Magnetic resonance enema versus rectal water contrast transvaginal ultrasonography in the diagnosis of rectosigmoid endometriosis

Umberto Leone Roberti Maggiore [1,2], Ennio Biscaldi [3], Gaetano Valerio Vellone [4], Pier Luigi Venturini [1,2], Simone Ferrero [1,2]

[1] Academic Unit of Obstetrics and Gynaecology, IRCCS AOU San Martino – IST, Largo R. Benzi 10, 16132 Genoa, Italy

[2] Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DiNOGMI), University of Genoa, Italy

[3] Department of Radiology, Galliera Hospital, via Mura delle Capuccine 14, 16128 Genoa, Italy

[4] Department of Surgical and Diagnostic Sciences, IRCCS San Martino Hospital and National Institute for Cancer Research, University of Genoa, Largo Rosanna Benzi, 1, 16132 Genoa, Italy

Corresponding author:

Simone Ferrero MD, PhD

Unit of Obstetrics and Gynaecology, IRCCS AOU San Martino – IST, Largo R. Benzi 10, 16132 Genoa, Italy

Telephone 01139 010 511525

Mobile 01139 3477211682

Fax 01139 010511525

E-mail: simone.ferrero@unige.it

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/uog.15934

Abstract

Objectives: To compare the accuracy of magnetic resonance enema (MR-e) and rectal water transvaginal ultrasonography (RWC-TVS) in the diagnosis of rectosigmoid endometriosis.

Methods: This prospective study included 286 patients of reproductive age with clinical suspicion of rectosigmoid endometriosis. Patients underwent MR-e and RWC-TVS before laparoscopic excision of endometriosis. The findings of MR-e and RWC-TVS were compared with surgical and histological results.

Results: Out of 286 patients included in the study, 151 (52.8%) had rectosigmoid endometriosis. MR-e and RWC-TVS had similar accuracy in the diagnosis of rectosigmoid endometriosis ($p = 0.063$). The sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratio positive and likelihood ratio negative of MR-e and RWC-TVS (%, 95% C.I.) in the diagnosis of recto-sigmoid endometriosis were 95.36% (90.68%-99.11%), 97.78% (93.63%-99.51%), 97.96% (94.14%-99.55%), 94.96% (89.89%-97.94%), 42.91 (14.01-131.46), 0.05 (0.02-0.10) and 92.72% (87.34%-96.30%), 97.04% (92.58%-99.17%), 97.22% (93.03%-99.22%), 92.25% (86.56%-96.06%), 31.29 (11.90-82.25), 0.08 (0.04-0.13), respectively. Both MR-e and RWC-TVS underestimated the size of the endometriotic nodules; in both imaging techniques the underestimation was greater for nodules with diameter ≥30 mm. There was no significant difference in the mean intensity of pain experienced by the patients during the two exams.

Conclusions: RWC-TVS should be the first line investigation in patients with clinical suspicion of rectosigmoid endometriosis and physicians should be trained in performing this exam. Considering that MR-e is more expensive that RWC-TVS, it should be used only when the findings of RWC-TVS are unclear.

Keywords: Bowel endometriosis; Diagnosis; Endometriosis; Magnetic resonance; Transvaginal ultrasonography

Introduction

Rectosigmoid endometriosis is a chronic and progressive benign disease characterized by the infiltration of the intestinal wall (at least the muscularis propria), which may cause severe pain, gastrointestinal symptoms, infertility and, in some patients, it may cause bowel occlusion [1]. Early diagnosis and adequate therapy are mandatory in the management of patients affected by this condition. Medical therapies (such as progestins, combined estroprogestin contraceptives and gonadotropin releasing hormone analogues) may be administered to treat symptoms caused by rectosigmoid endometriotic nodules that do not cause subocclusive symptoms [2-4]. Surgery, intestinal shaving [5, 6] or segmental resection [7], should be considered according to the characteristics of the nodules (size and depth of infiltration in the intestinal wall, degree of stenosis of the bowel lumen) and the preference of the patients (desire to conceive or to avoid hormonal therapies). The assessment of the presence and characteristics of rectosigmoid endometriotic nodules is relevant to provide the patient an appropriate and exhaustive informed consent, to plan the type of surgery and to schedule the assistance of a colorectal surgeon.

Until recently, the ultrasonographic diagnosis of endometriosis was limited to patients with ovarian endometriomas and other imaging techniques were used for the assessment of rectosigmoid endometriosis including rectal endoscopic ultrasonography [8], double-contrast barium enema [9], magnetic resonance imaging (MRI) [10], multidetector computerized tomography enema [11] and virtual colonoscopy [12]. However, two recent meta-analyses showed that rectosigmoid endometriosis can be accurately diagnosed by transvaginal ultrasonography (TVS) [13, 14]. Rectosigmoid distension may facilitate the identification of intestinal lesions during both MRI [15-17] and TVS [18, 19]. However, no previous study compared the accuracy of magnetic resonance enema (MR-e) and rectal water contrast transvaginal ultrasonography (RWC-TVS) in the diagnosis of rectosigmoid endometriosis.

The objective of this prospective study was to compare the accuracy of MR-e and of RWC-TVS in diagnosing rectosigmoid endometriotic nodules.

Materials and methods

This prospective study included all consecutive patients that were referred to our institution because of clinical suspicion of rectosigmoid endometriosis between November 2008 and December 2013. During this period, the imaging workup required that both MR-e and RWC-TVS were performed in patients with suspicion of rectosigmoid endometriosis. The local Ethics Committee approved the study protocol. Patients participating in the study signed a written consent form.

The inclusion criteria for the study were: reproductive age and suspicion of deep pelvic endometriosis on the basis of gynaecological symptoms and vaginal examination and/or presence of gastrointestinal symptoms that might be caused by rectosigmoid endometriosis. The following exclusion criteria were used: previous bilateral ovariectomy, previous exams diagnosing bowel endometriosis (such as double contrast barium enema, rectal endoscopic ultrasonography or multidetector computed tomography enema), previous bowel surgery (except appendectomy), renal or hepatic failure, presence of contraindications to MR examination.

Symptoms were systematically investigated during the study period and they were recorded in a database. The presence of dysmenorrhea, deep dyspareunia, chronic pelvic pain, and dyschezia was assessed; the intensity of these symptoms was rated on a 100 mm visual analogue scale (VAS), the left extreme of the scale representing the absence of pain and the right extreme of the scale indicating the maximal intensity of pain. The presence of the following gastrointestinal symptoms was assessed: diarrhoea (more than three bowel movements per day), constipation during the menstrual cycle, abdominal bloating, intestinal cramping, and feeling of incomplete evacuation after bowel movements. A symptom analogue scale questionnaire was used to estimate the severity of each gastrointestinal symptom (1 indicated the absence of the symptom; 10 indicated the highest severity of the symptom).

Two physicians independently performed MR-e and RWC-TVS. The radiologist (E.B.) and the ultrasonographer (S.F.) knew the clinical data and that the presence of rectosigmoid endometriosis was suspected; however, they were blinded to the findings of the other imaging technique. All patients included in the study underwent laparoscopy within three months from the completion of diagnostic investigations.

Intestinal endometriosis was defined as the disease infiltrating at least the muscularis propria. Endometriotic foci located on the bowel serosa were considered peritoneal and not bowel endometriosis. The decision to perform segmental bowel resection was based on the intraoperative findings.

The findings of MR-e and RWC-TVS were compared with surgical and histological results, which were considered the gold standard. The primary objective of the study was to assess the accuracy of the two imaging techniques in diagnosing the presence of rectosigmoid endometriosis. The secondary objective of the study was to assess the accuracy of the two imaging techniques in diagnosing the presence of infiltration of the mucosal layer of the bowel wall. The tertiary objective of the study was to compare the precision of the two techniques in estimating the size of the rectosigmoid endometriotic nodules.

Magnetic resonance enema technique - A radiologist (E.B.) performed all the exams according to a standardized procedure [17]. MR-e was performed on a 1.5 T magnet (Signa Excite HDx, GE Medical Systems, Waukesha, WI, USA) using an 8 channels phased array coil. The position of the patient was preferably prone and the MR entry position in the gantry was feet first. The pelvic volume was evaluated. The studies followed a standardized protocol consisting of: T2W FrFSE axial images (FOV = 30–36 cm; TE = 150 ms; TR = 5500 ms; matrix, 320 × 224; slice thickness = 3 mm; spacing = 1; acceleration factor = 1; 4 NEX); T2W FrFSE fat sat coronal images (FOV = 31–33 cm; TE = 150 ms; TR = 4250 ms; matrix, 384 × 254; slice thickness = 4 mm; spacing = 1; acceleration factor = 1; 4 NEX), T1W FSE coronal images (FOV = 31–33 cm; TE = min full; TR = 550 ms; matrix, 320 × 224; slice thickness = 4 mm; spacing = 1; acceleration factor = 1; 2 NEX), FIESTA

sequence in coronal plane (FOV = 37 cm; slice thickness = 3 mm; spacing = 1; matrix, 256 × 256; 2 NEX), T2W FrSE sagittal images (FOV = 31–33 cm; TE = 150 ms; TR = 4250 ms; matrix, 384 × 256; slice thickness = 3 mm; spacing = 1; acceleration factor = 1; 6 NEX), T2W FrFSE fat sat sagittal images (FOV = 31–33 cm; TE = 120 ms; TR = 4600 ms; matrix, 384 × 256; slice thickness = 4 mm; spacing = 1; acceleration factor = 1.5; 4 NEX), diffusion weighted EPI (b = 800) axial images (FOV = 30–36 cm; TR = 3000 ms; matrix, 128 × 128; slice thickness = 4 mm; spacing = 1; 8 NEX). T1 W images were acquired, employing fat-suppression even after contrast enhancement (gadobutrol at a dosage of 0.2 mmol/kg body-weight; Gadovist 1.0, Schering, Berlin, Germany) (Figure 3). After the patient lied on the MR bed, the retrograde distension was performed initially on the left lateral decubitus, then on the prone position to reduce abdominal wall movements and respiratory artefacts. 300-400 ml of ultrasonographic gel (Aquasonic, Parker Laboratories, Fairfield, NJ, USA) diluted with saline solution (1:8) were introduced to distend the rectum and the sigmoid colon by using a syringe connected to a 20-Fr Foley catheter. Intestinal hypotonization was not used.

Endometriotic nodules appear as solid masses outside the rectosigmoid wall, frequently with hypointense signal due to their fibrous nature [10, 20]. Visible penetration of the nodules in the intestinal wall was the main parameter to diagnose the infiltration of the muscularis propria [17] (Figure 6).

Rectal water contrast transvaginal ultrasonography technique - Few hours before the ultrasonography, a rectal enema (133 ml of monobasic sodium phosphate anhydrous; Clisma Lax; Sofar, Milan, Italy) was used to clean the rectosigmoid colon from fecal residues. The examinations were assessed in real time and archived with images saved as Tif files. A physician (S.F.) performed the exams according to a standardized protocol by using a Voluson E6 ultrasound machine (GE Healthcare Ultrasound, Milwaukee, WI, USA). After the transducer was introduced into the vagina, an assistant inserted a 6-mm (18 Ch) flexible catheter through the anal os into the rectal lumen up to a 15-cm distance from the anus. A gel infused with lidocaine (Luan, Molteni &

C., Scandicci, Italy) was used to minimize the discomfort due to the passage of the catheter. After the connection of a 50-mL syringe to the catheter, warm sterile saline solution was injected inside the rectosigmoid under ultrasonographic control. 100 ml of saline solution were infused continuously at the beginning of the procedure; subsequently, additional saline solution (up to 300 ml) was injected if requested by the ultrasonographer depending on the distensibility of the intestinal wall. During the examination, a Klemmer forceps was placed on the catheter to prevent backflow of the saline solution through the catheter when the solution was not being injected. There was no significant leakage of saline solution into the space between the catheter and the anus. Images were obtained before, during and after saline injection.

At ultrasonography, the intestinal serosa is hyperechoic; the two layers of the muscularis propria appear as hypoechoic strips separated by a fine hyperechoic line; the submucosa is hyperechoic; the muscularis mucosa is hypoechoic and the interface between the lumen and the mucosal layer is hyperechoic [21]. Rectosigmoid endometriotic nodules appear as nodular, solid, hypoechoic lesions, adjacent to and/or penetrating the muscularis propria; these nodules usually cause a thickening of the intestinal wall (Figure 5). Hyperechoic foci may sometimes be present within the nodule. Retraction and adhesions are often present; this results in the so-called "Indian Headdress" or "comet" sign [22, 23]. Distension of the intestinal wall with saline solution facilitated the identification of the limits of the intestinal nodules.

Tolerability of the exams - Patients were asked to rate the pain experienced during MR-e and RWC-TVS by using a 100 mm visual analogue scale (VAS); the left extreme represented the absence of pain, and the right extreme represented the worst possible pain. Mild pain was defined as VAS score <2, moderate pain as VAS score ≥2 and ≤5, and severe pain as VAS score >5.

Surgical technique - Before laparoscopy, the surgeons examined the reports and the images of both MR-e and RWC-TVS. A team of gynaecological and colorectal surgeons with extensive experience in the surgical treatment of pelvic and rectosigmoid endometriosis performed all the procedures laparoscopically. After adequate adhesiolysis, the sigmoid colon and the rectum were systematically

examined to identify the presence of endometriotic lesions. All visible endometriotic nodules (except those on the diaphragm) were excised. Segmental bowel resection was performed when rectosigmoid endometriotic lesions infiltrated at least the muscularis propria. The landmark used to define the transition from the sigmoid colon to the rectum was the loss of the taenia coli, the appendices epiploicae and the surgical mesocolon that anatomically is located at about the level of the third sacral vertebra. In particular, we defined the level where gradual convergence of the teniae coli started as rectosigmoid junction, while the point where teniae coli could not be seen anymore was considered as the beginning of upper rectum. The surgical specimens were histologically evaluated; the depth of infiltration of the endometriotic nodules in the bowel wall was assessed [24]. In addition, the presence of multifocal disease (presence of one or more lesions that affected the sigmoid colon and that were associated with the colorectal primary lesion) was assessed.

Statistical analysis - Accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) were calculated for both MR-e and RWC-TVS. In case of multifocal disease, the main nodule affecting the bowel was considered for the analysis. The McNemar's test with the Yates continuity correction was used to compare the accuracy of MR-e and RWC-TVS in the diagnosis of rectosigmoid endometriosis.. The precision of the measurement of nodule size by imaging techniques was estimated by subtracting the size of the nodule as measured by the techniques from the size of the nodule as measured at histology. The nonparametric Mann-Whitney test was used to compare the intensity of pain experienced by the patients during MR-e and RWC-TVS. The χ^2 test was used to compare the type of pain (mild, moderate and severe) experienced by the patients undergoing the two exams. Data were analysed using the SPSS software version 20.0 (SPSS Science, Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

A total of 286 women who performed both diagnostic exams and underwent surgery were included in the study. The main characteristics of the study population are summarized in Table 1.The path of the patients through the study is shown in Figure 1. The intensity of pain and gastrointestinal symptoms is presented in Table 2.

Surgery and histology demonstrated that 151 women (52.8%; 95% C.I., 47.0–58.6%) had rectosigmoid endometriotic nodules. The endometriotic nodules were located on the sigmoid colon in 90 patients (59.6%), on the rectosigmoid junction in 22 patients (14.6%) and on the rectum in 39 patients (25.8%). Multifocal disease was found in 21 patients (13.9%) who had two endometriotic nodules affecting the bowel. The mean (±SD) length of the resected bowel segment was 12.5 cm (± 2.8 cm). The diagnosis of endometriosis was confirmed in all the excised nodules by histological exam. The deeper nodule infiltrated the intestinal muscularis propria in 107 patients (70.9%), the submucosa in 31 women (20.5%) and the mucosa in 13 patients (8.6%).

Accuracy of MR-e and RWC-TVS

The accuracy, sensitivity, specificity, PPV, NPV, LR+ and LR− of MR-e and RWC-TVS in the diagnosis of rectosigmoid endometriosis are described in Table 3. The two techniques had similar accuracy in the diagnosis of rectosigmoid endometriosis (p=0.063) (Figure 2, Figure 4).

The accuracy, sensitivity, specificity, PPV, NPV, LR+ and LR− of MR-e and RWC-TVS in the diagnosis of the presence of mucosal infiltration are described in Table 4. The accuracy of RWC-TVS was superior to that of MR-e in the detection of infiltration of the mucosal layer ($p<0.001$).

Both MR-e and RWC-TVS underestimated the size of the endometriotic nodules; in both imaging techniques the underestimation was greater for nodules with diameter ≥30 mm (Table 5).

The mean (±SD) overall scanner room occupation time was 45.7 ± 3.9 min for MR-e; the mean (±SD) time required to perform RWC-TVS was 18.2 ± 2.9 min ($p < 0.001$).

Tolerability and adverse effects of MR-e and RWC-TVS

MR-e was safely performed in all the patients; there was no adverse reaction to paramagnetic contrast medium. During the injection of the ultrasonography jelly in the rectosigmoid, none of the patients showed signs of severe discomfort or allergic reactions. RWC-TVS was always well tolerated and no patient requested to interrupt the exam.

The mean (±SD) intensity of pain experienced was similar in patients undergoing MR-e (3.6 ± 1.5) than in those undergoing RWC-TVS (3.4 ± 1.2; p = 0.098). Severe pain was experienced by 44 women (15.4%) undergoing MR-e and 27 women (9.4%) undergoing RWC-TVS, moderate pain was experienced by 115 women (40.2%) undergoing MR-e and by 108 women (44.4%) undergoing RWC-TVS, mild pain was experienced by 127 women (44.4%) undergoing MR-e and by 151 women (52.8%) undergoing RWC-TVS (p = 0.042).

Discussion

This is the first study demonstrating that MR-e and RWC-TVS have similar accuracy in the diagnosis of rectosigmoid endometriosis. In both techniques, rectosigmoid distension was used to facilitate the identification of rectosigmoid endometriotic nodules. Over the last ten years, several ultrasound techniques other than 2D grayscale ultrasound have been used to study women with suspected rectosigmoid endometriosis including tenderness-guided ultrasound [25], sonovaginography with saline or gel [26-28] and three dimensional ultrasonography [29]. The choice of the ultrasonographic technique is often based on the experience of the sonographer rather than on evidence of superiority of one technique compared to the others. In this study, RWC-TVS was chosen for the comparison with MR-e because of the personal experience of the authors and of the common criterion of bowel distension with fluid. Previous studies applied intestinal jelly distension to MR for the diagnosis of deep endometriosis [16, 30-33]. Ten years ago, a prospective study showed that the injection of ultrasonography jelly in the vagina (20 to 30 ml) and the rectum (150 ml) during MR facilitates the identification of complete cul-de-sac obliteration in 31 patients with suspected rectovaginal endometriosis [30]. The usefulness of this technique was subsequently confirmed by the same authors in larger series [31, 33]. Furthermore, other authors confirmed that intestinal distension and opacification using ultrasound gel helps to visualize rectosigmoid endometriotic nodules [16, 32] and applied this technique also to the 3.0-T MR study of patients with suspected endometriosis [34]. A recent study compared the accuracy of MR-e to multidetector computerized tomography enema (MDCT-e) in estimating the presence of rectosigmoid endometriotic nodules. This study showed that both techniques were accurate in the diagnosis of rectosigmoid endometriosis; in particular, MR-e had an accuracy, sensitivity, specificity, positive predictive value and negative predictive value of 96.9%, 97.2%, 96.4%, 98.3%, 94.1%, respectively, in line with the results of current study [17].

Our group was the first to apply the criteria of retrograde bowel distension to TVS [18, 19, 35] and this technique was subsequently studied by other authors [36]. More recently, 3D ultrasonography

combined with intestinal distension demonstrated promising results in the diagnosis of rectosigmoid endometriosis [37]. The effectiveness of RWC-TVS in the diagnosis of rectosigmoid endometriosis observed in this study is similar to that previously reported by us [18] and by other authors [36].

A potential limitation of this study may be the experience of the radiologist in performing MR-e and of the ultrasonographer in RWC-TVS that may influence the accuracy of these techniques in diagnosing rectosigmoid endometriosis. However, the referral to a tertiary centre with large expertise in endometriosis is mandatory when bowel involvement is suspected to guarantee to the patient the best diagnostic and therapeutic pathway. A further limitation of this study is that the surgeons were aware of the findings of MR-e and RWC-TVS. Although in an ideal prospective study the surgeons should be blinded to the findings of the preoperative investigations, this theoretical study design appears unethical in clinical practice because diagnostic imaging may facilitate the identification of intestinal endometriotic nodules during surgery. Furthermore, the knowledge of the findings of the preoperative investigations may only help the surgeons in identifying endometriotic nodules that were actually present. A strength of the current study is the large sample size. Out of 286 women with the suspicion of rectosigmoid endometriosis, over 50% of the patients actually had bowel nodules.

This study demonstrates that both MR-e and RWC-TVS are accurate in the diagnosis of rectosigmoid endometriosis. RWC-TVS has some advantages in comparison with MR-e: it is faster and it does not require the use of contrast medium that may potentially cause allergic reactions. Furthermore, TVS is superior to MR in terms of cost-effectiveness [38], it allows to assess the degree of infiltration of the muscularis propria [18, 19, 35, 36] and to estimate the degree of stenosis of the intestinal lumen [36] and, thus, it should be considered the first-line technique to diagnose rectosigmoid endometriosis. The use of MR to study all symptomatic women before any form of treatment (medical or surgical) would increase the cost of preoperative assessment without a true increase of diagnostic performance. However, TVS must be performed by highly skilled ultrasonographers. In fact, it has been recently estimated that the learning curve for an accurate

diagnosis of deep pelvic endometriosis by TVS requires performing about 40 cases [39]; therefore, it may be difficult for sonographers working in small centres to achieve such experience. The main advantage of MR-e could be that, with a retrograde distension of the entire colon, this technique may provide a complete overview of the whole colon [40]. In the current study, the distension was targeted to the rectosigmoid because the aim of the study was the comparison with RWC-TVS and endometriotic lesions of the right colon are beyond the field of view of a transvaginal approach. Furthermore, the whole colon MR-e study requires longer time, a complete colonic distension may be difficult to be tolerated for the time required to complete all MR-e sequences, and, last but not least, an appropriate intestinal cleansing is required. In the current study we did not compare the accuracy of RWC-TVS with TVS alone, which was the objective of a previous study [18].

In conclusion, this study shows that RWC-TVS and MR-e have similar accuracy in the diagnosis of rectosigmoid endometriosis. The mean intensity of pain perceived during RWC-TVS and MR-e is similar but severe pain is perceived by the patients more frequently during MR-e. However, the methodology of the two exams was different (in terms of type of catheters used and volume of fluid instilled) and this may have influenced the discomfort perceived by the patients. Given also the better cost-effectiveness, in our opinion, TVS should be the first line investigation for patients with clinical suspicion of rectosigmoid endometriosis. Educational programs should be developed to offer sonographers who are familiar with the general use of TVS the opportunity to improve their skillness in the diagnosis of rectosigmoid endometriosis.

Tables

Table 1. Characteristics of the study population

	n = 286
Age (mean ± SD; years)	31.9 ± 4.8
BMI (mean ± SD; kg/m^2)	23.6 ± 2.2
Smokers (n, %)	91 (31.8)
Educational level (n, %):	
Primary	7 (2.4)
Secondary	204 (71.3)
University	75 (26.2)
Previous live births (n, %)	68 (23.7)
Previous surgery for endometriosis (n, %)	126 (44.1)
Hormonal therapy (n, %):	
None	165 (57.7)
Sequential oral contraceptive	57 (19.9)
Continuous oral contraceptive	18 (6.3)
Contraceptive vaginal ring	18 (6.3)
Norethisterone acetate	28 (9.8)

Table 2. Intensity of pain and gastrointestinal symptoms in the study population (n = 286)

Symptoms	Patients with symptom (n, %)	Severity (mean ± SD)
Dysmenorrhea*	244 (85.3)	63.4 ± 17.0
Non-menstrual pelvic pain*	235 (82.2)	55.0 ± 13.4
Dyspareunia*	230 (80.4)	58.9 ± 15.8
Dyschezia*	166 (58.0)	52.5 ± 17.0
Persistent constipation§	106 (37.1)	5.4 ± 2.2
Constipation during the menstruation§	57 (19.9)	6.0 ± 1.6
Diarrhoea§	80 (28.0)	7.6 ± 1.3
Diarrhoea during the menstruation§	94 (32.9)	8.0 ± 0.9
Intestinal cramping§	180 (62.9)	6.4 ± 1.6
Abdominal bloating§	169 (59.1)	6.7 ± 1.7
Feeling of incomplete evacuation§	105 (36.7)	6.3 ± 1.4
Passage of mucus§	103 (36.0)	5.8 ± 1.8
Cyclical rectal bleeding§	46 (16.1)	5.0 ± 1.0

* Measured using 100-mm visual analogue scale (VAS)

§ Measured using a 10-point symptom analogue scale questionnaire

Table 3. Diagnostic performance of magnetic resonance imaging enteroclysis (MR-e) and rectal water contrast transvaginal ultrasonography (RWC-TVS) in the diagnosis of rectosigmoid endometriosis (n=286)

	Accuracy	Sensitivity	Specificity	PPV	NPV	LR+	LR-
MR-e (%, 95% C.I.)	96.50 (94.37-98.63)	95.36 (90.68-99.11)	97.78 (93.63-99.51)	97.96 (94.14-99.55)	94.96 (89.89-97.94)	42.91 (14.01-131.46)	0.05 (0.02-0.10)
RWC-TVS (%, 95% C.I.)	94.76 (92.18-97.43)	92.72 (87.34-96.30)	97.04 (92.58-99.17)	97.22 (93.03-99.22)	92.25 (86.56-96.06)	31.29 (11.90-82.25)	0.08 (0.04-0.13)

MR-e, magnetic resonance imaging enteroclysis. RWC-TVS, transvaginal ultrasonography combined with water-contrast in the rectum. PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio.

Table 4. Diagnostic performance of magnetic resonance imaging enteroclysis (MR-e) and rectal water contrast transvaginal ultrasonography (RWC-TVS) in the diagnosis of infiltration of the mucosal layer of the bowel wall (n=286)

	Accuracy	Sensitivity	Specificity	PPV	NPV	LR+	LR-
MR-e	84.27% (80.05%-88.49%)	66.67% (34.89%-90.08%)	85.04% (80.25%-89.04%)	16.33% (7.32%-29.66%)	98.31% (95.74%-99.54%)	4.46 (2.73-7.27)	0.39 (0.18-0.87)
RWC-TVS (%, 95% C.I.)	86.36% (82.38%-90.34%)	76.92% (46.19%-94.96%)	86.08% (81.40%-89.96%)	20.83% (10.47%-34.99%)	98.74% (96.36%-99.74%)	5.53 (3.63-8.40)	0.27 (0.10-0.72)

MR-e, magnetic resonance imaging enteroclysis. RWC-TVS, transvaginal ultrasonography combined with water-contrast in the rectum. PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio.

Table 5. Difference between size of the largest nodule estimated by imaging techniques and that measured on histopathology

	Histology Largest diameter (mm, mean ± SD)	MR-e Mean difference (mm, 95% CI)[a]	MR-e Limits of agreement (mm)[b]	RWC-TVS Mean difference (mm, 95% CI)[a]	RWC-TVS Limits of agreement (mm)[b]
All nodules (n=286)	27.6 ± 6.6	1.531 (1.146-1.916)	-5.110 to 8.173	1.647 (1.266-2.028)	-4.921 to 3.284
Nodules with diameter <30 mm (n=198)	23.9 ± 3.6	0.874 (0.575-1.173)	-3.420 to 5.167	1.106 (0.769-1.443)	-3.728 to 5.940
Nodules with diameter ≥30 mm (n=88)	36.1 ± 3.2	3.011 (2.020-4.002)	-6.474 to 12.497	2.864 (1.931-3.797)	-6.066 to 11.793

MR-e, magnetic resonance imaging enteroclysis. RWC-TVS, transvaginal ultrasonography combined with water-contrast in the rectum.

[a] Mean difference calculated by subtracting size of nodule measured by imaging technique from size of nodule measured on histology.

[b] Limits of agreement calculated as mean difference ± 2 SDs of the difference.

Legend to figures

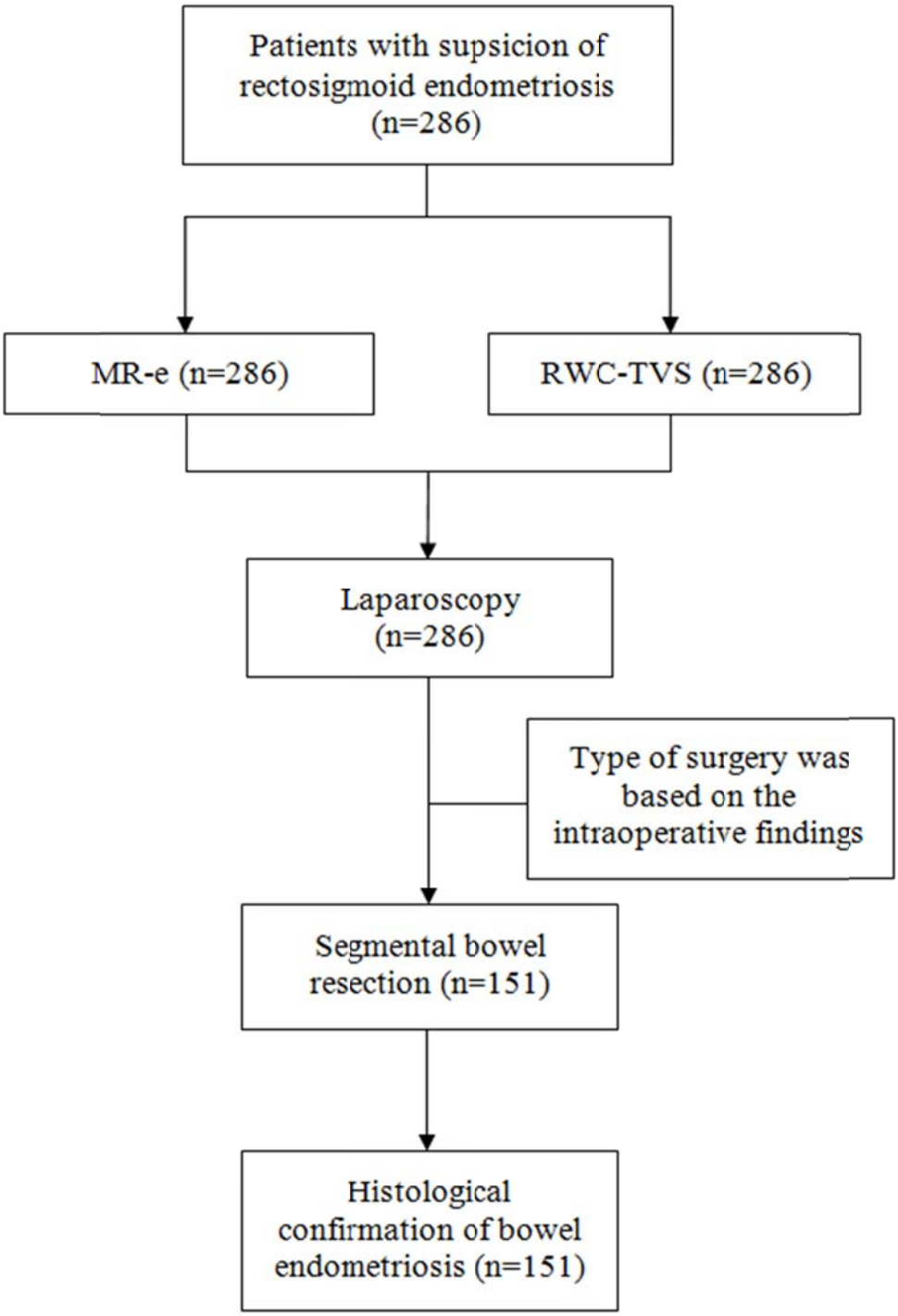
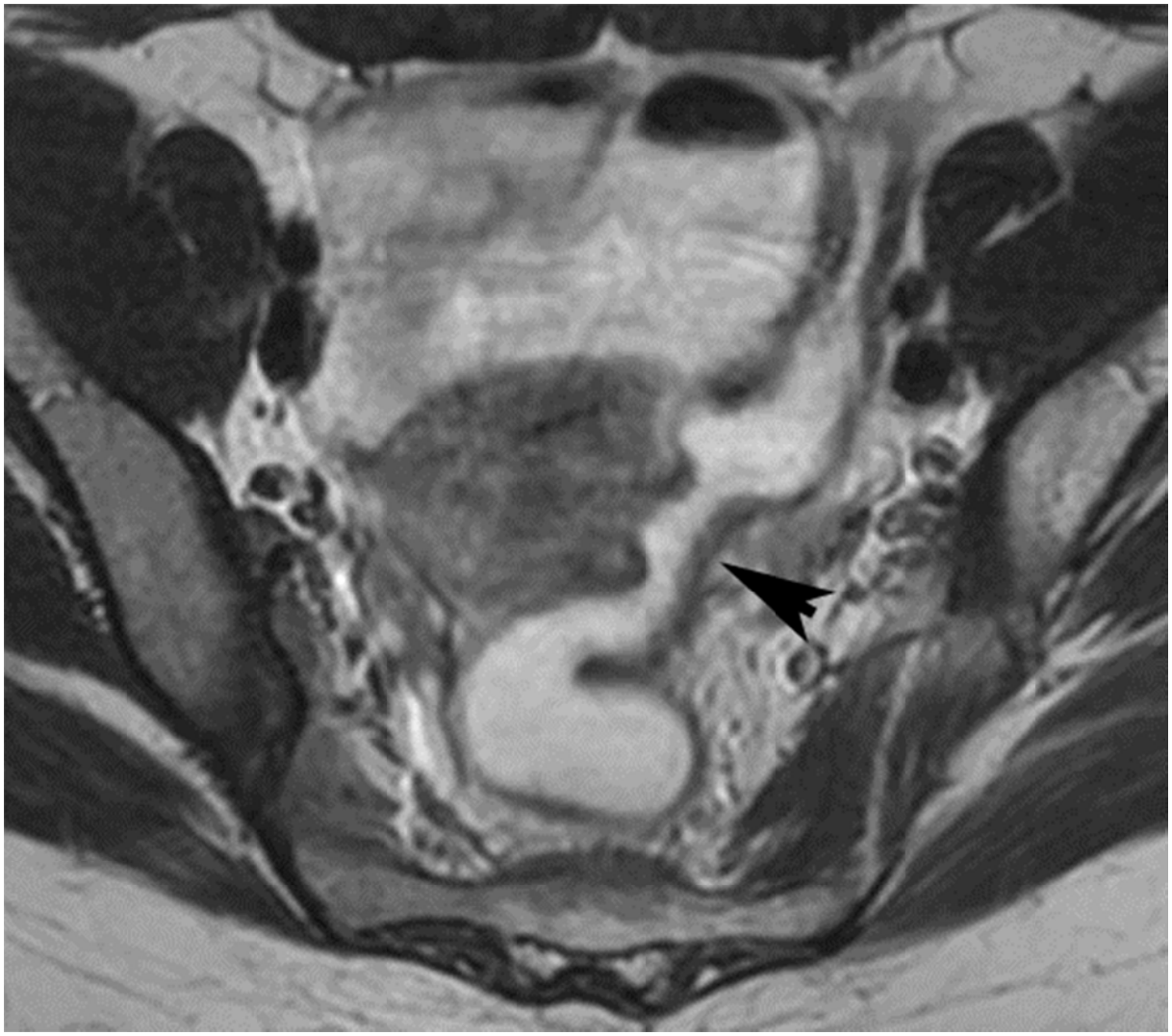


Figure 1. The flowchart shows the path of the patient through the study



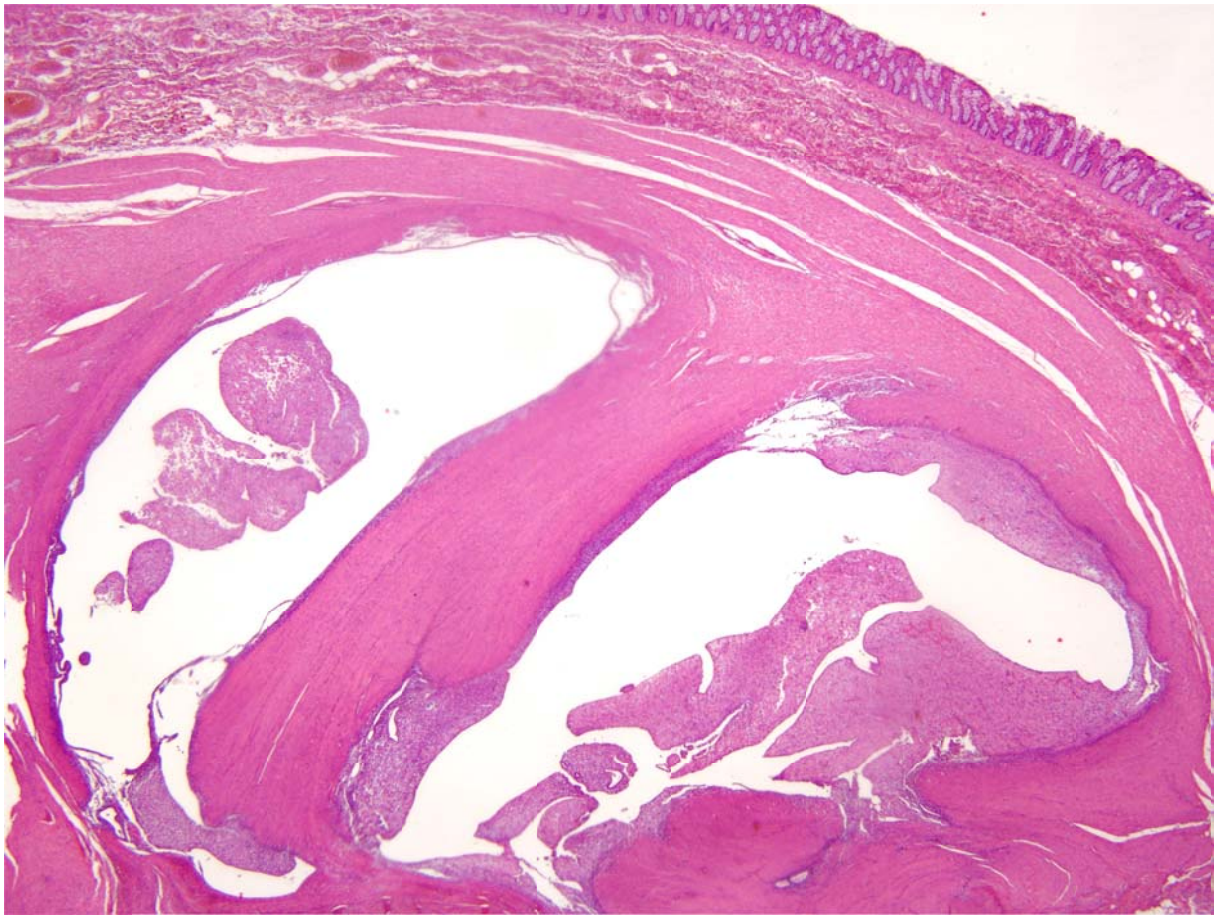


Figure 2. Rectal endometriotic nodule

a. RWC-TVS image demonstrating the hypoechoic nodule penetrating the thickened rectal wall (asterisk), some hyperechoic foci can be observed. The water contrast (WC) shows that the muscularis mucosa (hypoechoic) and the interface between the lumen and the mucosal layer (hyperechoic) are not infiltrated.

b. MR-e sagittal plane, FSE T2W sequence. After retrograde distension of the rectosigmoid, an endometriotic nodule deeply infiltrating the anterior wall of the lower rectum is well detectable (arrows). The posterior wall of the uterus is attracted toward the nodule.

c. MR-e axial plane, FSE T2W sequence. The rectal wall is infiltrated by the endometriosis: the intestinal wall is concentrically thickened (arrow).

d. Haematoxylin and eosin stained section of the resected rectal nodule (magnificantion 20X). Endometriotic cysts can be observed within the muscular layer of the rectal wall; columnar

endometrial epithelial cells and endometriotic stroma can be observed. The endometriotic cysts are surrounded by a thin fibrous capsule and muscle cells. The intestinal submucosa and mucosa are not infiltrated by endometriosis.

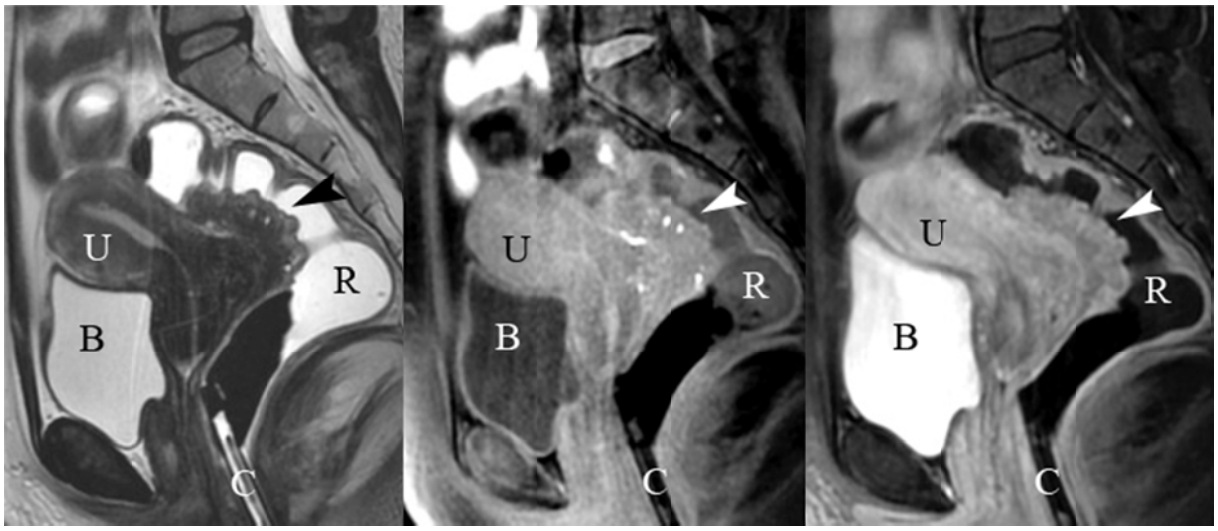


Figure 3. MR-e T1W and T2W sagittal images of rectal endometriotic nodule

On the left, FrFSE T2W sequence; the nodule has T2 hyperintense spots. In the middle, FSE T1W fat sat sequence; the nodule has hemorrhagic focal hyperintense spots. On the right, FSE T1W fat sat sequence after gadolinium injection: the nodule shows a generic enhancement that is similar to the uterine and rectal wall. The arrowhead indicates the endometriotic nodule infiltrating the muscularis mucosae of the middle rectum. B, bladder; R, rectum; U, uterus; C, catheter used to dilate the rectosigmoid colon.

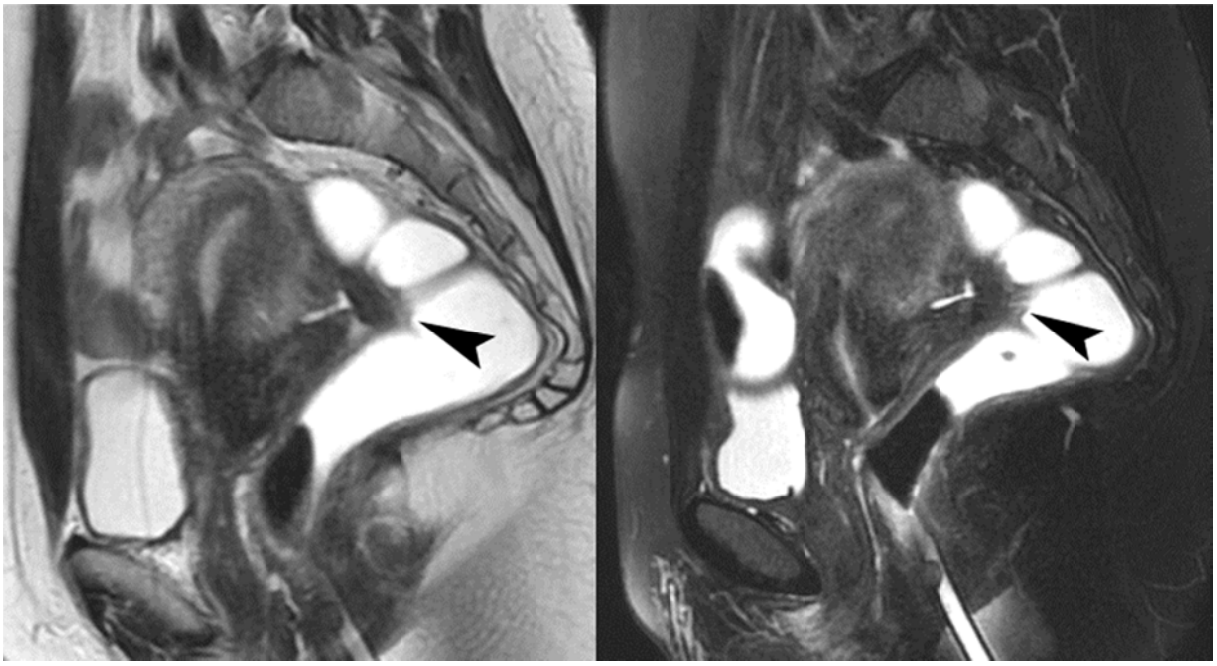


Figure 4. Rectal endometriotic nodule

a. RWC-TVS image. The water contrast (WC) facilitates the identification of a rectal endometriotic nodule (asterisk) with larger diameter of 35 mm.

b. MR-e FrFSE T2 (on the left) and T2W fat sat sequence (on the right) sagittal images. A rectal nodule (arrowhaed) infiltrates the anterior wall of the lower rectum; the nodule is inhomogeneously hypointense in both sequences. The liquid in the rectum enhances the intestinal wall visibility and the detection of the nodule. The muscular wall is infiltrated.

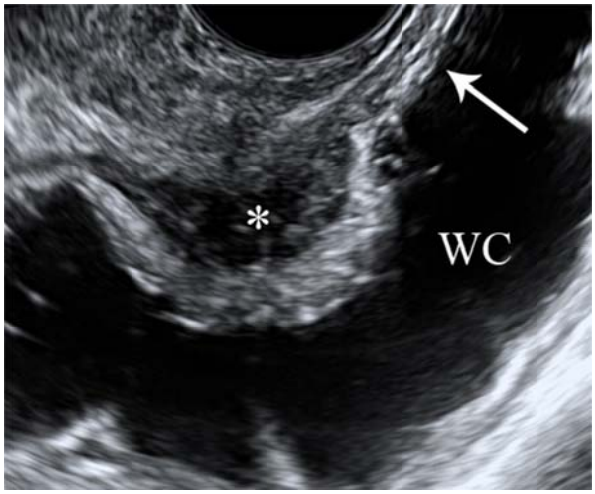
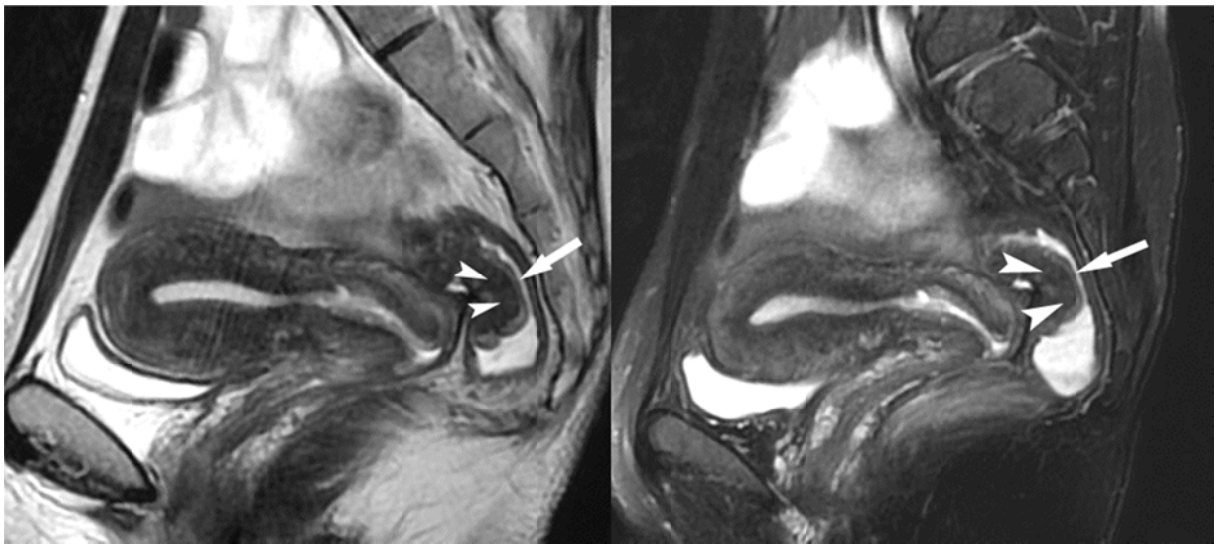


Figure 5. RWC-TVS image of a rectal endometriotic nodule

The endometriotic nodule (asterisk) penetrates the muscularis propria of the rectum causing a thickening of the intestinal wall. The normal layers of the rectal wall can be observed distally to the nodule (arrow). WC, water contrast.



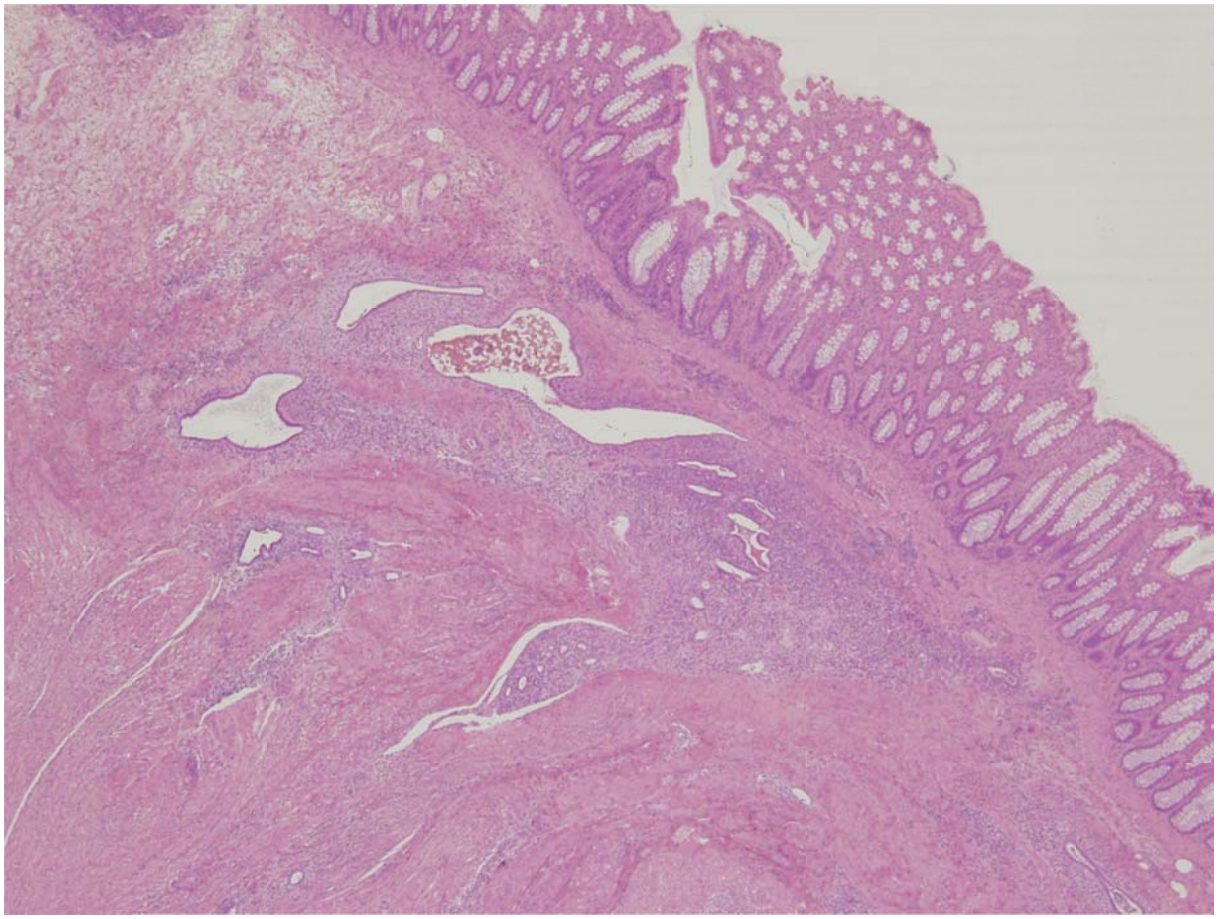


Figure 6. Rectal endometriotic nodule

a. MR-e FrFSE T2 (on the left) and T2W fat sat sequence (on the right) sagittal images.

A rectal nodule deeply infiltrating the anterior wall of the lower rectum. The nodule is inhomogeneously hypointense in both sequences. The liquid inserted in the rectum enhances the lesion detectability. The fat saturation confirms that the space between rectum and uterus is infiltrated. It is possible to detect two layers peripherally to the nodule: deeply the infiltration of the muscular wall is appreciable (arrow head), on the surface of the nodule (arrow) the mucosa of the rectum is not infiltrated.

b. Haematoxylin and eosin stained section of the resected rectal nodule (magnification 40X). Histology shows that the rectal mucosa is not infiltrated by endometriosis.

References

1. Remorgida V, Ferrero S, Fulcheri E, Ragni N, Martin DC. Bowel endometriosis: presentation, diagnosis, and treatment. *Obstet Gynecol Surv* 2007; **62** : 461-470.

2. Ferrero S, Camerini G, Ragni N, Venturini PL, Biscaldi E, Remorgida V. Norethisterone acetate in the treatment of colorectal endometriosis: a pilot study. *Hum Reprod* 2010; **25** : 94-100.

3. Ferrero S, Camerini G, Ragni N, Menada MV, Venturini PL, Remorgida V. Triptorelin improves intestinal symptoms among patients with colorectal endometriosis. *Int J Gynaecol Obstet* 2010; **108** : 250-251.

4. Leone Roberti Maggiore U, Remorgida V, Scala C, Tafi E, Venturini PL, Ferrero S. Desogestrel-only contraceptive pill versus sequential contraceptive vaginal ring in the treatment of rectovaginal endometriosis infiltrating the rectum: a prospective open-label comparative study. *Acta Obstet Gynecol Scand* 2014; **93** : 239-247.

5. Donnez J, Squifflet J. Complications, pregnancy and recurrence in a prospective series of 500 patients operated on by the shaving technique for deep rectovaginal endometriotic nodules. *Hum Reprod* 2010; **25** : 1949-1958.

6. Roman H. Rectal shaving using PlasmaJet in deep endometriosis of the rectum. *Fertil Steril* 2013; **100**: e33.

7. Darai E, Dubernard G, Coutant C, Frey C, Rouzier R, Ballester M. Randomized trial of laparoscopically assisted versus open colorectal resection for endometriosis: morbidity, symptoms, quality of life, and fertility. *Ann Surg* 2010; **251** : 1018-1023.

8. Bazot M, Lafont C, Rouzier R, Roseau G, Thomassin-Naggara I, Darai E. Diagnostic accuracy of physical examination, transvaginal sonography, rectal endoscopic sonography, and magnetic resonance imaging to diagnose deep infiltrating endometriosis. *Fertil Steril* 2009; **92** : 1825-1833.

9. Faccioli N, Foti G, Manfredi R, Mainardi P, Spoto E, Ruffo G, Minelli L, Mucelli RP. Evaluation of colonic involvement in endometriosis: double-contrast barium enema vs. magnetic resonance imaging. *Abdom Imaging* 2010; **35** : 414-421.

10. Bazot M, Darai E, Hourani R, Thomassin I, Cortez A, Uzan S, Buy JN. Deep pelvic endometriosis: MR imaging for diagnosis and prediction of extension of disease. *Radiology* 2004; **232** : 379-389.

11. Biscaldi E, Ferrero S, Fulcheri E, Ragni N, Remorgida V, Rollandi GA. Multislice CT enteroclysis in the diagnosis of bowel endometriosis. *Eur Radiol* 2007; **17** : 211-219.

12. van der Wat J, Kaplan MD. Modified virtual colonoscopy: a noninvasive technique for the diagnosis of rectovaginal septum and deep infiltrating pelvic endometriosis. *J Minim Invasive Gynecol* 2007; **14** : 638-643.

13. Hudelist G, English J, Thomas AE, Tinelli A, Singer CF, Keckstein J. Diagnostic accuracy of transvaginal ultrasound for non-invasive diagnosis of bowel endometriosis: systematic review and meta-analysis. *Ultrasound Obstet Gynecol.* 2011; **37** : 257-263.

14. Guerriero S, Ajossa S, Orozco R, Perniciano M, Jurado M, Melis GB, Alcazar JL. Diagnostic accuracy of transvaginal ultrasound for diagnosis of deep endometriosis in the recto-sigmoid: a meta-analysis. *Ultrasound Obstet Gynecol* 2016; **47**: 281-9.

15. Chassang M, Novellas S, Bloch-Marcotte C, Delotte J, Toullalan O, Bongain A, Chevallier P. Utility of vaginal and rectal contrast medium in MRI for the detection of deep pelvic endometriosis. *Eur Radiol* 2010; **20** : 1003-1010.

16. Loubeyre P, Copercini M, Frossard JL, Wenger JM, Petignat P. Pictorial review: rectosigmoid endometriosis on MRI with gel opacification after rectosigmoid colon cleansing. *Clin Imaging* 2012; **36**: 295-300.

17. Biscaldi E, Ferrero S, Leone Roberti Maggiore U, Remorgida V, Venturini PL, Rollandi GA. Multidetector computerized tomography enema versus magnetic resonance enema in the diagnosis of rectosigmoid endometriosis. *Eur J Radiol* 2014; **83** : 261-267.

18. Valenzano Menada M, Fortunato T, Ferrero S, Petrera P, Fulcheri E, Bogliolo S. Massive ovarian edema: a case of over 30 cm ovarian mass in young woman. *Minerva Ginecol* 2008; **60** : 345-348.

19. Ferrero S, Biscaldi E, Morotti M, Venturini PL, Remorgida V, Rollandi GA, Valenzano Menada M. Multidetector computerized tomography enteroclysis vs. rectal water contrast transvaginal ultrasonography in determining the presence and extent of bowel endometriosis. *Ultrasound Obstet Gynecol* 2011; **37** : 603-613.

20. Biscaldi E, Ferrero S, Remorgida V, Fulcheri E, Rollandi GA. Rectosigmoid endometriosis with unusual presentation at magnetic resonance imaging. *Fertil Steril* 2009; **91** : 278-280.

21. Goncalves MO, Podgaec S, Dias JA, Jr., Gonzalez M, Abrao MS. Transvaginal ultrasonography with bowel preparation is able to predict the number of lesions and rectosigmoid layers affected in cases of deep endometriosis, defining surgical strategy. *Hum Reprod* 2010; **25** : 665-671.

22. Guerriero S, Ajossa S, Gerada M, Virgilio B, Angioni S, Melis GB. Diagnostic value of transvaginal 'tenderness-guided' ultrasonography for the prediction of location of deep endometriosis. *Hum Reprod* 2008; **23** : 2452-2457.

23. Benacerraf BR, Groszmann Y, Hornstein MD, Bromley B. Deep infiltrating endometriosis of the bowel wall: the comet sign. *J Ultrasound Med* 2015; **34** : 537-542.

24. Valenzano Menada M, Remorgida V, Abbamonte LH, Nicoletti A, Ragni N, Ferrero S. Does transvaginal ultrasonography combined with water-contrast in the rectum aid in the diagnosis of rectovaginal endometriosis infiltrating the bowel? *Hum Reprod* 2008; **23** : 1069-1075.

25. Guerriero S, Ajossa S, Gerada M, D'Aquila M, Piras B, Melis GB. "Tenderness-guided" transvaginal ultrasonography: a new method for the detection of deep endometriosis in patients with chronic pelvic pain. *Fertil Steril* 2007; **88** : 1293-1297.

26. Saccardi C, Cosmi E, Borghero A, Tregnaghi A, Dessole S, Litta P. Comparison between transvaginal sonography, saline contrast sonovaginography and magnetic resonance imaging in the diagnosis of posterior deep infiltrating endometriosis. *Ultrasound Obstet Gynecol* 2012; **40** : 464-469.

27. León M, Vaccaro H, Alcázar JL, Martinez J, Gutierrez J, Amor F, Iturra A, Sovino H. Extended transvaginal sonography in deep infiltrating endometriosis: use of bowel preparation and an acoustic window with intravaginal gel: preliminary results. *J Ultrasound Med* 2014; **33** : 315-321.

28. Reid S, Lu C, Hardy N, Casikar I, Reid G, Cario G, Chou D, Almashat D, Condous G. Office gel sonovaginography for the prediction of posterior deep infiltrating endometriosis: a multicenter prospective observational study. *Ultrasound Obstet Gynecol* 2014; **44** : 710-718.

29. Guerriero S, Saba L, Ajossa S, Peddes C, Angiolucci M, Perniciano M, Melis GB, Alcázar JL. Three-dimensional ultrasonography in the diagnosis of deep endometriosis. *Hum Reprod* 2014; **29** : 1189-1198.

30. Takeuchi H, Kuwatsuru R, Kitade M, Sakurai A, Kikuchi I, Shimanuki H, Kinoshita K. A novel technique using magnetic resonance imaging jelly for evaluation of rectovaginal endometriosis. *Fertil Steril* 2005; **83** : 442-447.

31. Kikuchi I, Takeuchi H, Kuwatsuru R, Kitade M, Kumakiri J, Kuroda K, Takeda S. Diagnosis of complete cul-de-sac obliteration (CCDSO) by the MRI jelly method. *J Magn Reson Imaging* 2009; **29** : 365-370.

32. Loubeyre P, Petignat P, Jacob S, Egger JF, Dubuisson JB, Wenger JM. Anatomic distribution of posterior deeply infiltrating endometriosis on MRI after vaginal and rectal gel opacification. *AJR Am J Roentgenol* 2009; **192** : 1625-1631.

33. Kikuchi I, Kuwatsuru R, Yamazaki K, Kumakiri J, Aoki Y, Takeda S. Evaluation of the usefulness of the MRI jelly method for diagnosing complete cul-de-sac obliteration. *Biomed Res Int* 2014; **2014** : 437962.

34. Hottat N, Larrousse C, Anaf V, Noël JC, Matos C, Absil J, Metens T. Endometriosis: contribution of 3.0-T pelvic MR imaging in preoperative assessment--initial results. *Radiology* 2009; **253** : 126-134.

35. Menada MV, Remorgida V, Abbamonte LH, Fulcheri E, Ragni N, Ferrero S. Transvaginal ultrasonography combined with water-contrast in the rectum in the diagnosis of rectovaginal endometriosis infiltrating the bowel. *Fertil Steril* 2008; **89** : 699-700.

36. Bergamini V, Ghezzi F, Scarperi S, Raffaelli R, Cromi A, Franchi M. Preoperative assessment of intestinal endometriosis: A comparison of transvaginal sonography with water-contrast in the rectum, transrectal sonography, and barium enema. *Abdom Imaging* 2010; **35** : 732-736.

37. Philip CA, Bisch C, Coulon A, de Saint-Hilaire P, Rudigoz RC, Dubernard G. Correlation between three-dimensional rectosonography and magnetic resonance imaging in the diagnosis of rectosigmoid endometriosis: a preliminary study on the first fifty cases. *Eur J Obstet Gynecol Reprod Biol* 2015; **187** : 35-40.

38. Guerriero S, Alcazar JL, Ajossa S, Melis GB. Modified ultrasound scanning is a cost-effective method for the detection of deep infiltrating endometriosis. *Fertil Steril* 2009; **91** : e38; author reply e39.

39. Tammaa A, Fritzer N, Strunk G, Krell A, Salzer H, Hudelist G. Learning curve for the detection of pouch of Douglas obliteration and deep infiltrating endometriosis of the rectum. *Hum Reprod* 2014; **29** : 1199-1204.

40. Scardapane A, Bettocchi S, Lorusso F, Stabile Ianora AA, Vimercati A, Ceci O, Lasciarrea M, Angelelli G. Diagnosis of colorectal endometriosis: contribution of contrast enhanced MR-colonography. *Eur Radiol* 2011; **21** : 1553-1563.