of patients that are evaluated for DIE [2]. The natural history of DIE is still unknown, but the infiltration depth of lesions increases with time and is correlated to the intensity of pain [14, 18]. Most common sites of bowel involvement are the rectum and rectosigmoid (65.7%) with involvement of the sigmoid in 17.4% patients [8]. Symptoms of bowel endometriosis are dyschezia, cyclic hematochezia, pencil-like stools, and bowel obstruction.

Endometriosis infiltrating the bowel is difficult to detect at physical examination. Transvaginal sonography (TVS) is usually the first imaging technique performed by the gynecologist for evaluation of pelvic diseases and has demonstrated accurate diagnosis of endometriosis infiltrating the bowel [3, 4, 17]. It is a useful imaging modality for screening, although normal TVS findings do not rule out diagnosis of DIE [4], and TVS is of limited value in assessing the areas far from the probe [17, 22], including the sigmoid. Magnetic resonance (MR) imaging, a non-invasive method, has the advantage over other methods of investigation, as it can make

a complete survey of the anterior and posterior compartments of the pelvis at one time [1] and it provides information about the inaccessible areas to laparoscopy [6] and TVS [22]. This is valuable, because DIE lesions are multifocal in a large number of patients and may present retroperitoneally as well [7]. MR imaging has shown accurate diagnosis of DIE previously [2, 16] and bowel wall infiltration assessment correlated well with pathologic findings [16]. However, in the latter study, only 3 patients underwent segmental bowel resection and in 4 patients rectosigmoid nodule excision was performed.

Preoperative mapping of disease extension is important, first, to decide whether surgical intervention is indicated, and second for planning of complete surgical excision, since success of treatment depends on radical surgical removal [13]. The indication for bowel wall resection, apart from symptoms [20], is based on dimensions of the nodule >2 cm or 3 cm and/or on muscularis involvement and/or the percentage of circumference involvement [10, 11]. Shaving or limited disk resection procedures could be a less invasive alternative for segmental resection in patients in which extension and/or infiltration of endometriosis is limited [12].

The aim of this study is to describe MR imaging morphologic- and signal intensity abnormalities of DIE infiltrating the bowel, to help improve diagnosis, and to assess the value of MR imaging in predicting depth and extent of bowel wall infiltration in the largest group of patients so far.

Materials and methods

Study population

This single-center, retrospective study was performed in a tertiary referral center for endometriosis between April 2004 and January 2010. All patients that underwent segmental bowel resection were identified using the hospital archive system, and the MR exams of these patients were retrieved and retrospectively studied. Clinical data were assessed (symptoms and surgical history) in all patients. The institutional review board (IRB) granted permission for this study; the requirement for informed consent was waived.

MR imaging

MR imaging of the pelvis was performed at 1.5 Tesla (Sonata or Avanto, Siemens, Erlangen, Germany) using a pelvic phased-array coil, and included high resolution turbo spin echo T2-weighted imaging (repetition time (TR)/echo time (TE) 6000–10000/136 ms, echo train length 61, number of acquisitions: 3) in the axial, coronal, and sagittal plane, and fat-suppressed spin echo T1 weighted imaging (TR/TE 740–790/19 ms, number of acquisition 2) in the axial and sagittal plane, using a

Fig. 1. A 31-year-old woman who presented with dyschezia and hematochezia. Segmental bowel resection was performed, as hormonal therapy did not decrease pain symptoms in this patient. **A** and **B** Sagittal and axial T2-weighted images (6000–10000/137) show a lesion with isointense to slightly hyperintense signal compared to muscle in the posterior fornix that is infiltrating the bowel wall. The lesion was scored on MR imaging as infiltrating the serosa of the bowel wall without prominent thickening of the muscularis. **C** Histopathology shows endometriosis of the bowel serosa with fibrosis (*curved black arrow*) and minor local involvement of the muscular layer at this site. The indigenous smooth muscle is locally only minimally thickened (*black arrow*)

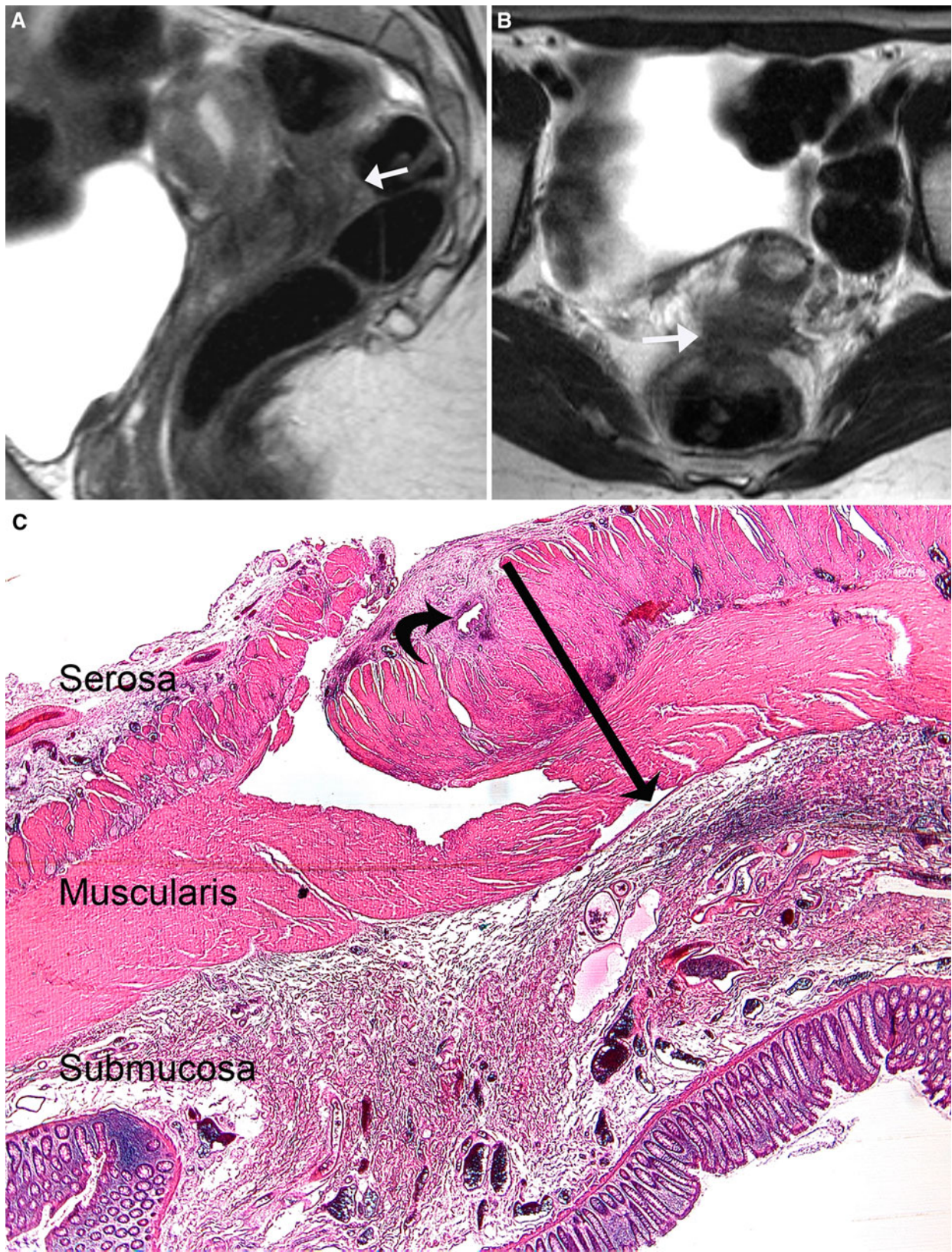
multislice technique. Slice thickness varied from 4 to 6 mm with a 0.8–1.2 mm interslice gap. Matrix varied from 512 to 256 (the latter for T1-weighted images) and field of view ranged from 350 to 400. Three patients were excluded from this study because of poor quality of the images. No intravenous contrast was used [5].

MR analysis

Examinations were analyzed 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 performed in patients who underwent segmental bowel resection (2004–2010) were analyzed by two independent, experienced readers, specializing in abdominal imaging, blinded for pathology results. Inter-rater agreement for diagnosis of DIE infiltrating the muscular layer of the bowel was calculated.

Analysis included the presence of DIE infiltrating the bowel wall, number of lesions (single or multiple), location, lesion length (mm), location in relation to the anus (cm), depth of bowel wall infiltration (no infiltration (adhesions), serosal, muscular or mucosal infiltration), signal intensities (homogeneous/heterogeneous, hyper/hypo/isointense), thickness of the muscularis in the axial plane (mm), thickness of the (sub)mucosa in the axial plane (mm), presence of circular involvement of the bowel, and presence of endometriosis at locations other than the bowel wall (DIE and endometrial cysts).

The following criteria were used for diagnosis: (1) DIE: The joint presence of signal intensity abnormalities and morphologic abnormalities as previously described by Bazot et al. [2]; (2) Endometrial cysts: hyperintensity on T1- and hypointensity on T2-weighted images (shading) [23]. Bowel involvement was scored as “adhesive” when a strand of fibrous tissue was found in the fat plane between uterus and bowel, showing hypointense signal intensity, causing disappearance of the high signal intensity of the fat. Bowel wall involvement was scored as infiltrating the serosal layer when “minimal” bowel wall thickening was found, showing slightly high signal



intensity compared to muscle, in continuity with a mass at the serosal side of the bowel wall, showing hypointense signal (Fig. 1). The infiltration depth was scored as

infiltrating the muscular layer, when thickening of the muscularis was found, showing a “fan shaped” configuration with isointense signal compared to muscle with

or without thickening of the (sub)mucosa that demonstrated slightly high to high signal intensity at the luminal side of the bowel wall [23]. Suspicion of mucosal infiltration was raised when extensive muscular thickening of the bowel wall was found, showing isointensity compared to muscle with thickening of the (sub)mucosa (slightly high to high signal intensity compared to muscle at the luminal side of the bowel wall) and irregularities (e.g., interruption) at this site.

Histopathology

All histopathological slides of the surgical resections were revised by one pathologist. Diagnosis of endometriosis with bowel involvement was made when endometrial glands and stroma were found within the lesion that infiltrated the bowel [9].

Analysis included depth of bowel wall infiltration (“no infiltration”, serosal, muscular, submucosal, or mucosal infiltration). If the lesion was infiltrating the serosa and in addition minor superficial (microscopic) infiltration of the muscularis propria was found, then it was assessed as serosal involvement. Thickening of the muscularis propria was assessed, comparing the site of infiltration of endometriosis in the bowel wall with a site without infiltration of endometriosis in the same specimen (present or absent).

Statistical analysis

Statistical parameters (e.g., mean and standard deviation) were calculated using the Statistical Package for Social Sciences, version 15.0 (SPSS, Inc, Chicago, IL). The inter-rater agreement was calculated using Cohen’s kappa coefficient. The degree of agreement was defined according to Landis and Koch (<0: no agreement; 0.00–0.20: slight agreement; 0.21–0.40: fair agreement; 0.41–0.60: moderate agreement; 0.61–0.80: substantial agreement; 0.81–1.00: excellent agreement). Sensitivity, specificity, positive, and negative predictive values were determined for diagnosis of endometriosis infiltrating the muscular of the bowel wall.

To compare (sub)mucosal thickness on MR imaging, the Mann–Whitney *U* test was used. A *P*-value of less than 0.05 was considered statistically significant.

Results

Patient characteristics

In 28 patients, segmental bowel resection was performed (mean age: 32 years; range: 25–44 years), because patients did not respond to hormonal therapy and/or there was suspicion of a clinically relevant stenosis of the bowel. Segmental resection of the rectum, rectosigmoid, or sigmoid was performed in 3, 21, and 4 patients, respectively, by a multidisciplinary team, including

gynecologists and a gastrointestinal surgeon. In one patient a colostomy and in another three patients an ileostomy was performed previously in another hospital, because of symptoms of acute bowel obstruction. Symptoms and previous surgical history are shown in Table 1.

MR imaging

On MR imaging, a total of 28 DIE lesions were found adhesive with or infiltrating the bowel wall. One patient showed a retrocervical nodule that demonstrated hypointense signal, adhesive with the bowel. Lesions were located at the rectum, rectosigmoid, and sigmoid in 15, 6, and 7 lesions, respectively. DIE lesions infiltrating the bowel muscularis showed a characteristic “fan shaped” configuration depicting isointense signal compared to muscle on T2-weighted imaging and slightly high to hyperintense signal compared to muscle at the luminal side of the bowel wall. On T1-weighted fat suppressed imaging, lesions showed isointensity compared to muscle. Foci of high signal intensity were present in five lesions on T2-weighted imaging and five lesions on T1-weighted fat suppressed imaging. The mean distance relative to the anus was 13 cm (range: 8–30 cm). The mean lesion length was 48 mm (range: 20–170 mm).

Table 1. Patient characteristics in 28 patients diagnosed with endometriosis infiltrating (or adhesive with) the bowel wall on MR imaging that underwent segmental bowel resection

	Number of patients (%)
Symptoms	
Dyschezia	20 (71)
Hematochezia	18 (64)
Dysparunia	16 (57)
Dysmenorrhea	24 (86)
Pencil-like stool	6 (21)
Ileus	4
Previous surgeries related to endometriosis	
Diagnostic laparoscopy	7 (25)
Therapeutic laparoscopy	9 (32)
Laparotomy	4 (14)

Table 2. Correlation between MR imaging and histopathology in 28 patients who underwent segmental bowel resection

MR imaging	Number of lesions	Histopathology	Number of lesions
Adhesive	1	Endometriosis separate from bowel	1
Serosa	2	Serosa	2
Mucularis	22	Mucularis ^a	20
		Serosa	1
		Focal infiltration of mucosa	1
Mucosa	3	Mucularis ^b	2
		Focal infiltration of mucosa	1

^aOf which nine lesions infiltrated the submucosal layer in addition to infiltration of the muscularis

^bIn one of these lesions endometriosis was also found in the submucosal layer

Depth of infiltration is shown in Table 2. In 6 patients, there was suspicion of circular involvement of the bowel on MR imaging.

Presence of endometriosis at locations other than the bowel (DIE and/or endometrial cysts) was found in all patients. Ovarian endometrial cysts were found in 20 out of 28 patients (71%), DIE was found retrocervical in 28 out of 28 patients (100%), and infiltrating the bladder wall in 3 out of 28 patients (11%).

Correlation with histopathology

The correlation between MR imaging and histopathology is shown in Table 2. The mean interval between MR imaging and surgery was 168 days (range 4–388 days).

Histopathological evaluation of 28 surgical bowel specimens showed endometriosis limited to the serosa in 3 cases (11%), involvement of the muscularis propria in 22 cases (79%), and mucosal involvement in 2 cases (7%). In one patient, no infiltration of the bowel wall was found at histopathology, but a nodule, which could be excised separate from the bowel during surgery, revealed endometriosis.

Inter-rater agreement for diagnosis of DIE infiltrating the muscular layer of the bowel on MR imaging was 0.84. The sensitivity, specificity, positive and negative predictive values, and accuracy for infiltration of the muscular layer of the bowel wall were 100%, 75%, 96%, 100%, and 96%, respectively. Regarding infiltration of the muscular layer of the bowel on MR imaging, 24 cases were true-positive, none were false-negative, one was false-positive, and three were true-negative cases. The “fan shaped” configuration seen on MR imaging, corresponded to thickening and distortion of the muscularis propria and smooth muscle hyperplasia at histopathology and macroscopic images (Figs. 2, 3, and 4), as a consequence of infiltration by endometrial glands and stroma. The thickness of the muscularis, measured on MR imaging in 12 patients with muscular infiltration of endometriosis (mean: 10.0 mm) at histopathology, was not significantly different from the muscular thickness in patients with infiltration of the muscularis and (sub)mucosa (mean: 11.4 mm; $P = 0.496$).

The slightly high to hyperintense signal compared to muscle at the luminal side of the bowel wall on MR imaging (Fig. 5), which was present in all lesions infiltrating the muscular layer of the bowel, corresponded to (sub)mucosal thickening, as a consequence of “non-specific inflammation” with or without infiltration of endometriosis at histopathology.

The mean (sub)mucosal thickness was measured on MR imaging in 11 out of 12 patients with muscular infiltration and 11 patients with muscular and (sub)mucosal infiltration of endometriosis at histopathology, as in two lesions it was not possible to distinguish the different layers of the bowel wall on MR

imaging. The (sub)mucosal thickness in patients with muscular infiltration of endometriosis (mean: 3.8 mm) did not significantly differ from the (sub)mucosal thickness in 12 lesions that infiltrated the muscularis and (sub)mucosa (mean: 4.5 mm; $P = 0.145$).

Discussion

This study shows that MR imaging is useful to predict muscular infiltration of the bowel in endometriosis. Muscular infiltration was diagnosed on MR imaging with a sensitivity of 100% and specificity of 75%. On T2-weighted imaging lesions showed a characteristic “fan shaped” configuration, demonstrating isointense signal compared to muscle and slightly high to hyperintense signal at the luminal side of the bowel wall. On T1-weighted fat suppressed imaging, most lesions showed homogeneous isointensity compared to muscle. Foci of high signal intensity were present in a minority of lesions. The “fan shaped” configuration of lesions, showing isointensity compared to muscle on MR imaging corresponded to muscular thickening at histopathology, predominantly due to proliferation and distortion of indigenous smooth muscle and smooth muscle hyperplasia, as a consequence of infiltration by endometriosis. Previously, this configuration, demonstrated in a small patient population ($n = 6$), was named “mushroom cap”, because of a pattern of intraluminal endophytic growth [24]. However, if the bowel wall is involved over a long distance, the “mushroom cap” cannot be recognized anymore.

Moreover, lesions showed slightly hyperintense to hyperintense signal at the luminal side of the bowel wall, corresponding to the (sub)mucosal layer of the bowel at histopathology. The slightly high to hyperintense signal may be caused by submucosal swelling (edema), which is also seen at colonoscopy. At histopathology in some lesions “non-specific inflammation” of the submucosa and submucosal thickening was observed. These (sub)mucosal changes might be caused by submucosal distortion and elevation [15], by (underlying) endometriosis [21]. Thickening of the submucosa on MR imaging was not related to infiltration of endometriosis into this layer of the bowel wall, therefore this finding solely cannot be used to predict depth of infiltration. Although infiltration of the (sub)mucosa may be very difficult to assess on MR imaging, in some lesions extensive irregularities at this site may raise suspicion of (sub)mucosal involvement.

MR imaging previously showed accurate diagnosis of DIE infiltrating the bowel [2, 16]. Furthermore, a high correlation between colon wall infiltration scores and histopathology was reported in a small group of patients at 3.0 T [16]. In the latter study however, the method of colon wall infiltration assessment was not described. They reported that readers gave colon wall invasion

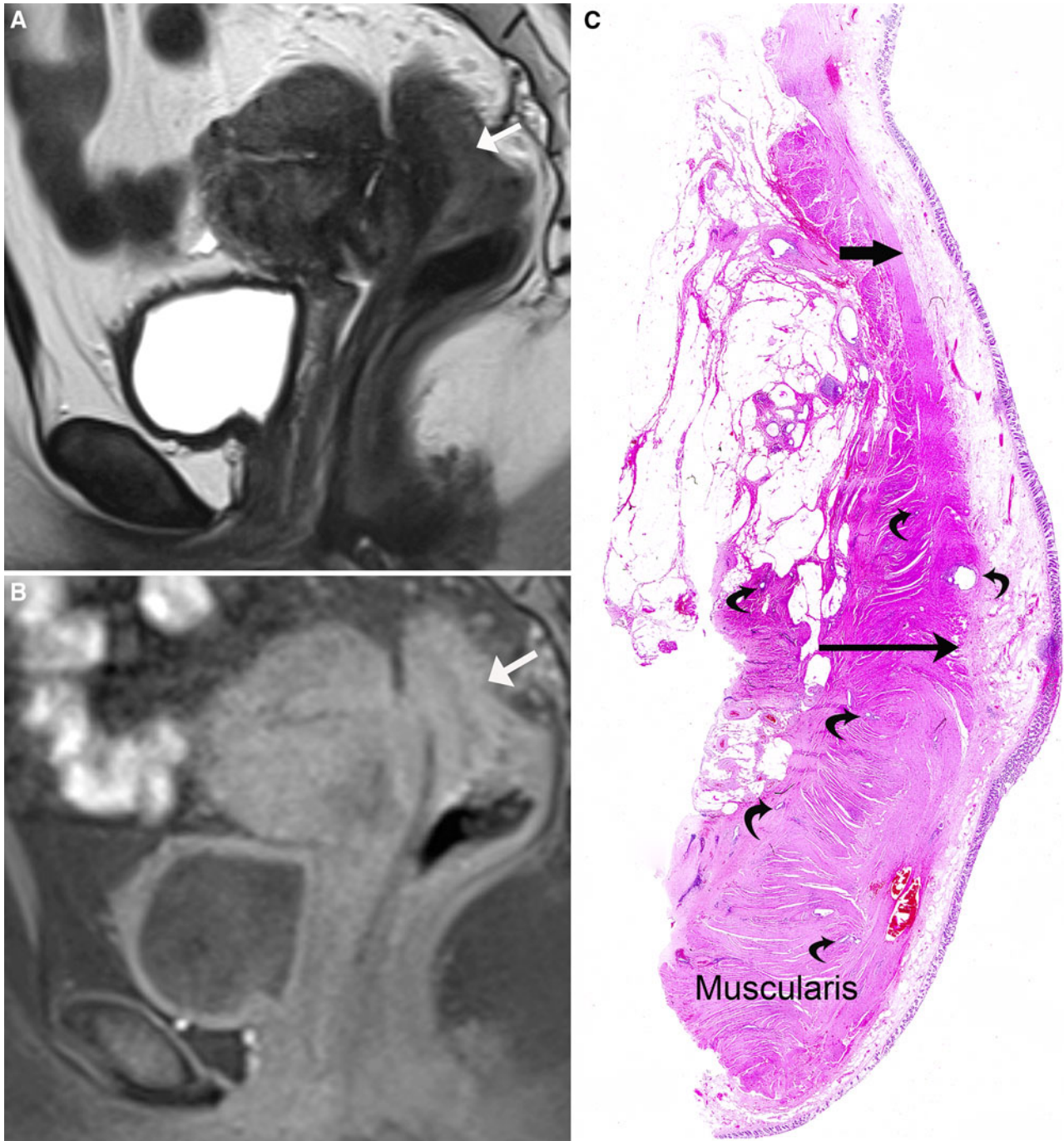


Fig. 2. A 30-year-old woman known with endometriosis previously presented elsewhere with complete bowel obstruction, due to endometriosis infiltrating the rectosigmoid. Colostomy was performed before referral to our hospital. Thereafter, a segmental bowel resection was performed in our hospital. At histopathology, the endometriotic lesion was diagnosed as infiltrating the muscular and submucosal layers of the bowel wall. **A** Sagittal T2-weighted image (6000–10000/137) shows

“fan shaped” configuration with isointense signal compared to muscle. **B** Sagittal T1-weighted image (740–790/19) shows isointensity of the lesion. **C** Histopathology shows endometriosis infiltrating the muscular and submucosal layer of the bowel wall (*curved black arrows*). At the site of endometriosis, thickening of indigenous smooth muscle is seen (*black arrow*) compared to the thickness of the indigenous smooth muscle in another area (*thick black arrow*).

scores that were higher than scores at pathologic examination in a couple of patients. In our study, only one out of 28 lesions was scored to infiltrate deeper into the

bowel wall on MR imaging compared to histopathology. Due to the retrospective nature of our study, there is a possibility of sampling errors at histopathology. Samples

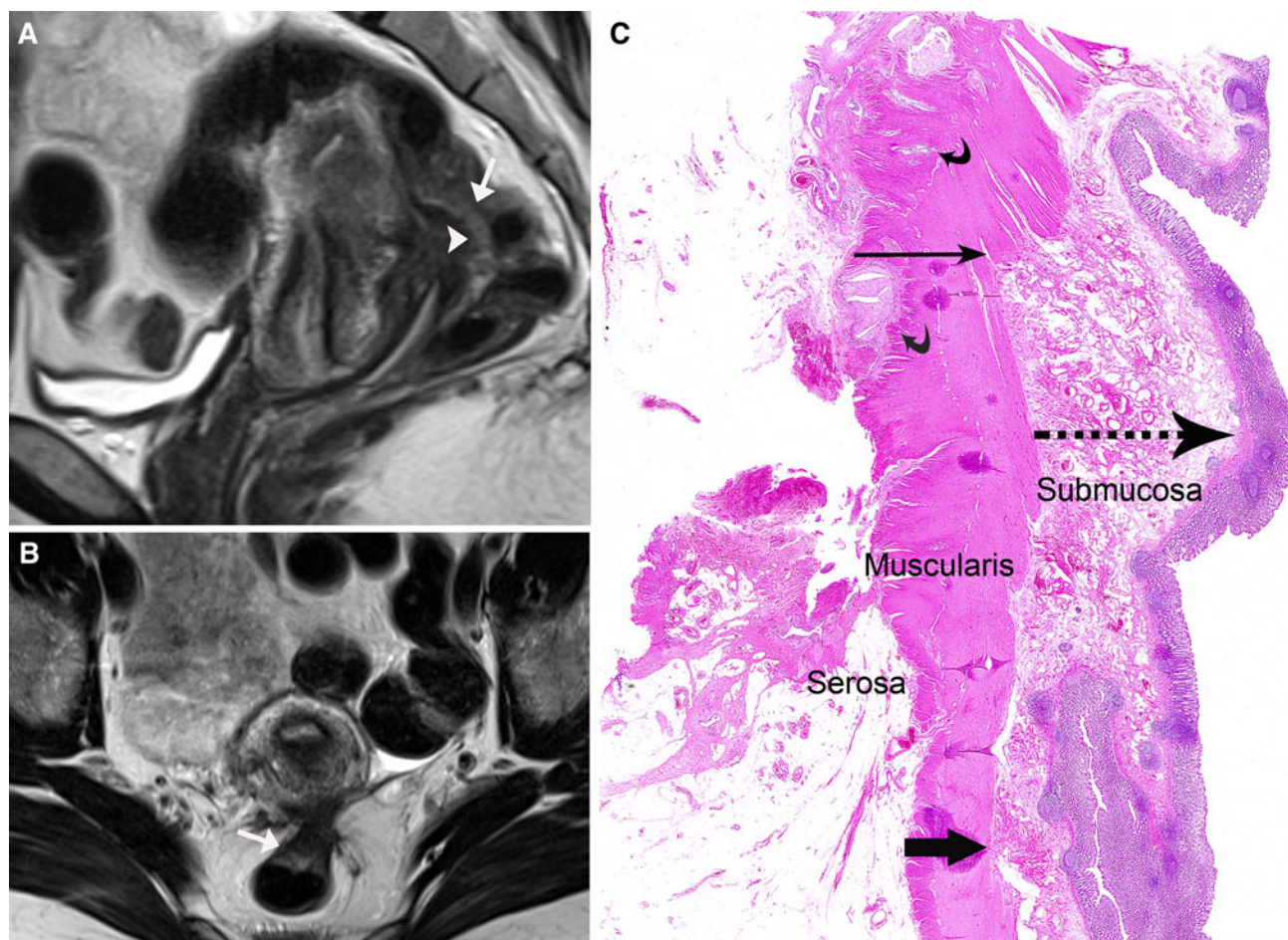


Fig. 3. A 36-year-old woman presented with progressive dyschezia and pencil-like stools. At colonoscopy, 10 cm from the anal canal swollen, edematous mucosa was seen with small submucosal bleedings. **A** and **B** Sagittal and axial T2-weighted images (6000–10000/137) show “fan shaped” configuration (*white arrow*) located at the torus uterinus with isointense signal compared to muscle and slightly high signal intensity at the luminal side of the

bowel wall (*arrowhead*). **C** Histopathology shows endometriosis infiltrating the muscular layer of the bowel wall (*curved black arrows*). The image shows thickening of the muscular layer of the bowel wall at the site of endometriosis (*black arrow*), compared to a site without infiltration of endometriosis (*thick black arrow*). Furthermore “non-specific” inflammation with thickening of the submucosa (*dotted arrow*) is shown.

are taken from locations that are most affected macroscopically, but we cannot exclude that occasionally the most affected part of the bowel wall has not been sampled adequately. TVS also showed high accuracy in predicting infiltration of the muscular layer of the rectum previously [17, 19]. However, accuracy for predicting infiltration of the mucosal layer was also low [17]. Predicting depth of bowel wall infiltration by TVS may be valuable, although TVS is of limited value in locating endometriosis infiltrating the sigmoid, because the location above the level of the uterine fundus is too far from the probe to visualize accurately [22].

A limitation of this study may be that the mean time between MR imaging and surgery was 168 days. However, as DIE is usually a slowly progressive disease, we expect this bias to be of minimal influence to our results.

Furthermore, patients whom segmental bowel resection is performed are in general patients with more extensive disease compared to patients that do not undergo surgery. Therefore a bias exists, as most lesions infiltrated the muscular layer of the bowel wall in our patient group. The standard MR imaging protocol for analysis of DIE did not include intravenous contrast, as this has been demonstrated to be of no additional value [5].

In conclusion, MR imaging is valuable to predict muscular infiltration of the bowel. The “fan shaped” configurations on MR imaging may help diagnose and determine the extent of DIE infiltrating the muscular layer of the bowel. Infiltration of the (sub)mucosa may be difficult to assess on MR imaging, as (sub)mucosal thickening may be caused by edema without infiltration of endometriosis.

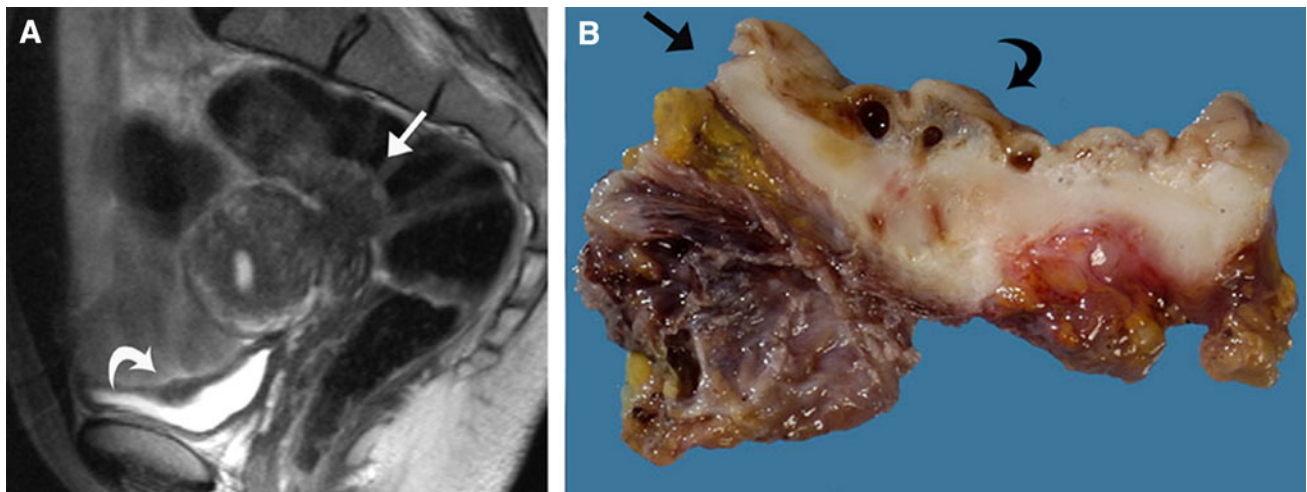


Fig. 4. A 35-year-old woman, known with endometriosis previously presented with dyschezia, hematochezia, and pencil-like stools. Segmental bowel resection was performed and histopathology showed the lesion infiltrated the muscular and submucosal layer of the bowel wall. Non-specific inflammation was found with thickening of the submucosa. **A** Sagittal T2-weighted image (6000–10000/137) shows lesion infiltrating

the rectosigmoid with isointense signal compared to muscle and slightly high signal intensity at the luminal side of the bowel wall (*white arrow*). Furthermore endometriosis is also found infiltrating the bladder wall (*white curved arrow*). **B** Macroscopic appearance shows bowel wall (*black arrow* corresponding to the rectum) with endometriosis infiltrating the muscular and submucosal layers (*black curved arrow*).

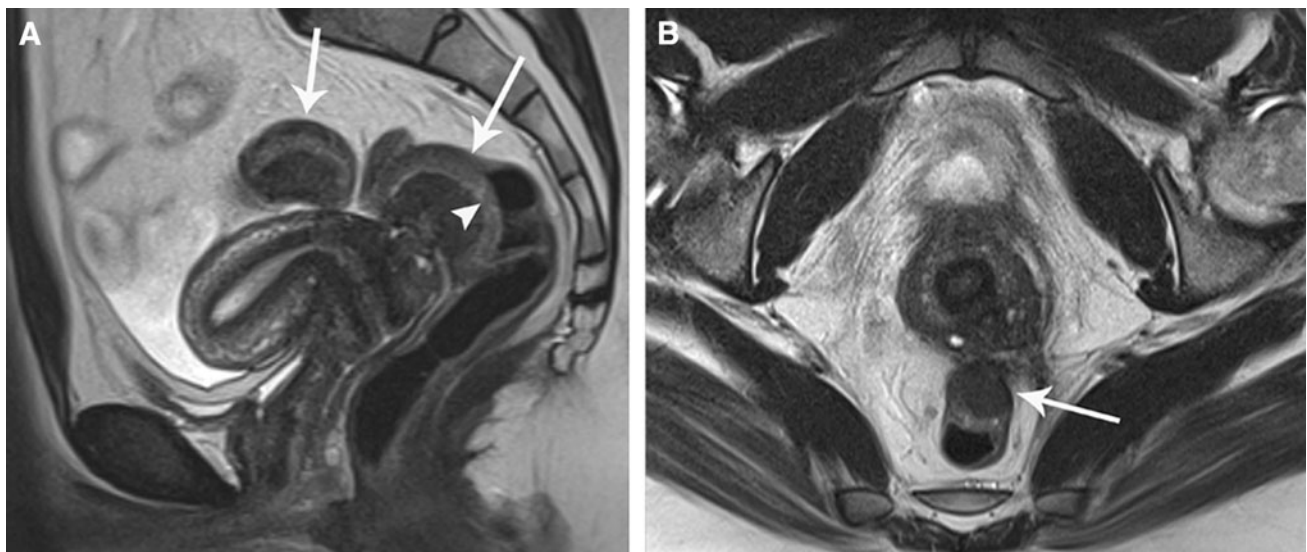


Fig. 5. A 28-year-old woman diagnosed with two DIE lesions infiltrating the rectosigmoid and sigmoid. **A** and **B** Sagittal and axial T2-weighted images (6000–10000/137) show two lesions depicting “fan shaped” configurations

(*arrows*), demonstrating isointense signal compared to muscle. In addition, hyperintense signal compared to muscle is found at the luminal side of the bowel wall (*arrowhead*).

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