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Transvaginal sonography vs. clinical examination in the preoperative diagnosis of deep infiltrating endometriosis

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KEYWORDS: deep infiltrating endometriosis; diagnosis; transvaginal ultrasound

ABSTRACT

Objective *The aim of this study was to compare the diagnostic performance of clinical vaginal examination with that of transvaginal sonography (TVS) in the presurgical diagnosis of deep infiltrating endometriosis.*

Methods *One-hundred and fifty-five women with symptoms suggestive of endometriosis were included. One-hundred and twenty-nine patients met the inclusion criteria and were prospectively and independently assessed by vaginal examination and TVS prior to a diagnostic laparoscopy and, where appropriate, radical resection and histological confirmation of endometriosis was performed. Sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV) and positive and negative likelihood ratios (LR+ and LR−) were calculated for each test method.*

Results *In total, 83 (64%) women had histological confirmation of endometriosis, 52 (40%) of whom had deep infiltrating endometriosis. The prevalence of endometriosis on the uterosacral ligaments, pouch of Douglas, vagina, bladder, rectovaginal space and rectosigmoid was 23.3%, 16.3%, 8.5%, 3.1%, 6.9% and 24%. PPV, NPV, LR+ and LR− for vaginal examination were 92%, 87%, 41.56 and 0.60 for ovarian endometriosis; 43%, 84%, 2.48 and 0.63 for uterosacral ligament disease; 64%, 95%, 9.14 and 0.26 for involvement of the pouch of Douglas; 80%, 97%, 42.91 and 0.28 for vaginal endometriosis; 78%, 98%, 46.67 and 0.23 for endometriosis of the rectovaginal space; 100%, 98%, 75.60 and 0.75 for bladder involvement; 86%, 84%, 18.97 and 0.63 for rectosigmoidal endometriosis. Values for TVS were similar with regard to vaginal and rectovaginal space endometriosis, but were clearly superior to vaginal examination in cases of ovarian (87%, 99%, 24.56 and 0.04), uterosacral ligament (91%, 90%, 31.35 and 0.37) and rectosigmoidal (97%, 97%, 88.51 and 0.1) endometriosis.*

Conclusions *TVS is a more useful test than is vaginal examination in detecting endometriosis in the ovaries and rectosigmoid. Copyright © 2011 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Endometriosis is one of the most challenging gynecological disorders. Hospital-based studies have reported prevalence rates of up to 15%[1], whereas two large community-based analyses have found a prevalence rate of 2%[2,3]. Studies report that between 15% and 30% of women with endometriosis will have deep infiltrating disease[4,5], although this is likely to be influenced by referral patterns. The most common sites for deep infiltrating endometriosis are the rectovaginal space and the rectosigmoid, with the majority of women being found to have disease in these areas[6].

Although studies have identified frequently reported symptoms associated with endometriosis[7], a definitive diagnosis can only be achieved following surgery, ideally with histological confirmation. This need for a surgical diagnosis has contributed to an average diagnostic delay of between 6[8] and 8 years[9]. Although patient and doctor awareness of endometriosis is increasing, diagnostic, and

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therefore therapeutic, delay confers a heavy economic and social price, and pervades several aspects of a woman's life[10,11]. In addition, the organ-destructive growth of deep infiltrating endometriosis may lead to long-term impairment of organ function, particularly in cases of intestinal and ureteral endometriosis.

In an attempt to reduce the diagnostic delay associated with endometriosis, studies have investigated the diagnostic accuracy of imaging tests such as magnetic resonance imaging (MRI), computed tomography (CT) and transvaginal sonography (TVS). Although TVS has been shown to be accurate at diagnosing endometriomas[12], some evidence suggests that it may not be a particularly useful test for diagnosing pelvic endometriosis[13]. Recent studies, however, have shown that TVS, when carried out by experienced sonographers, may indeed be a highly valuable test for the detection of deep infiltrating endometriosis affecting the uterosacral ligament, rectovaginal space, posterior pelvic pouch, vagina, urinary bladder and rectosigmoid[14–20]. Although evidence is increasing that TVS should be the first-line investigation to detect deep infiltrating endometriosis presurgically, evaluation of the patient's symptoms and vaginal examination are still regarded as the standard approach in everyday clinical practice.

The aim of this study was to compare the diagnostic performance of TVS with that of clinical examination with regard to the diagnosis of deep infiltrating endometriosis.

METHODS

Study setting

The study was designed as a prospective diagnostic study of premenopausal (i.e. < 50 years and menses within the past 6 weeks – except patients with a history of a permanent intake of combined oral contraceptive pills or Mirena®) women with suspected endometriosis attending one of three pelvic pain clinics, two UK-based (Worthing and Chertsey HS Hospital) and one Austrian (Centre for Endometriosis, Villach, Austria). The patient population consisted of: (a) women who were referred to the pelvic pain clinic for laparoscopy because of suspected endometriosis based on clinical history and the referring physician's clinical findings, and (b) self-referred women (coming to the pain clinic without having seen any gynecologist before for their current problems).

All women underwent a gynecological and TVS examination before deciding for surgical intervention. However, women were also booked for laparoscopy in case of normal clinical and TVS findings where there was a presence of endometriosis-associated symptoms or a history of primary subfertility.

Women with a history of gynecological cancer, previous surgery for deep infiltrating endometriosis or other disease entities requiring resection of the bladder, and/or dissection of the rectovaginal space and/or anterior rectosigmoidal wall were excluded from this study. In addition, patients with congenital anatomical abnormalities of the genital tract and cases where the patient was a virgin (exclusion for performance of TVS) were excluded. The study was approved by the local Institutional Ethics Review Board (IRB) and informed consent was obtained from all patients enrolled in this study.

Vaginal examination

Vaginal examination was performed by one of five experienced clinical examiners who were all blinded to TVS results. Vaginal examination was undertaken prior to TVS. The bimanual per vaginam examination was considered positive and therefore suggestive of endometriotic infiltration if the following criteria were met, palpable nodule or thickened area or a palpable cystic expansion with topographic-anatomical correlation to the following sites: left and/or right uterosacral ligaments, vagina, rectovaginal space, pouch of Douglas, the rectosigmoid and the urinary bladder (posterior wall). Owing to the limited ability to differentiate adnexal masses by vaginal examination, any palpable cystic expansion located within the right and/or left adnexal region was considered as cystic ovarian endometriosis until proven otherwise by laparoscopy and histological analysis.

Transvaginal sonography

All TVS scans were performed by one examiner (G.H.) who was blinded to the results of the vaginal examinations but was aware that the women were being investigated for chronic pelvic pain and therefore endometriosis was suspected.

TVS was carried out with either a Logic 9 (GE Healthcare Ultrasound, Milwaukee, WI, USA) or Accuvix XQ (Accuvix Sonoace, Medison Co., Ltd, Seoul, Korea) scanner using a 5–9-MHz transducer for transvaginal visualization of the urinary bladder, both adnexa, the uterus, the vagina and rectovaginal space, the uterosacral ligaments and the rectosigmoid. In order to achieve adequate visualization of these structures, the transducer was first introduced into the posterior vaginal fornix and withdrawn backwards to assess the pouch of Douglas, uterosacral ligaments, urinary bladder and the vagina. Following this, the probe was advanced for visualization of the uterus and the adnexal regions in the sagittal and horizontal planes. Finally, the probe was moved upwards to achieve full visualization of the rectosigmoidal wall layers. Rotation of the probe and up and down movements were necessary to visualize the rectosigmoid in women with axial or anteverted uteruses. In patients with a fixed and/or retroverted uterus, we tried to extend the visualization of the bowel as far as technically feasible. The bowel was not prepared prior to the investigation. The TVS diagnosis of endometriosis was based on sono-anatomical changes in the following pelvic structures and/or organs: endometriotic involvement of the ovaries was considered in the presence of a cyst

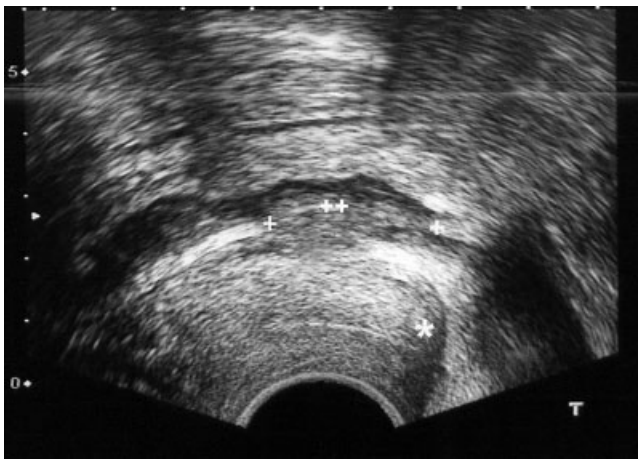

Figure 1 Transvaginal sonography showing a thickened, hypoechogenic irregular structure (++) disrupting the echo of the posterior vaginal wall (+) situated posterior to the cervix (*), corresponding to an endometriotic lesion involving the upper part of the posterior vaginal fornix also infiltrating the adjacent rectosigmoid.

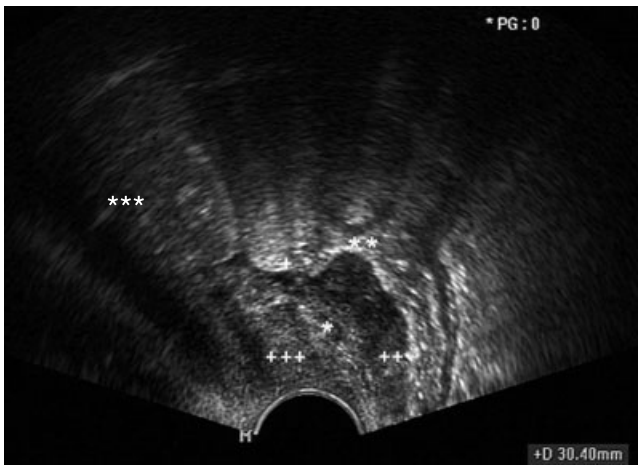

Figure 2 Transvaginal sonography showing a solid, partly cystic hypoechogenic nodule (++) situated posterior and inferior to the pouch of Douglas (+), partly infiltrating the posterior vaginal wall (*) and the anterior rectosigmoidal wall (**), corresponding to deep infiltrating endometriosis of the rectovaginal space and rectosigmoid. +++, cervix; ***, uterus.

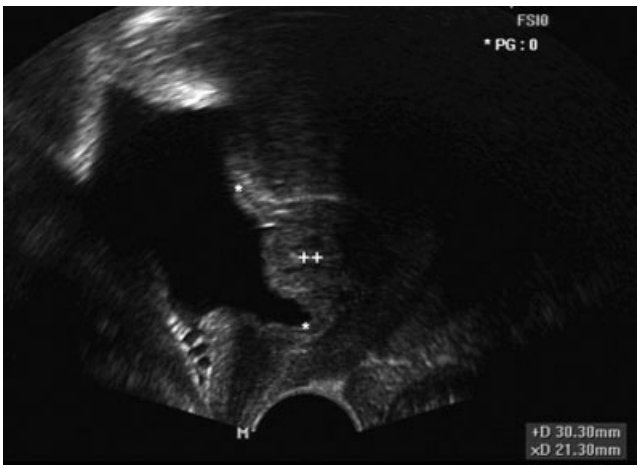

Figure 3 Transvaginal sonography showing a solid isoechogenic nodule (++) arising from the posterior wall of the urinary bladder (*), corresponding to deep infiltrating endometriosis of the bladder.

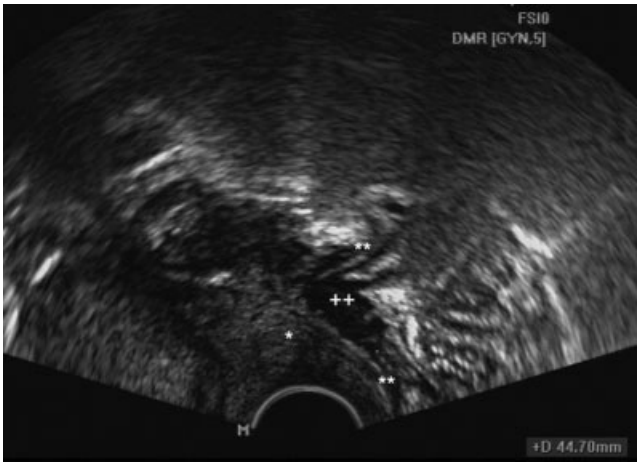

Figure 4 Transvaginal sonography demonstrating a solid hypoechogenic nodule (++) behind the cervix (*) situated within the anterior rectosigmoidal wall (**), corresponding to deep infiltrating endometriosis of the rectosigmoid with a hyperechogenic rim reflecting the rectosigmoidal submucosa. The hypoechogenic area represents infiltration and hypertrophy of the rectosigmoidal muscle.

or multiple cysts containing diffuse low-level echoes suggestive of an endometrioma, as defined by Kupfer *et al.*[21]. In accordance with the criteria defined by Bazot *et al.*[15], uterosacral ligament involvement was defined by a regular or irregular hypoechogenic nodular structure or hypoechogenic linear thickening with regular or irregular margins near the site of cervical insertion. Thickening and/or the presence of a hypoechogenic cystic or noncystic nodule within the posterior vaginal wall was considered as vaginal involvement (Figure 1). Similarly, the rectovaginal space, defined as the area between the rectum and the posterior vaginal wall from the level of the introitus up to a level defined by the lower border of the posterior lip of the cervix, was considered positive in the presence of a hypoechogenic nodule or cystic mass (Figure 2). Endometriosis of the bladder was suspected if a hypoechogenic nodule with or without cystic features was visualized within the posterior wall of the urinary bladder (Figure 3). Posterior pelvic pouch obliteration was considered complete when the uterus, adnexa and rectosigmoid colon were adherent, with disappearance of the peritoneal structure and incomplete when peritoneal limits were partially identified with the presence or absence of suspended or lateralized fluid collection[16]. Finally, sonographic features of endometriotic disease of the rectosigmoid included the presence of a regular or irregular hypoechogenic mass distorting and replacing the normal appearance of the muscular layer of the rectosigmoidal wall (a hypoechogenic thin line in the midsagittal plane adjacent to a hyperechogenic layer representing the rectosigmoidal submucosa) (Figure 4).

Laparoscopy, radical resection of endometriosis and histology

All patients included in the study underwent laparoscopy and, where present, resection and histological confirmation of endometriosis. In accordance with previous studies, deep infiltrating endometriosis was defined as subperitoneal endometriotic infiltration of tissues > 5 mm[22]. A histological presence of endometriosis was taken to represent a 'true positive' diagnosis of endometriosis.

A total of three surgeons performed the laparoscopy, all of whom had more than 10 years experience in radical laparoscopic surgery for deep infiltrating endometriosis (J.E., J.W., J.K.). The surgeons were blinded to the results of the vaginal examination and TVS in one of the centers (triple-blinded setting – clinical examiner, TVS examiner and surgeon blinded), but were aware of the vaginal examination and TVS results in the other two centers (double-blinded setting – clinical examiner and TVS examiner blinded). Prior to laparoscopy, all patients with symptoms suggestive of deep infiltrating endometriosis underwent chemical and physical cleansing of the bowel 24 h prior to surgery.

All cases of complete obliteration of the pouch of Douglas secondary to endometriosis were cleared surgically in order to achieve full resection of disease and to adequately assess the extent of endometriotic infiltration of structures such as the lower rectum, posterior vaginal wall or rectovaginal space. All cases of intestinal endometriosis, i.e. involvement of the small intestine and/or the rectosigmoid, were either treated with segmental resection of the bowel followed by side-to-end or end-to-end anastomosis using an EndoGia® stapling device or disc resection. Resection and removal of the endometriotic rectosigmoidal nodule was performed via a 4–5 cm minilaparotomy as described by Keckstein *et al.*[4] and Chapron *et al.*[23]. In addition, all patients with deep infiltrating endometriosis of the urinary bladder were treated with complete resection of the endometriotic nodule infiltrating the bladder wall.

Statistical analysis

Test accuracy was assessed by calculating the sensitivity and specificity for each site of possible endometriotic infiltration. Positive predictive values (PPV), negative predictive values (NPV) and positive and negative likelihood ratios (LR+ and LR−) were calculated to determine the ability of the tests to predict the presence or absence of disease. Ninety-five percent confidence intervals were calculated for each of the test results to determine the precision of the results. Data were analyzed using *R* statistical software[24] (The R Foundation, Vienna, Austria) and the DiagnosisMed package[25]. The tests were considered to be: very useful if LR+ was above 10 and LR− was below 0.1; moderately useful if LR+ was between 5 and 10 and LR− was between 0.1 and 0.2; somewhat useful if LR+ was between 2 and 5 and LR− was between 0.2 and 0.5; and useless if LR+ was between 1 and 2 and LR− was between 0.5 and 1[26]. Comparison of test accuracies were performed using Fisher's exact test.

RESULTS

Patient data

One hundred and fifty-five women were invited to participate in this study and 153 agreed to take part; 24 were excluded because they did not meet the inclusion criteria (18 had a history of previous surgery for deep infiltrating endometriosis, three had a history of gynecological cancer and three women were virgins). A total of 129 women were therefore included in the study. Women were 17–44 years of age (mean 32.2 years, SD 5.4 years). As shown in Table 1, the most common symptoms were dysmenorrhea (86%) and dyspareunia (55.8%).

Surgical findings

Endometriosis was histologically confirmed in 83/129 (64.3%) women. Deep infiltrating endometriosis was diagnosed in 52/129 (40.3%) women. Thirty (23.3%) women had uterosacral ligament involvement, with bilateral presence of endometriosis in 19 (14.7%) patients. Eleven (8.5%) women had vaginal endometriosis, 21 (16.3%) had pouch of Douglas endometriosis, 31 (24%) had rectosigmoidal involvement, nine (7%) had rectovaginal space involvement and four (3.1%) had urinary bladder involvement.

Fifty-four women (41.9%) were found to have peritoneal disease (25 with exclusively peritoneal endometriosis and 29 in combination with other affected sites). As shown in Table 2, the prevalence of cystic ovarian endometriosis was 27/129 (16.2%) with bilateral involvement in nine cases. A total of 213 sites were found to be affected by endometriosis with a mean of two affected locations per patient (Table 2).

Forty-six women (35.7%) did not have any signs of endometriotic disease during laparoscopic inspection of the pelvis. Thirty-one of these women did not have any apparent pelvic abnormalities and four women had macroscopic features consistent with chronic pelvic inflammatory disease (PID). Pelvic adhesions were observed in 11/46 women.

Table 1 Symptoms in 129 patients undergoing vaginal examination, transvaginal sonography and laparoscopy for pelvic endometriosis

Symptom	n *(%)*
Dysmenorrhea	111 (86.0)
Dyspareunia	72 (55.8)
Dyschezia	39 (30.2)
Dysuria	6 (4.6)
Chronic pelvic pain	45 (34.8)
Subfertility	20 (15.5)

Table 2 Location of endometriosis diagnosed by radical resection and histopathological analysis in 129 patients undergoing vaginal examination, transvaginal sonography and laparoscopy for suspected pelvic endometriosis

Site of disease	n *(%) or* n
Pelvic peritoneum	54 (41.9)
Ovary	27 (20.9)
Deep infiltrating endometriosis	52 (40.3)
Uterosacral ligaments	30 (23.3)
Pouch of Douglas	21 (16.3)
Vagina	11 (8.5)
Rectovaginal space	9 (6.9)
Urinary bladder	4 (3.1)
Rectosigmoid	31 (24.0)
Total number of sites affected	213
One site affected	31
Two sites affected	19
Three sites affected	11
> 3 sites affected	22

Preoperative findings of vaginal examination and TVS

Data on sensitivity, specificity, NPV, PPV, test accuracies, LR+ and LR− for vaginal examination and TVS are shown in Tables 3 and 4.

Vaginal examination findings

As shown in Table 3, vaginal examination suggested a diagnosis of cystic ovarian endometriosis in 12/129 (9.3%) women. One was a false-positive diagnosis that was explained by a luteal cyst at surgery. Vaginal examination yielded a diagnosis of uterosacral ligament endometriosis in 35/129 (27.1%) women with 20 false-positive results. None of the 20 women with a false-positive result was found to have abnormal uterosacral ligaments during surgery, but seven exhibited deep infiltrating endometriosis of the rectum and five of the vagina. Endometriosis of the pouch of Douglas was diagnosed with vaginal examination in 25/129 (19.4%) women with nine false-positive results. Of the women with a false-positive result, five had deep infiltrating endometriosis of the uterosacral ligaments and four had rectosigmoidal deep infiltrating endometriosis. Vaginal examination diagnosed vaginal endometriosis in 10/129 (7.8%) patients, including two false-positive results. One woman with a false-positive result was diagnosed with deep infiltrating endometriosis in the uterosacral ligaments, whereas the other had rectosigmoidal deep infiltrating endometriosis. Vaginal examination diagnosed endometriosis of the rectovaginal space in 9/129 (6.9%) cases with two false-positive results. One woman with a false-positive result was found to have isolated vaginal endometriosis, the other one exhibited rectosigmoidal deep infiltrating endometriosis.

No false-positive diagnosis of bladder endometriosis was made. Rectosigmoidal deep infiltrating endometriosis was diagnosed via vaginal examination in 14/129 (10.9%) women with two false-positive results. The two women with false-positive results showed uterosacral ligament disease.

Transvaginal sonography findings

As shown in Table 4, TVS yielded a diagnosis of cystic ovarian endometriosis in 30/129 (23.3%) women. Three of the four women with false-positive results were found to have luteal cyst, whereas one had an ovarian malignancy. TVS yielded a diagnosis of uterosacral ligament endometriosis in 21/129 (16.3%) women with two false-positive results. The two women with a false-positive diagnosis were both found to have rectosigmoidal deep infiltrating endometriosis. TVS diagnosed vaginal endometriosis in 8/129 (6.2%) women, yielding one false-positive result. The false-positive case was surgically diagnosed with deep infiltrating endometriosis infiltrating the right uterosacral ligament.

Bladder endometriosis was found to be present by TVS in 4/129 (3.1%) patients with two false-positive cases. No

Table 3 Diagnostic performance of vaginal examination for preoperative diagnosis of endometriosis

Location	*Sensitivity*	*Specificity*	*PPV*	*NPV*	*Accuracy (%)*	*LR+ (95% CI)*	*LR− (95% CI)*
Ovary	11/27 41 (22–61)	101/102 99 (95–100)	11/12 92 (62–100)	101/117 87 (79–92)	87	41.56 (5.61–307.88)	0.60 (0.44–0.82)
Uterosacral ligaments	15/30 50 (31–69)	79/99 80 (71–87)	15/35 43 (26–61)	79/94 84 (75–91)	73	2.48 (1.46–4.21)	0.63 (0.43–0.91)
Pouch of Douglas	16/21 76 (53–92)	99/108 92 (85–96)	16/25 64 (43–82)	99/104 95 (89–98)	89	9.14 (4.68–17.86)	0.26 (0.12–0.56)
Vagina	8/11 73 (39–94)	116/118 98 (94–100)	8/10 80 (44–98)	116/119 97 (93–100)	96	42.91 (10.36–177.69)	0.28 (0.11–0.73)
Rectovaginal space	7/9 78 (40–97)	118/120 98 (94–100)	7/9 78 (40–97)	118/120 98 (94–100)	97	46.67 (11.30–192.68)	0.23 (0.07–0.77)
Urinary bladder	1/4 25 (0–81)	125/125 100 (96–100)	1/1 100 (1–100)	125/128 98 (93–100)	98	75.60 (3.50–1633.9)	0.75 (0.43–1.32)
Rectosigmoid	12/31 39 (22–58)	96/98 97 (93–100)	12/14 86 (57–98)	96/115 84 (75–90)	84	18.97 (4.49–80.17)	0.63 (0.47–0.83)

Data for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) are given as *n* and % (95% CI). LR+, positive likelihood ratio; LR−, negative likelihood ratio.

Table 4 Diagnostic performance of transvaginal sonography for preoperative diagnosis of endometriosis

Location	*Sensitivity*	*Specificity*	*PPV*	*NPV*	*Accuracy (%)*	*LR + (95% CI)*	*LR − (95% CI)*
Ovary	26/27	98/102	26/30	98/99	96	24.56	0.04
	96 (81–100)	96 (90–99)	87 (69–96)	99 (95–100)		(9.37–64.35)	(0.01–0.26)
Uterosacral ligaments	19/30	97/99	19/21	97/108	90	31.35	0.37
	63 (44–80)	98 (93–100)	91 (70–99)	90 (83–95)		(7.74–126.95)	(0.23–0.60)
Pouch of Douglas	16/21	108/108	16/16	108/113	96	163.50	0.23
	76 (53–92)	100 (95–100)	100 (71–100)	96 (90–99)		(10.18–2624.8)	(0.11–0.51)
Vagina	7/11	117/118	7/8	117/121	96	75.09	0.37
	64 (31–89)	99 (95–100)	88 (47–100)	97 (92–99)		(10.14–556.03)	(0.17–0.80)
Rectovaginal space	7/9	120/120	7/7	120/122	99	181.50	0.22
	78 (40–97)	100 (96–100)	100 (47–100)	98 (94–100)		(11.16–2952.4)	(0.07–0.75)
Urinary bladder	2/4	123/125	2/4	123/125	97	31.25	0.51
	50 (7–93)	98 (94–100)	50 (7–93)	98 (94–100)		(5.78–169.07)	(0.19–1.35)
Rectosigmoid	28/31	97/98	28/29	97/100	97	88.51	0.10
	90 (74–98)	99 (94–100)	97 (82–100)	97 (92–99)		(12.55–624.23)	(0.03–0.29)

Data for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) are given as *n* and % (95% CI). LR+, positive likelihood ratio; LR−, negative likelihood ratio.

abnormalities were found at cystoscopy and laparoscopy in the two women with a false-positive diagnosis. Rectosigmoidal deep infiltrating endometriosis was diagnosed via TVS in 29/129 (22.5%) women with one false-positive result. The woman with a false-positive diagnosis was surgically diagnosed with uterosacral ligament endometriosis without rectosigmoidal infiltration.

Finally, test accuracies of the double- vs. triple-blinded setting were compared to evaluate a possible review bias of the surgeon if aware of presurgical TVS and/or vaginal examination findings. However, no significant differences in test accuracies (Fisher's exact test) could be observed (Tables S1 and S2 online).

DISCUSSION

In order to clearly differentiate between various anatomical sites of deep infiltrating endometriosis, all patients included in this study underwent full resection of deep infiltrating endometriosis and dissection of the pouch of Douglas if it was occluded, steps which enhanced the accuracy of the gold standard test. The results of this study strongly suggest that, especially in patients with cystic ovarian and deep infiltrating disease, vaginal examination alone may be insufficient to detect endometriosis prior to laparoscopy. In 27 women with proven endometriomas, vaginal examination yielded a sensitivity and NPV of only 41% and 87%, in contrast to the findings obtained by TVS with corresponding values of 96% and 99%, respectively. These differences were less obvious for the rectovaginal space or vaginal deep infiltrating endometriosis with lower sensitivities and NPVs for both modalities when compared with values for ovarian or rectosigmoidal endometriosis. The most striking finding of this study was the diagnostic value of TVS and the differences of corresponding values from vaginal examination regarding the detection of rectosigmoidal endometriosis. In our study, 31/129 women (24.0%) had rectosigmoidal deep infiltrating endometriosis, of which 39% were diagnosed positive for rectosigmoidal deep infiltrating endometriosis with vaginal examination with a NPV of 84%. By contrast, 90% of the women with proven rectosigmoidal disease tested positive by TVS with a NPV of 97%. The obviously lower sensitivity, PPV, NPV and accuracy of vaginal examination may be explained by two factors.

First, rectosigmoidal endometriotic nodules situated at or above the level of the uterine fundus cannot be palpated digitally but can be visualized by TVS due to the extended acoustic window of the transvaginal probe. Second, palpable nodules situated posterior to the cervix can only be allocated to anatomical structures nearby (uterosacral ligaments, rectovaginal space, vagina, rectosigmoid) with great difficulty and a lack of specificity, thereby causing false-negative findings with regard to rectosigmoidal deep infiltrating endometriosis. By contrast, TVS clearly facilitates the differential visualization and possible endometriotic involvement of these locations, thereby gaining high accuracy. Nevertheless, it should be stated that vaginal examination and evaluation of specific symptoms should not be completely omitted as a basic diagnostic tool in detecting endometriosis and planning further therapeutic interventions.

Digital examination, in addition to TVS, may help to gain a better understanding of the anatomical extent and dimension of deep infiltrating endometriosis which is of crucial importance for the surgeon. In addition, TVS is highly operator dependent and good diagnostic results may only be achieved by medical staff trained and experienced in using TVS.

To date, only two previous studies have independently compared vaginal examination with TVS for the detection of deep infiltrating endometriosis[14,27]. Although the results of these studies are in accordance with the data presented in this study with respect to rectosigmoidal endometriosis, the study designs do raise some concern. First, in both studies, the decision regarding the surgical procedure to be carried out in each individual patient was based on both the clinical and imaging results,

which may influence the results of the reference test. Second, the authors did not provide the reader with detailed information on the type and extent of the surgical procedure in cases of extensive and occluding deep infiltrating endometriosis[14] and even state that dissection of the pouch of Douglas was not performed in affected patients[15,16]. Because the final diagnostic endpoint and therefore reference value in any study evaluating a diagnostic modality is the accurate determination and evaluation of the extent of deep infiltrating endometriosis, the adequate and accurate surgical evaluation of the pelvic situs is of crucial importance for the final results of the gold standard diagnostic procedure.

Finally, our data were generated in three different institutions. Although the TVS examiner did not differ between the three centers, it should be noted that the multicenter setting underlines the general applicability of TVS, independent of the local infrastructure, i.e. outpatient clinic setting, different ultrasound machines, etc.

A possible weakness of this study is the operator dependency of TVS. Because a direct correlation may exist between the level of experience of the operator and the results of the test, i.e. TVS, it should be stated that the results of this study cannot necessarily be extrapolated to any gynecological unit with TVS facilities. Adequate training may be necessary to apply these data to other pelvic pain clinics.

In addition, this study was conducted in three different tertiary referral centers. As a consequence, NPVs and PPVs of vaginal examination and TVS, which are affected by the prevalence of the disease, may not be comparable with a non-tertiary hospital setting.

Taken together, our results strongly suggest that vaginal examination alone may be insufficient to detect endometriosis prior to laparoscopy. The use of TVS, performed by well-trained staff clearly enhances diagnostic accuracy, especially in patients with cystic endometriosis of the ovaries or deep infiltrating endometriosis of the uterosacral ligaments bladder and rectosigmoid, but appears to be equally efficient in cases of deep infiltrating endometriosis of the vagina and pouch of Douglas. Based on these data and the availability of TVS and vaginal examination, TVS can be recommended as the method of choice for the primary and preoperative assessment of pelvic pain patients with suspected endometriosis. In centers where TVS is not used on a routine basis, it should be included in the standard assessment of patients with pelvic pain.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Comparison of accuracies of the results of vaginal examination for double-blinded vs. triple-blinded setting.

Table S2 Comparison of accuracies of the results of transvaginal sonography for double-blinded vs. triple-blinded setting.