Magnetic resonance imaging versus transvaginal ultrasound for complete survey of the pelvic compartments among patients with deep infiltrating endometriosis

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Synopsis:

Transvaginal ultrasound showed a higher accuracy compared to magnetic resonance in diagnosing recto-vaginal endometriosis. Magnetic resonance should be recommended if suspicion of bladder endometriosis exists.

Abstract

Objective: To compare the performance of magnetic resonance imaging (MRI) and transvaginal ultrasound (TVU) in detecting deep infiltrating endometriosis (DIE), using Enzian classification. Secondarily, to evaluate the influence of nodule size on the accuracy of MRI and TVU.

Methods: A retrospective study was carried out at "La Paz" University Hospital, Madrid, Spain, between April 2012 and December 2014. Inclusion criteria were suspicion of DIE at gynecologic examination, indication to undergo TVU, MRI and surgery.] Exclusion criteria were previous hysterectomy, bowel resection, or urinary tract surgery. The diagnosis of DIE using MRI or TVU was considered positive when it correlated with histology. Sensitivity, specificity, accuracy, and mean size of the nodule were calculated.

Results: In the present study involving 48 women, TVU demonstrated greater accuracy than MRI for recto-vaginal (77% vs 69%) and vaginal (94% vs 89%) endometriosis. MRI showed greater accuracy (96%) than TVU (92%) for bladder endometriosis. The size of the nodule did not have a significantly different effect on the accuracy of TVU compared with MRI.

Conclusion: In the present study, TVU provided a more accurate localization of vaginal and recto-vaginal endometriosis as compared with MRI, however MRI should

be recommended if a suspicion of bladder endometriosis exists. The nodule size did not seem to influence the accuracy of the two techniques.

1 INTRODUCTION

Deep infiltrating endometriosis (DIE) is defined as endometriosis which infiltrates the peritoneum more than 5 mm [1]. Most DIE lesions are known to originate from the posterior part of the cervix and secondarily infiltrate the anterior wall of the rectum [2]. The nodule could infiltrate the recto-sigmoid, uterosacral ligaments, vaginal fornix, recto-vaginal septum, and the bladder [3]. The revised American Fertility Society classification of endometriosis (rAFS) [4] is still the most used, however this classification has limitations in terms of localization and mapping of the lesions of DIE [5]. The Enzian classification [6] is not a score in the same way as the rAFS, but a morphological description of lesions, including their size. Indeed, it provides a complete description of all endometriotic lesions of the pelvis compartments.

The preoperative assessment of DIE is important for the decision making around surgical strategy, and for informing the patient about the risks. Several imaging techniques have been proposed, such as transvaginal ultrasound (TVU), magnetic resonance imaging (MRI), transrectal sonography, rectal endoscopic sonography, and computed tomography [7, 8]. Surgery with histopathologic examination provides the definitive diagnosis; the main role of surgery, however, is therapeutic [9]. Until now, there has not been a unanimous consensus on the gold standard technique for diagnosing DIE. Saline contrast sonovaginography has been described as an accurate method for exploring the depth of infiltration of the bowel, and its diagnostic value was considered similar to MRI [10]. Some authors described MRI and rectal

endoscopic sonography as second line imaging for the detection of upper gastrointestinal lesions and the depth of colorectal lesions, respectively [11]. The computed tomography-based virtual colonoscopy (CTC) was proposed by Roman et al. [12] in the preoperative assessment of bowel endometriosis. It revealed accurate data on the length and height of colorectal involvement by DIE and on stenosis of the gastrointestinal tract lumen. Undoubtedly, MRI and TVU are the most used imaging techniques in the clinical practice of the majority of the centers. Despite continuing controversy in the literature, it is not yet established which of the techniques is the most accurate for the preoperative mapping of DIE [13].

The purpose of the present study was to compare the diagnostic performance of MRI and TVS in the detection of DIE, using Enzian classification. A secondary aim was to evaluate the influence of the nodule size on the accuracy of MRI and TVU in the diagnosis of DIE. The study received Institutional Review Board approval.

2 MATERIAL AND METHODS

The present retrospective study was carried out at the Endometriosis Unit of "La Paz" University Hospital, Madrid, Spain, between April 1, 2012, and December 31, 2014. Inclusion criteria were clinical objectivity at gynecologic examination, indication to undergo TVU and MRI and finally surgical treatment. Exclusion criteria were previous hysterectomy, bowel resection, or urinary tract surgery (partial cystectomy or ureter reimplantation).

TVU scans were performed by a gynecologist who was an expert in gynecological ultrasound. MRI was performed by a radiologist skilled in abdominal and pelvic radiology for endometriosis. The radiologist was blinded to the ultrasound results. Both sonographers and radiologists used Enzian classification to report the localization of DIE in the following sites: compartment A—recto-vaginal space and vagina; compartment B—uterosacral ligaments (USL), cardinal ligaments, pelvic sidewall; compartment C—recto-sigmoid junction. According to the Enzian classification, the lesions were classified as FU (involvement of the ureter) and FB (involvement of the bladder). Furthermore, within the compartments A, B, and C, three subgroups were classified, depending on the size of the nodule: subgroup 1 if the nodule size is smaller than 1 cm; subgroup 2 if the nodule size measures 1–3 cm; and subgroup 3 for nodules larger than 3 cm. In the same way, the Enzian classification was used to describe the anatomical distribution of the endometriosis lesions removed by surgery.

The diagnosis of endometriosis using MRI or TVU was considered to be positive when it correlated with surgical and histological findings. Surgical data and preoperative symptoms of the patients were investigated. The nodule size of each compartment of the pelvis detected by surgery was calculated. Patients had a maximum interval of 2 months between imaging (MRI and TVU) and surgery.

Transvaginal ultrasound protocol

The procedure was performed after obtaining verbal consent and using GE Voluson ultrasound machines (730 Pro and E6. GE Healthcare, Chicago, IL, USA), equipped with 4–8 MHz abdominal probes and a transvaginal 5-9 MHz probe. The standardized protocol included bowel preparation with a simple rectal enema 12

hours prior to initiation of the examination. Transabdominal scan with panoramic view of the pelvic organs and abdomen was systematically performed, with special attention to the renal pelvis and ureters. This was followed by vaginal ultrasound examination. All the examinations included systematic analysis of the uterus and ovaries, the uterosacral ligaments (which are not generally visible if normal), posterior vaginal fornix, recto-vaginal septum, recto-sigmoid, and bladder. The endometriotic lesion was described when there was a regular or irregular nodular hypoechoic thickening (Figure S1). Recto-vaginal endometriosis was visible as a solid nodular hypoechoic thickening (Figure 1).

Recto-sigmoid involvement by endometriosis was considered if the muscularis propria layer was infiltrated by solid irregular spiculated hypoechoic nodule involvement, described as "Indian head dress", with or without peripheral vascular Doppler [14] (Figure S2). Finally, the transducer was positioned in the anterior vaginal fornix to visualize the eventual involvement of the bladder in longitudinal and transverse sections. In order to do this, a moderate repletion of bladder was necessary. The DIE implant could be represented as a hypoechoic or isoechoic nodule in the bladder wall, or as a nodule with a heterogeneous echostructure containing numerous anechoic ("bubble-like") areas [15] (Figure S3).

Magnetic resonance imaging protocol

The MRI was performed using a 1.5T MRI device (GE Signa Explorer, GE Healthcare, Milwaukee, Wisconsin). All patients signed a written informed consent document. They underwent bowel preparation, which consisted of one dose of Puntualex (Senósidos A+B sal cálcica, Lainco SA, Barcelona, Spain) with abundant

hydration every 8 hours, 3 days prior to the procedure. The study was conducted outside the menstrual period. The procedure required a moderate repletion of the patient's bladder [16]. MRI imaging was performed with the patient lying in the supine position. Sonographic gel (Telic Group, Barcelona, Spain), 150 mL, diluted with saline solution (1:2), was introduced using a syringe connected to a 20-Fr Foley catheter to distend the rectum and the sigmoid colon. Sonographic gel (25-50 cm^3) was introduced into the vagina. The following sequences were obtained: sagittal T2 field of view (FOV) 240 mm, matrix 512 pixels; axial T1 FOV 260, matrix 512; coronal T2 with fatty saturation FOV 360, matrix 512; axial T2 FOV 240, matrix 512; axial T1 with fatty saturation FOV 340, matrix 512; sagittal T1 with fatty saturation FOV 280, matrix 256. Slice thickness 5 mm. The diagnosis of DIE was based on a hypointense signal of nodules on T2-weighted images and eventually hyperintense signal on fatty saturation T1-weighted image, usually typical of bladder (Figure 2) and recto-sigmoid nodule (Figure S4). The eventual involvement of the ureters by endometriosis was evaluated.

Statistical analysis was carried out using SAS 9.3 software (SAS Institute, Cary, NC, USA). Continuous variables were expressed as mean, SD and percentiles. Qualitative variables were expressed as absolute values and percentiles. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for TVS and MRI. Furthermore, accuracy and likelihood ratios (95% confidence intervals [CI]) were calculated. Quantitative variables between the two imaging techniques were compared using student *t* test and Mann–Whitney *U* test. All statistical tests were bilateral, and a *P* value of <0.05 was considered statistically significant. Cohen's kappa test evaluated the agreement among MRI, TVS, and

surgery. Kappa values between 0.81 and 1.0 were interpreted as excellent agreement, 0.61–0.80 as good agreement, 0.41–0.60 as moderate agreement, 0.21–0.40 as fair agreement, and values less than 0.20 as poor agreement.

3 RESULTS

Among 69 eligible patients who presented, 48 fulfilled the inclusion criteria described above. A total of 21 patients were excluded for the following reasons: seven declined to undergo MRI; six declined surgical intervention; five were considered not eligible owing to previous surgical intervention; and three had missing data. The mean age of the 48 patients was 34 ± 6 years, and the mean body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) was 22 ± 2.7. At the preoperative evaluation, patients showed the following symptoms: 32 (67%) patients reported dysmenorrhea; 13 (27%) had chronic pelvic pain; 35 (73%) complained of dyspareunia; and 10 (21%) of dysuria. The surgical procedures performed were: hysterectomy in 18 patients (37%); monolateral adnexectomy in 4 (8%); bilateral adnexectomy in 13 (27%); ovarian cystectomy in 22 (46%); ureteroneocystostomy in 3 (6%); bladder resection in 6 (12%); recto-sigmoid nodule shaving in 9 (19%); discoid bowel resection in 5 (10%); segmentary bowel resection in 18 (37%); and partial colpectomy in 13 (27%). Deep infiltrating endometriosis was detected in all 48 (100%) patients and confirmed by histology. All of the surgical procedures were performed by laparoscopy. The performance data of TVU and MRI for each specific location of endometriosis are shown in Table 1: the highest accuracy (94%) for TVU was for diagnosing vaginal endometriosis (compartment A of Enzian classification). The highest accuracy (96%) for MRI was for diagnosing bladder endometriosis (that is compartment FB of Enzian classification).

In relation to each single localization, the degree of concordance (Cohen's kappa test) was calculated (Tables 2 and 3): TVU showed a moderate agreement with surgery for diagnosis of endometriosis of compartment A (vagina–recto-vaginal endometriosis), compartment C (recto-sigmoid), compartment FB (bladder), and compartment FU (ureter). MRI showed a good agreement with surgery for diagnosis of endometriosis of compartment FB, moderate agreement for compartment C, and fair agreement for compartments A and FU. Both of the two techniques showed poor agreement with surgery for detecting endometriosis of uterosacral ligaments (compartment B).

The mean diameter of the nodules was as follows: recto-vaginal nodule 27.9 ± 7.5 mm; vaginal nodule 36.6 ± 2.9 mm; uterosacral ligament nodule 20.4 ± 8.2 mm; recto-sigmoid nodule 29.9 ±13.4 mm; bladder nodule 37.1 ± 9.9 mm; ureteral nodule 19.5 ± 1.6 mm. The student t test and the Mann–Whitney U test showed that there were no statistically significant differences between the mean size of DIE nodules and TVU (compartment A, P=0.512; compartment B, P=0.334; compartment C, P=0.473; compartment FB, P=0.701; compartment FU, P=0.702) or MRI accuracy (compartment A, P=0.932; compartment B, P=0.164; compartment C, P=0.193; compartment FB, P=1.0; compartment FU, P=0.531).

4 DISCUSSION

The present study showed that TVU had better accuracy than MRI for predicting recto-vaginal (77% versus 69%) and vaginal (94% versus 89%) endometriosis. In contrast, for the diagnosis of bladder endometriosis, MRI showed a good agreement with surgery and better accuracy (96%) than TVU (92%).

The findings of the present study are in agreement with other investigators [17] who showed that TVU was more effective than MRI in detecting recto-vaginal endometriosis (TVU accuracy 97% vs MRI accuracy 71%). Savelli [18] showed that TVU was an accurate method for detecting posterior DIE, but that this imaging technique strictly depended on the experience of the physician and the size of the nodule.

Regarding the diagnosis of bladder endometriosis, the present study reported similar values of sensitivity and specificity of MRI (67% and 100%) to those described by others authors [19, 20, 21]. Furthermore, the present study showed that MRI had good concordance ((Cohen's kappa test: 0.77) with surgery and reliable likelihood ratios (LR+ infinitive, LR– 0.3) for bladder location of DIE. It was concluded that MRI was more performant than TVU for detection of bladder nodule, however Gauche Cazalis et al. [22] showed better sensitivity with lower specificity (33% and 89%) of MRI, compared with TVU (17% and 100%), for diagnosing bladder endometriosis.

A strength of the present study was that it clarified the value of MRI for correct localization of bladder endometriosis. Indeed, the majority of studies in the literature [8, 16, 17] investigated the accuracy of the different imaging techniques only for intestinal endometriosis. The authors of the present study suggest that MRI is the gold standard in the management of women who complain of dysuria, bladder pain, urgency, and less often hematuria [21] with a gynecologic examination and ultrasound findings suspicious for bladder endometriosis. Another strength of the present study was the use of Enzian classification of DIE, as this provided adequate mapping of deep endometriosis localizations [5] and enabled radiologists, sonographers, and gynecologic surgeons to easily share the diagnostic findings. To

our knowledge, only one study correlates the MRI to Enzian score to evaluate the localization of DIE [5], however TVU was not included in the analysis.

In the comparison of TVU and MRI for diagnosing DIE of USL, the present study showed poor agreement of the two techniques (TVU [Cohen's kappa test]: 0.02; MRI [Cohen's kappa test]: 0.09) with surgery with low sensitivity and specificity (59% and 43% for TVU and 67% and 43% for MRI). The authors suggest that the reasons for misdiagnosis could include the fibrosis that often involves USL in the presence of "frozen pelvis", and the prolapse of the uterus in a retroverted position with severe adhesions and large "kissing ovaries" [7].

In the present study, high specificity (95%) associated with low sensitivity (50%) and good accuracy (89.6%) were obtained in the diagnosis of deep endometriosis of the ureters using TVU. Indeed an expert sonographer can easily identify mono/bilateral ureteral nodules, with dilatation of the pelvic ureter [7]. However, MRI showed the same accuracy value (90%) and similar specificity (98%), but low sensitivity (33%). Regarding intestinal endometriosis, the findings showed the same accuracy of MRI and TVU to detect recto-sigmoid endometriosis (75%) with a moderate degree of agreement (TVU (Cohen's kappa test 0.43, MRI (Cohen's kappa test 0.50) with surgery for both techniques. Similar results were reported in the literature [7, 13, 16, 21].

Considering the size of the DIE nodules, surprisingly the present study did not show statistically significant differences in the accuracy of the two imaging techniques.

Di Paola et al. [5] showed that nodules of the bladder smaller than 2 cm were not recognizable by MRI. Other investigators agreed that TVU was the most accurate imaging technique in defining the size of endometriotic lesions, but the underestimation was great for nodules larger than 3 cm [21]. The authors suggest that the low number of patients and the complex measurement of the nodule owing to the surrounding fibrosis could justify the present study results. Furthermore, there were no nodules smaller than 1 cm (subgroup 1 of Enzian classification), and this could represent a bias of the present study.

Another limitation of the study could be the high prevalence of DIE in the data (100% of patients included in the study) which could influence the sensitivity and specificity of the imaging techniques: this is because the study was conducted in an endometriosis referral center.

Finally, the study is ongoing at our Institution, and we look forward to recruiting more patients in order to achieve a more definitive conclusion.

All pelvic compartments can be accurately mapped by using the two complementary methods for diagnosis of DIE. In particular, TVU provided a more accurate preoperative localization of vaginal and recto-vaginal endometriosis as compared with MRI, however MRI should be recommended when involvement of the bladder is suspected. TVU and MRI showed the same accuracy for detection of recto-sigmoid endometriosis. Finally, the nodule size did not seem to influence the accuracy of the two techniques.

Author contributions

AH contributed to the conception and design of the study, and writing the manuscript. ES contributed to the conception and design of the study, collection of data, and writing the manuscript. IZ contributed to data collection and statistical analysis. PH and AL contributed to the interpretation and analysis of the data. RR contributed to the interpretation and analysis of the data, and revising the manuscript.

Conflicts of interest

The authors have no conflict of interests.

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Figure legends

Figure 1. Transvaginal ultrasound. Regular hypoechoic nodule affecting the upper part of the recto-vaginal septum.

Abbreviations: Bl, bladder; R, rectum; V, posterior vaginal wall.

Figure 2. Magnetic resonance imaging in a patient with endometriotic nodule of the bladder. Low intensity signal at T2-weighted axial (a) and sagittal (b) images. Hyperintense signal on fatty saturation T1-weighted sagittal image (c).

Abbreviations: bl, bladder; cer, cervix; re, rectum; ut, uterus; vag, vagina.

Figure S1. Transvaginal parasagittal plane of the uterus. Nodular solid enlargement of uterosacral ligament bearing an endometriotic nodule (between calipers). Associated endometriotic nodule of the recto-sigmoid (*).

Abbreviations: Bl, bladder; Ut, uterus.

Figure S2. Transvaginal ultrasound. Sagittal view of the recto-sigmoid area with an endophytic hypoechoic, irregular and spiculate nodule (*) involving the muscularis propria layer. Arrows: normal aspect of the muscularis propria layer.

Abbreviation: Ut, uterine cervix.

Figure S3. Transvaginal ultrasound showing a vesical and ureteral endometriotic solid nodule (+ marks), involving bladder wall and distal ureter. Note the double-J stent (arrow) inside the bladder.

Abbreviations: Bl, bladder; Ur, ureter.

Figure S4. Magnetic resonance imaging in a patient with voluminous nodule of recto-sigmoid, attached to kissing ovaries. Low intensity signal at T2-weighted sagittal image.

Abbreviations: ov, ovaries; vag, vagina.

Table 1 Sensitivity, specificity, accuracy, PPV, NPV, LR+, and LR– data of transvaginal ultrasound and magnetic resonance imaging for diagnosing deep infiltrating endometriosis.

Imaging	Site	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+ (CI 95%)	LR- (CI 95%)	Accuracy (%)
TVU	Recto-vaginal space	65	88	83	73	5.43 (1.80–16.37)	0.39 (0.22–0.70)	37/48 (77)
MRI	Recto-vaginal space	74	64	65	73	2.05 (1.15–3.65)	0.40 (0.19–0.86)	33/48 (69)
TVU	Vagina	67	96	50	98	15.1 (3.11–72.35)	0.34 (0.07–1.73)	45/48 (94)
MRI	Vagina	33	93	25	95	4.97 (0.72–34.73)	0.71 (0.32–1.60)	43/48 (89)
TVU	Utero-sacral ligaments	59	43	57	45	1.03 (0.64–1.68)	0.94 (0.49–1.86)	25/48 (52)
MRI	Utero-sacral ligaments	67	43	60	50	1.16 (0.74–1.84)	0.77 (0.38–1.61)	27/48 (56)
TVU	Recto-sigmoid	81	62	81	62	2.16 (1.13–4.17)	0.30 (0.13–0.68)	36/48 (75)
MRI	Recto-sigmoid	69	87	92	58	5.50 (1.47–20.53)	0.35 (0.21–0.62)	36/48 (75)
TVU	Bladder	50	98	75	93	20.8 (2.58–70.69)	0.51 (0.23–1.14)	44/48 (92)
MRI	Bladder	67	100	100	95	-	0.33 (0.11–1.03)	46/48 (96)
TVU	Ureter	50	95	60	93	10.4 (2.18–50.55) 13.8	0.52 (0.24–1.17) 0.6	43/48 (90) 43/48 (90)
MRI	Ureter	33	98	67	91	(1.49–31.89)	(0.39–1.20)	

Abbreviations: CI, confidence interval; DIE, deep infiltrating endometriosis; LR+, positive likelihood ratio; LR–, negative likelihood ratio; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value; TVU, transvaginal ultrasound.

Table 2 Transvaginal ultrasound and surgical Enzian classification for all observed lesions, with relative degree of concordance (k-Cohen). [a]

Enzian compartment[b]	TVU n (%)	Surgery n (%)	Cohen K test CI 95%
A1	0	0	0.53 (0.30–077)
A2	16 (33)	18 (37)	
A3	6 (12)	8 (17)	
B1	0	0	0.02 (0.0–0.30)
B2	27 (56)	24 (50)	
B3	1 (2)	3 (6)	
C1	0	0	0.43 (0.16–0.70)
C2	25 (52)	22 (46)	
C3	7 (14)	10 (21)	
FB	4 (8)	6 (12)	0.55 (0.17–0.94)
FU	5 (10)	6 (12)	0.48 (0.10–0.87)

Abbreviations: A, vagina–recto-vaginal endometriosis; B, uterosacral ligament endometriosis; C, recto-sigmoid endometriosis; CI, confidence interval; FB, bladder endometriosis; FU, ureteral endometriosis; TVU, transvaginal ultrasound.
[a] n=48.
[b] Size of nodule: 1 = <1 cm; 2 = 1–3 cm; 3 = >3 cm.

Table 3 Magnetic resonance imaging and surgical Enzian classification for all observed lesions, with relative degree of concordance (k-Cohen). [a]

Enzian compartment[b]	MRI n (%)	Surgery n (%)	Cohen K test CI 95%
A1	0	0	0.37 (0.11–0.63)
A2	25 (52)	18 (37)	
A3	5 (10)	8 (17)	
B1	0	0	0.09 (0–0.37)
B2	29 (60)	24 (50)	
B3	1 (2)	3 (6)	
C1	0	0	0.50 (0.26–0.73)
C2	19 (39)	22 (46)	
C3	5 (10)	10 (21)	
FB	4 (8)	6 (12)	0.77 (0.48– 1)
FU	3 (6)	6 (12)	0.39 (0–0.81)

Abbreviations: A, vagina–recto-vaginal endometriosis; B, uterosacral ligament endometriosis; C, recto-sigmoid endometriosis; CI, confidence interval; FB, bladder endometriosis; FU, ureteral endometriosis; MRI, magnetic resonance imaging.
[a] n=48.
[b] Size of nodule: 1 = <1 cm; 2 = 1–3 cm; 3 = >3 cm.