Diagnostic value of transvaginal 'tenderness-guided' ultrasonography for the prediction of location of deep endometriosis

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BACKGROUND: The aim was to evaluate the diagnostic accuracy of transvaginal tenderness-guided ultrasonography in the identification of location of deep endometriosis. METHODS: Consecutive women scheduled for surgery in our Department for clinically suspected endometriosis were included in this prospective study. All women underwent modified transvaginal ultrasonography using a stand-off in the week before surgery, which also evaluated the painful sites evocated by a gentle pressure of the probe. Five locations of deep endometriosis were considered: vaginal walls, rectovaginal septum, rectosigmoid involvement, uterosacral ligaments and anterior compartment (anterior pouch and/or bladder). Sensitivity, specificity and likelihood ratios (LR+/−) were calculated with 95% confidence intervals (CIs). RESULTS: We included 88 women; surgery associated with histopathological evaluation revealed deep endometriosis in different pelvic locations in 72 patients. With respect to the vaginal walls, transvaginal ultrasonography had a sensitivity of 91% (95% CI, 79–97%), specificity of 89% (95% CI, 81–93%), an LR+ of 8.2 and an LR− of 0.09. For endometriosis of rectovaginal septum, transvaginal ultrasonography had a sensitivity of 74% (95% CI, 64–80%), specificity of 88% (95% CI, 4–8%), an LR+ of 6.2 and an LR− of 0.3. For other locations, the sensitivity was lower (ranging from 67% to 33%) with a comparable specificity. CONCLUSIONS: This technique shows a high specificity and sensitivity in the detection of vaginal and rectovaginal endometriosis. Good specificity associated with a lower sensitivity was obtained in the diagnosis of deep endometriosis of uterosacral ligaments, rectosigmoid involvement or anterior deep endometriosis.

Keywords: transvaginal ultrasonography; deep endometriosis; sensitivity; specificity

Introduction

Deep invasive endometriosis is defined by the presence of endometriotic implants that penetrate the retroperitoneal space for a distance of 5 mm or more. This disease involves the Douglas pouch, the rectovaginal septum, intestine, anterior pouch and the uterosacral ligaments (Koninckx *et al.*, 1991) but seems difficult to assess by physical examination only (Chapron *et al.*, 2002; Abrao *et al.*, 2007). Preoperative evaluation is mandatory for the selection of different medical or surgical options and the selection of an appropriate surgeon with sufficient experience in this kind of surgery (Angioni *et al.*, 2006). In addition, the identification of different locations of deep endometriosis has a crucial role because in certain sites as, e.g. intestine or bladder, the surgery is particularly difficult and risky. Transvaginal ultrasonography should be considered the first-line procedure, but in the diagnosis of deep endometriosis this technique seems to have controversial results.

Sensitivities of plain transvaginal ultrasonography have been reported to range from 44% to 89% and specificity from 50% to 85% (Bazot *et al.*, 2003, 2004a,2007a; Dessole *et al.*, 2003). Recently, more encouraging results have been obtained by Abrao *et al.* (2007) that have evaluated the capacity of transvaginal ultrasonography to diagnose only rectosigmoid and retrocervical involvement in patients with clinically suspected endometriosis. On the contrary, other authors have reported the sensitivity to be <30% in the rectovaginal septum location (Bazot *et al.*, 2004a). Dessole *et al.* (2003) have proposed a new technique called sonovaginography for the assessment of rectovaginal endometriosis, based on transvaginal ultrasonography combined with the introduction of saline solution to the vagina that creates an acoustic window between the transvaginal probe and the surrounding structures of the vagina. As an alternative, Guerriero *et al.* (2007) created a new modality of ultrasonographic evaluation called 'tenderness-guided' ultrasonography,

using an acoustic window between the transvaginal probe and the surrounding vaginal structures by increasing the amount of ultrasound gel inside the probe cover. In addition, because the endometriotic nodule itself can induce pain, they asked patients to indicate during the ultrasonographic examination which points felt tender under gentle pressure of the probe, and they paid particular attention to evaluate those sites. Using this approach, they obtained a specificity of 95% with a sensitivity of 90% (Guerriero et al., 2007). No studies have been reported illustrating the role of this new technique in the identification of different locations of deep endometriosis.

The aim of the present study was to evaluate the diagnostic accuracy of transvaginal tenderness-guided ultrasonography in the identification of location of deep endometriotic implants.

Materials and Methods

Consecutive women scheduled for laparoscopic surgery in our Department between December 2005 and December 2007 for clinically suspected endometriosis, on the basis of patient history of pelvic pain and/or clinical examination, were included in this prospective study. This observational study protocol was approved by our Institutional Review Board. All women underwent modified transvaginal ultrasonography using a stand-off, obtained by increasing the amount of ultrasonographic gel inside the probe's cover, for better visualization of the vaginal walls and posterior and anterior fornix (previously described in detail) (Guerriero et al., 2007) (Fig. 1), in the week before surgery. The operator also evaluated with particular attention the painful sites evocated by a gentle pressure of the probe. All scans were performed by one investigator (G.S.) who had more than 15 years of experience with transvaginal ultrasonography at the onset of the study.

On the basis of our desire to have a specificity and a sensitivity of 90%, we aimed to recruit a minimum of 80 symptomatic women, of whom 40% would have deep endometriosis in one of the different considered pelvis localization. This sample size would enable an estimation of sensitivity and specificity within 20%.

By ultrasonography, deep endometriosis implants were suspected from the presence of hypoechoic linear thickening or nodules/masses with or without regular contours in five locations: (i) vaginal walls (Fig. 2), (ii) rectovaginal septum (Fig. 3), (iii) rectosigmoid involvement (Fig. 4), (iv) uterosacral ligaments (Fig. 5) and (v) anterior compartment (anterior pouch and/or bladder) (Fig. 6). In particular, rectosigmoid involvement was suspected in cases which showed the presence of nodules which had thin band-like echoes

Figure 1: A normal vaginal wall of the anterior fornix (crosses) visualized using a stand-off obtained increasing the amount of ultrasound transmission gel in the probe cover.

Figure 2: An endometriotic nodule (curved arrow) in the vaginal wall.

Figure 3: A nodule involving the rectovaginal septum (curved arrows).
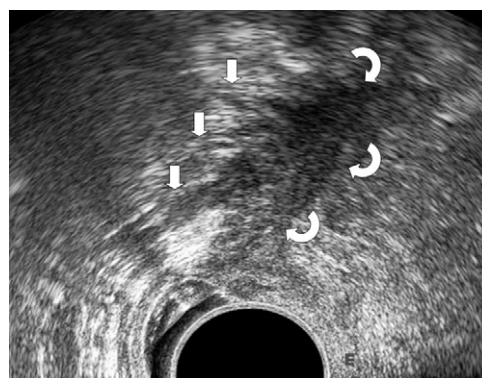The straight arrow indicates the vaginal wall.

Figure 4: A retrocervical nodule (curved arrows) with rectosigmoid involvement suspected by the presence of some thin band-like echoes (straight arrows) departing from the center of the mass as a 'Indian head dress'.

departing from the centre of the mass that were defined as 'Indian head dress' (Fig. 4). Also the anterior compartment was examined to evaluate the presence of bladder endometriosis (Figs 1 and 6).

The reproducibility of the technique was determined by evaluating 10 symptomatic patients by two examiners, each with a different level of expertise in ultrasonography in gynecology: a highly experienced examiner (S.A.) with 10 years experience and an expert (S.G.) with
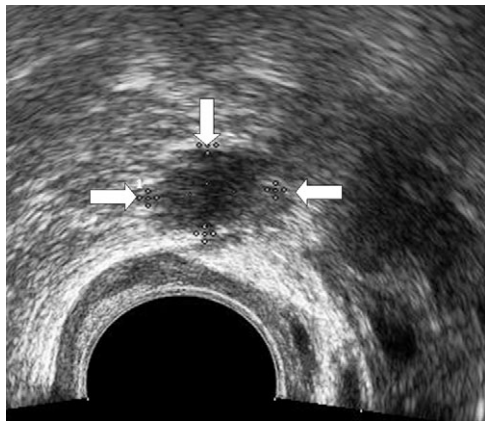
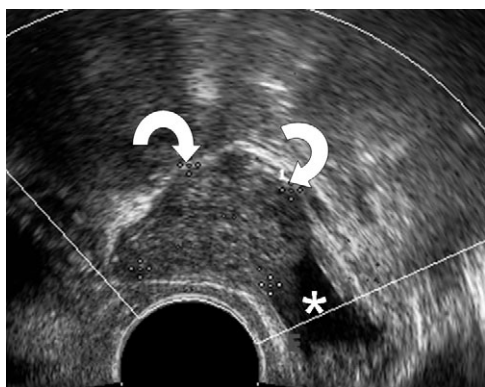**Figure 5:** A nodule of the uterosacral ligament (straight arrows).

Figure 6: A nodule of the anterior compartment (curved arrows) protruding in the bladder (asterisk).

more than 15 years experience. Intraobserver agreement was good or very good for both the examiners with different degrees of experience (kappa values ranging from 0.75 to 0.88). Interobserver agreement between expert and highly experienced operator was good (kappa value of 0.70).

In accordance with Bazot *et al.* (2004b), at laparoscopy, deep pelvic endometriosis was diagnosed from the following: (i) presence of endometrial tissue (endometrial gland and stroma) at histopathological examination of at least one resected subperitoneal lesion; (ii) direct visualization of a deep pelvic lesion of endometriosis associated with only fibrosis at biopsy, or without biopsy of the deep lesion (in this case, subperitoneal endometriosis was diagnosed on the basis of the presence of another histologically proved location of endometriosis) and (iii) complete cul-de-sac obliteration secondary to endometriosis was observed (in this case, the tissue that caused the obliteration was unresectable because the surgeons considered it too risky or because the patient refused to undergo surgical removal of

deep endometriosis). The findings at modified transvaginal ultrasonography were compared with the findings at surgery with histopathological confirmation of presence of endometriosis. Sensitivity, specificity and likelihood ratios (LR+/−) were calculated with 95% confidence intervals (CIs), according to STARD Statement for Reporting Diagnostic Accuracy Studies (Bossuyt *et al.*, 2003).

Results

We included in the study 88 women. The mean age ($\pm$ SD) of the study population was 33 ± 5 years, ranging from 20 to 45 years. The indication for surgery was clinically suspected endometriosis on the basis of patient clinical examination associated with pelvic pain in all 88 patients, of whom 10 patients had associated infertility. Forty patients (45%) reported the presence of dyspareunia and 71 (81%) the presence of dysmenorrhea. All 88 had previous treatment for persistent pelvic pain with medications (estroprogestins and/or GnRH agonist and non-steroidal anti-inflammatory drugs) for at least 2 years.

Surgery associated with histopathological evaluation revealed deep endometriosis in different pelvic locations in 72 patients. Vaginal walls involvement was present in 34 patients. Rectosigmoid involvement was present in 39 patients. Uterosacral ligaments involvement was present in 24 patients. Rectovaginal septum involvement was present in 46 patients. Anterior compartment (anterior pouch and/or bladder) involvement was present in 18 patients including four patients with bladder involvement. Isolated deep endometriosis was detected in the vagina in five (7%) cases, rectosigmoid involvement in one (1.3%) case, in the rectovaginal septum in nine cases (12.5%), in the uterosacral ligaments in 5 (7%) cases and in the anterior compartment in two cases (2.7%).

The mean time for the performance of the technique was 15–20 min in cases where the presence of deep endometriosis was suspected, less if not suspected. The mean ($\pm$ SD) ultrasonographic diameter of endometriotic nodules was 16 ± 8 mm, ranging from 10 to 34 mm. The sensitivity, specificity and LR for the five considered locations are reported in Table I. The pre-test probability of vaginal involvement of deep pelvic endometriosis in our population was 39% and this probability of disease rose to 84% when the test was positive and decreased to 6% when the test was negative. The pre-test probability of rectosigmoid involvement of deep pelvic endometriosis in our population was 44% and this probability of disease rose to 87% when the test was positive and decreased to 22% when the test was negative.

Table I. The sensitivity, specificity and LR with the 95% CI of modified transvaginal ultrasonography for the five considered locations.

Site	Specificity, % (*n*), 95% CI, %	Sensitivity, % (*n*), 95% CI, %	LR+95% CI	LR−95% CI
Vaginal involvement	89 (48/54), 83–97	91 (31/34), 79–97	8.21, 3.83–18	0.1, 0.03–0.29
Rectosigmoid involvement	92 (45/49), 37–61	67 (26/39), 55–73	8.17, 3.11–21	0.36, 0.23–0.57
Uterosacral ligaments involvement	94 (60/64), 92–100	50 (12/24), 34–60	8, 2.86–22	0.53, 0.36–0.80
Rectovaginal septum involvement	88 (37/42), 77–95	74 (34/46), 64–80	6.21, 2.68–14	0.3, 0.18–0.49
Anterior pouch (vesical and/or anterior) involvement	100 (70/70), 93–100	33 (6/18), 14–59	Infinity, 2.86–825	0.67, 0.48–0.92
Bladder involvement	100 (84/84), 94–100	100 (4/4), 40–100	Infinite, 9.50–2464	0, 0.01–1.40

The pre-test probability of uterosacral ligaments involvement of deep pelvic endometriosis in our population was 27% and this probability of disease rose to 75% when the test was positive and decreased to 17% when the test was negative. The pre-test probability of rectovaginal septum involvement of deep pelvic endometriosis in our population was 52% and this probability of disease rose to 87% when the test was positive and decreased to 25% when the test was negative. The pre-test probability of anterior pouch involvement of deep pelvic endometriosis in our population was 20% and this probability of disease rose to 100% when the test was positive and decreased to 67% when the test was negative.

Discussion

The delay in the diagnosis of endometriosis is extremely long for a disease associated with a wide rage of related symptoms including dysmenorrhea, pelvic pain, dyspareunia, bowel upset, bowel pain, infertility, presence of ovarian mass and dysuria, with the time to diagnosis reported as ranging from 5 to 8 years in recently published papers (Arruda *et al*., 2003; Husby *et al*., 2003; Sinaii *et al*., 2008). In addition, this delay does not seem to relate to the extent of the disease (Sinaii *et al*., 2008). A recent study performed among 1000 women with endometriosis showed that patients with milder disease have a time to diagnosis from the onset of symptoms which is not significantly different in comparison with patients with more severe disease including those with rectovaginal nodules (Sinaii *et al*., 2008). In our opinion, the awareness of the existence of a non-invasive technique such as ultrasonography that may be able to investigate also the different locations of deep endometriosis might reduce this delay, as previously suggested for pelvic adhesions (Guerriero *et al*., 1997; Okaro *et al*., 2006) and for ovarian endometriomas (Guerriero *et al*., 1998; Alcazar, 2001).

The use of an efficient but less invasive technique might not only decrease the waiting time for a laparoscopy, but may in some cases avoid this procedure if too risky, as in the case of a rectosigmoid involvement, and hence permit an effective medical therapy based on the administration of economic drugs such as oral contraceptives (Vercellini *et al*., 2008).

Magnetic resonance imaging (MRI) has also been used for the diagnosis of deep pelvic endometriosis and Bazot *et al*. (2004a) reported an overall good accuracy with a sensitivity of 90% and a specificity of 91%. However, other authors reported lower values (Abrao *et al*., 2007) and in certain locations this technique was found to lack sensitivity, as in the presence of rectal involvement (Kinkel *et al*., 1999). Also in cases of rectovaginal septum involvement, the sensitivity reported in a recent paper of Bazot *et al*. (2007b) was only 44%. For all these arguments and with regard to the greater expense of MRI, it can be considered to have less cost-effectiveness in comparison with ultrasonography.

Because of its high diffusion and relatively low cost and discomfort, transvaginal ultrasonography should be considered as the first-line procedure, even if it has had controversial results in the diagnosis of deep endometriosis (Table II). The present study demonstrates that our reproducible technique, guided by tenderness of the site during examination and by the creation of a stand-off to visualize the near field area of posterior and anterior fornices and the vaginal walls, shows a high specificity and sensitivity in the detection of vaginal and rectovaginal endometriosis (Table I). A good specificity, but associated with lower sensitivity, was also obtained in the diagnosis of deep endometriosis of uterosacral ligaments, rectosigmoid involvement or anterior deep endometriosis (Table I). Our results in the vaginal involvement are better than those reported by other authors who observed sensitivities ranging from 25% to 50% (Table II). Regarding rectovaginal involvement, a very wide range of sensitivities have been reported in the literature ranging from 11% to 98% (Table II). Our results are relatively good with a sensitivity of 74% (Table I).

One of the limitations of this study is the relatively small sample size for some locations as uterosacral involvement, which may lead to wide confidence intervals. Lesions involving uterosacral ligaments are also usually smaller than those at other locations. Bazot has reported in different studies a

Table II. The assessment of pelvic endometriosis by transvaginal sonography for some locations reported in the literature with the related prevalences.

Site	Authors	Sensitivity %	Specificity %	Prevalence %
Uterosacral ligaments involvement	Bazot *et al*. (2007a,b)	81	75	90
	Bazot *et al*. (2004a,b)	71	96	50
	Bazot *et al*. (2003)	75	83	81
	Present study	50	94	27
Vaginal involvement	Bazot *et al*. (2007a,b)	50	96	32
	Bazot *et al*. (2004a,b)	29	100	12
	Bazot *et al*. (2003)	25	100	13
	Present study	91	89	39
Rectovaginal septum involvement	Bazot *et al*. (2007a,b)	11	100	11
	Bazot *et al*. (2004a,b)	29	100	6
	Abrao *et al*. (2007)	98	100	51
	Present study	74	88	52
Rectosigmoid involvement	Bazot *et al*. (2007a,b)	93	100	67
	Bazot *et al*. (2004a,b)	87	97	35
	Bazot *et al*. (2003)	95	100	73
	Abrao *et al*. (2007)	98	100	39
	Present study	67	92	44

relatively wide range of sensitivity (81–71%) and specificity (96–75%) (Bazot *et al*., 2004a,2007a) (Table II) in this particular location. As reported byAbrao *et al*. (2007), the principal limiting factor of transvaginal evaluation, which was found in only a few patients and which did not significantly affects results, was that of significant pain in the Douglas pouch.

The wide range of accuracy reported in the literature (Table II) may be due to differences in the prevalence of deep endometriosis in the different locations among different studies (Table II) or because of the different 'definitions' of deep endometriosis that are presented by different authors (Bazot *et al*., 2003, 2004a, 2007a; Abrao *et al*., 2007). Concerning these relevant problems, a pioneer in the studies on endometriosis states that 'the enthusiasm to recognize and to treat deep endometriosis is already producing and will continue to produce a progressive shift of the severity of the reported series of deep endometriosis' (Koninckx, 1998). In our study, the endometriosis was extensively searched for in all the different pelvic locations, and for these reasons, lesions were isolated in only a few cases.

In our opinion, this technique may allow an accurate preoperative evaluation in selecting patients for the correct kind of surgery. In addition, this procedure should be used not only for the follow-up during medical therapy but also in the absence of therapy (Fedele *et al*., 2004) to evaluate the possible progression of the disease. This more detailed ultrasonography can be performed by every skilled operator in gynecological ultrasonography (as suggested by the good reproducibility demonstrated in the present study). However, the gynecologist who does not perform this procedure should know of the potential of this non-invasive procedure in the identification of deep endometriosis in different locations. Also the physicians should be made aware of this new technique, since it has been demonstrated that a specialist gynecologist sensitive to the problem of pelvic pain can decrease the delay in diagnosis (Greene *et al*., 2008). In conclusion, there has been an increase in the diagnostic accuracy of different imaging methodologies associated with the improvement in the capability of surgical techniques as laparoscopy. This, together with the wide range of effective drugs against the major symptoms, means that the creation of a one-stop endometriosis clinic can be finally proposed, enabling most patients to benefit from the need for a only single hospital visit and the availability of immediate results. This approach could significantly shorten 'the interval' between referral and initiation of treatment, surgical or medical, as previously demonstrated in cases of recurrent miscarriage (Habayeb and Konje, 2004).

Author's Role

Design and institution of the study protocol, collection and analysis of data, drafting the article, final preparation of the article and approval of the final version—S.G.

Review of the article, approval of the final version—S.A.

Collection and analysis of data, approval of the final version—M.G.

Acquisition of data, revising the article, approval the final version—B.V.

Revising the article, final approval—S.A.

Revision of the study protocol, review of the article, approval of the final version—G.B.M.

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