

Preoperative work-up for patients with deeply infiltrating endometriosis: transvaginal ultrasonography must definitely be the first-line imaging examination

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BACKGROUND: Transvaginal ultrasonography (TVUS) has important advantages compared with transrectal ultrasonography (TRUS): it is less invasive, is cost-effective, is a familiar and well-accepted approach, and anesthesia is not required. We compared the accuracy of TVUS and TRUS for diagnosing rectal wall involvement in patients presenting with histologically proved deeply infiltrating endometriosis (DIE).

METHODS: Prospective study of 134 patients with histologically proved DIE underwent preoperative investigations using both TVUS and TRUS. The radiologist (TVUS) and sonographer (TRUS) were unaware of the clinical findings but knew that DIE was suspected.

RESULTS: DIE was confirmed histologically for all the patients. A rectal wall involvement was histologically proved for 75 patients (56%). For the diagnosis of infiltration of the intestinal wall, TVUS and TRUS, respectively, had a sensitivity of 90.7% and 96.0%, a specificity of 96.5% and 100.0%, a positive predictive value of 97.1% and 100.0% and a negative predictive value of 88.9% and 95.2%.

CONCLUSIONS: TVUS and TRUS have similar degrees of accuracy for predicting intestinal involvement. TVUS must be the first-line imaging process to perform for patients presenting with clinically suspected DIE. The question for the coming years is to define if it is necessary for TRUS to be carried out systematically in cases of clinically suspected DIE.

Key words: deep endometriosis / deeply infiltrating endometriosis / preoperative work-up / transvaginal ultrasonography / transrectal ultrasonography

Introduction

There are three types of endometriotic lesions: superficial endometriosis (peritoneal and/or ovarian), ovarian endometriomas and deeply infiltrating endometriosis (DIE). DIE is a specific entity, histologically defined when endometriotic lesions penetrate more than 5 mm under the peritoneum (Koninckx *et al.*, 1991). DIE is responsible for pelvic pain symptoms (Fauconnier and Chapron, 2005), and

the type of pain is related to location of the DIE lesions (Fauconnier *et al.*, 2002), whereas the severity is correlated to depth of the DIE nodules (Koninckx *et al.*, 1991; Porpora *et al.*, 1999; Chapron *et al.*, 2003a).

Management of DIE can be either medical (Igarashi *et al.*, 1998; Fedele *et al.*, 2000; Fedele *et al.*, 2001; Hefler *et al.*, 2005; Vercellini *et al.*, 2005; Razzi *et al.*, 2007) or surgical (Urbach *et al.*, 1998; Chapron *et al.*, 2003b; Darai *et al.*, 2005; Vignali *et al.*, 2005;

Ribeiro *et al.*, 2006; Seracchioli *et al.*, 2007). Success of surgery is correlated with the radicality of the exeresis (Chopin *et al.*, 2005). A satisfactory work-up (questioning, clinical examination, imaging) is necessary preoperatively to establish the map of DIE lesions and to obtain the patient's consent (Chapron *et al.*, 2004a).

Preoperative knowledge about intestinal infiltration is essential because, if surgery is decided, a specific intestinal surgical procedure will be necessary (Chapron *et al.*, 2003b). In these situations, patients must be informed preoperatively concerning the surgical risks (Landi *et al.*, 2006; Dubernard *et al.*, 2008). Because clinical examination is of limited use for establishing the extent of the DIE lesions (Chapron *et al.*, 2002; Abrao *et al.*, 2007), it is necessary to use non-invasive imaging processes prior to surgery. Transrectal ultrasonography (TRUS) was demonstrated to be efficient for the diagnosis of rectal wall infiltration by DIE lesions (Chapron *et al.*, 1998; Fedele *et al.*, 1998; Delpy *et al.*, 2005; Bazot *et al.*, 2007a). Magnetic resonance imaging (MRI), also proposed, presents the great advantage of offering the possibility of obtaining a complete pelvic evaluation with a single imaging procedure (Siegelman *et al.*, 1994; Kinkel *et al.*, 1999; Bazot *et al.*, 2004; Chapron *et al.*, 2004b; Kataoka *et al.*, 2005; Abrao *et al.*, 2007). More recently, transvaginal ultrasonography (TVUS), which is the imaging method of choice for diagnosis of endometriomas (Mais *et al.*, 1993; Guerriero *et al.*, 1995), was proposed for the diagnosis of DIE (Gorell *et al.*, 1989; Bazot *et al.*, 2003; Koga *et al.*, 2003). This method of investigation offers the advantages of accessibility and cost-effectiveness when compared with MRI and tolerability when compared with TRUS.

The aim of this study is to compare the results of TVUS with those of TRUS, which is the investigation of choice for the diagnosis of rectal wall infiltration, and to clarify whether there are limits for TVUS.

Materials and Methods

Between January 2005 and July 2007, we performed a prospective study during which time patients suffering from pelvic pain (alone or associated with infertility) underwent complete surgical exeresis of DIE lesions (Chapron *et al.*, 2003b). DIE was suspected in all cases preoperatively (questioning, clinical examination, imaging). Diagnosis of DIE was histologically proven for each patient. DIE lesions were classified in five locations (bladder, uterosacral ligament(s) (USL), vagina, intestine, ureter) according to a previous classification (Chapron *et al.*, 2006). For each patient, data were collected: (i) general patients' characteristics (age, gravidity, parity, height, weight); (ii) history of previous medical and/or surgical treatment for endometriosis; (iii) preoperative painful symptoms scores (dysmenorrhea, deep dyspareunia, non-cyclic chronic pelvic pain, gastrointestinal and lower urinary tract symptoms) according to visual analogue scale; (iv) stage of the disease and mean revised American Fertility Society (AFS) scores (total, implant, adhesion) according to the AFS (AFS, 1985); (v) number and location of DIE lesions (bladder, USL, vagina, intestine, ureter); (vi) existence of associated ovarian endometrioma.

All women underwent both TVUS and TRUS prior to surgery. The radiologist (for the TVUS) and the sonographer (TRUS) were informed that DIE was suspected but were blinded to the results of clinical findings and previous imaging examinations. They were asked whether there was involvement of the digestive wall.

Transvaginal ultrasonography

TVUS was performed with a Toshiba ultrasound machine, using a 5–9 MHz transducer. TVUS was performed without bowel preparation by a single

experienced radiologist (A.E.M.B.). Routine analysis of uterus and ovaries took place first. Moreover, the protocol included the study of the peritoneal surfaces (pouch of Douglas, vesicouterine pouch) and the retroperitoneal space (i.e. USL, torus uterinum and posterior fornix of the vagina). The probe was first positioned in the lower vagina in front of the anal canal. The probe was moved slowly down and up to the posterior fornix of the vagina. By moving the probe, all the anterior rectosigmoid space could be analyzed. The normal aspect of the rectum/sigmoid colon muscularis propria is hypoechoic and thin (<3 mm). Intestinal DIE was defined as an irregular hypoechoic mass, with or without hypo/hyperechoic foci involving the rectum/sigmoid colon muscularis propria (Bazot *et al.*, 2007b). Particular attention was paid to the appendix and small. The aspect of torus uterinum and USL was observed at the same time with sagittal and parasagittal views of hypoechoic and irregular nodules.

Transrectal ultrasonography

TRUS was performed with an Olympus UM 160 Echoendoscope (SCOP Medecine Olympus, 94150 Rungis, France) by a single examiner (G.R.). It was carried out without sedation, 2 h after a rectal enema. Endoscopic examination of the rectum and the distal sigmoid colon was first performed, placing the probe in the sigmoid colon, over the aortic bifurcation and/or the upper part of the body of the uterus. The probe was then slowly withdrawn allowing optimum imaging of rectal and sigmoid colon walls, with instillation of water into the intestinal lumen and alternating use of 5, 7.5 and 12 MHz frequencies. Normal intestinal walls usually appear as a five-layer structure: the fourth hypoechoic layer corresponds to the muscularis propria. The surrounding areas were also imaged, with particular attention paid to the ovaries, cervix and body of the uterus, pouch of Douglas, USL areas and torus uterinum. DIE showed up as hypoechoic peri-digestive nodules of rounded or roughly triangular shape. A diagnosis of digestive tract infiltration was confirmed when a hypoechoic thickening of the muscularis propria was demonstrated at ultrasound (Chapron *et al.*, 1998), either isolated or involved in an adjacent pelvic location.

Statistical analysis

For each imaging process (TVUS and TRUS), sensitivity, specificity, positive and negative predictive value (PPV and NPV), 95% confidence intervals and kappa test of concordance in the diagnosis of rectal wall involvement for patients presenting histologically proved DIE were calculated (McKenzie *et al.*, 1997). Data are presented as mean \pm SD.

Results

During the study period, 134 patients were enrolled. Patients' characteristics are presented in Table I. Four hundred and ten ($n = 410$) histologically proved DIE lesions were removed during complete DIE surgical exeresis: USL (132 lesions; 32.2%); vagina (80 lesions; 19.5%); bladder (22 lesions; 5.4%); intestine (163 lesions; 39.7%) and ureter (13 lesions; 3.2%). The mean number of DIE lesions per patient was 3.1 ± 2.1 (range 1–10). Fifty-one patients ($n = 51$; 38.1%) had an ovarian endometrioma associated with the DIE lesions.

Patient distribution, according to the main location of the DIE Classification (Chapron *et al.*, 2006), was as follows: USL 25 patients (18.7%); vagina 23 patients (17.2%); bladder 11 patients (8.2%); intestine 66 patients (49.2%); and ureter 9 patients (6.7%) (Table II). A total of 75 patients (56.0%) presented with histologically proved intestinal involvement (the 66 patients classified as 'intestine' and 9 as 'ureter') (Table II). The mean number of intestinal DIE lesions per patient was 2.7 ± 1.5 (range 1–9). For 70 patients (93.3%), the

Table I Characteristics of patients with DIE in the study

Patients' characteristics (n = 134)	
Age (years) ^a	32.1 ± 5.0 (range 22–47)
Gravidity ^a	0.7 ± 1.1 (range 0–7)
Parity ^a	0.4 ± 0.8 (range 0–5)
Height (cm) ^a	164.7 ± 7.6 (range 146–197)
Weight (kg) ^a	59.6 ± 10.6 (range 37–87)
Previous treatment for endometriosis	
Hormonal treatment (%)	100.0
Surgery (%)	65.7
Mean number of previous surgeries	1.1 ± 1.1 (range 0–4)
Preoperative painful symptoms scores ^{a,b,c}	
Dysmenorrhea	7.8 ± 1.9 (range 0–10)
Deep dyspareunia	5.3 ± 3.0 (range 0–10)
Non-cyclic chronic pelvic pain	3.8 ± 3.0 (range 0–10)
Gastrointestinal symptoms	5.7 ± 3.4 (range 0–10)
Lower urinary tract symptoms	1.8 ± 3.0 (range 0–10)
Mean implant score rAFS ^{a,d}	14.8 ± 13.1 (range 4–46)
Mean adhesion score rAFS ^{a,d}	29.2 ± 26.8 (range 0–104)
Mean total score rAFS ^{a,d}	44.0 ± 35.7 (range 4–150)
rAFS stage ^d (%)	
Stages I + II	37.3
Stages III + IV	62.7

^aData are presented as mean ± SD.

^bSometimes more than one for the same patient.

^cVisual analogue scale.

^dScore according to the revised American Fertility Society Classification (AFS, 1985).

intestinal DIE lesions were associated with other DIE lesions (USL, vagina, bladder, ureter).

The anatomic distribution of intestinal DIE lesions (163 lesions for 75 patients) is presented in Table III. All the patients presented a

rectal and/or sigmoid DIE lesion. Ninety-six percent (96.0%; 72 cases) of the patients presented a rectal wall infiltration. Appendix ($n = 8$ patients) and omentum ($n = 3$ patients) DIE lesions were never isolated and always associated with rectal and/or sigmoid DIE lesions.

Among the patients with intestinal DIE lesions ($n = 75$), only 34 patients (45.3%) presented a single intestinal lesion (not taking omentum and appendix DIE lesions into account). Among the 41 patients with more than one intestinal DIE lesions (not taking omentum and appendix DIE lesions into account), 21 patients presented, associated with the rectal and/or sigmoid DIE lesions, a 'right intestinal DIE lesion' located at the cecum and/or ileum (cecum: $n = 4$ patients; ileum: $n = 13$ patients; cecum and ileum: 4 patients). So, for patients with rectal and/or sigmoid DIE lesions ($n = 75$), the rate of associated 'right intestinal involvement' (ileum and/or cecum) was 28% ($n = 21$ patients) (Fig. 1).

The sensitivity, specificity, PPV and NPV of TVUS and TRUS for the diagnosis of rectal wall involvement are presented in Table IV. TVUS and TRUS yielded a diagnosis of deep rectal endometriosis in 68 (90.7%) and 72 patients (96.0%), respectively. The kappa test of concordance was 0.86 for TVUS and 0.96 for TRUS.

Discussion

This prospective study demonstrates two points: first, TVUS is accurate to diagnose intestinal wall involvement for patients with DIE and results are similar than those observed with TRUS; second, in cases of rectal DIE lesions, there are associated cecum and/or ileum DIE lesions in 28% of the cases.

It is essential that these results, which agree with the conclusions of two recent studies (Abrao et al., 2007; Bazot et al., 2007b), should be taken into consideration when treating DIE patients. If surgery is decided, the DIE lesions must all be totally excised (Chapron et al., 2003b; Chopin et al., 2005; Fedele et al., 2005; Vignali et al., 2005). Consequently, if there is any deep intestinal infiltration, a specific segmental intestinal resection procedure is required (Remorgida et al., 2005; Abrao et al., 2008). Bowel segmental resection is by no

Table II Distribution of patients according to main location of the DIE

Main lesion ^a	n ^b	Associated lesions					Total ^c		
		USL			Va	Bl		In	Ur
		R	L	B					
USL	25	6	15	4				29 (7.1)	
Vagina	23	7	7	4	23			45 (11.0)	
Bladder	11	0	1	0	0	11		12 (2.9)	
Intestine	66	15	11	21	49	9	147	273 (66.6)	
Ureter	9	0	0	6	8	2	16	51 (12.4)	
	134	28	34	35 ^d	80	22	163	410	

Values in parentheses are percentages.

^aAccording to a previously published surgical classification for DIE (Chapron et al., 2006).

^bNumber of patients.

^cNumber of histologically proven DIE lesions.

^dEach lesion of bilateral pair counted as part of pair, so total number of individual lesions = 212.

Bl, bladder; USL, uterosacral ligament; Va, vagina; Bl, bladder; Ur, ureter; In, intestine; R, right; L, left; B, bilateral.

Table III Anatomic distribution of intestinal DIE lesions^a in 75 patients

Location	Patients n (%)	Intestinal DIE lesions	
		n	Mean number
Rectum	72 (96.0)	84	1.1 ± 0.5 (range 0–4)
Sigmoid	29 (38.7)	31	0.4 ± 0.5 (range 0–2)
Cecum	8 (10.7)	10	0.1 ± 0.4 (range 0–3)
Ileum	17 (22.7)	27	0.4 ± 0.9 (range 0–6)
Appendix	8 (10.7)	8	0.1 ± 0.3 (range 0–1)
Omentum	3 (4.0)	3	0.4 ± 0.2 (range 0–1)
Total	75 ^a	163	2.7 ± 1.5 (range 1–9)

^aSome patients presented several intestinal DIE lesions.

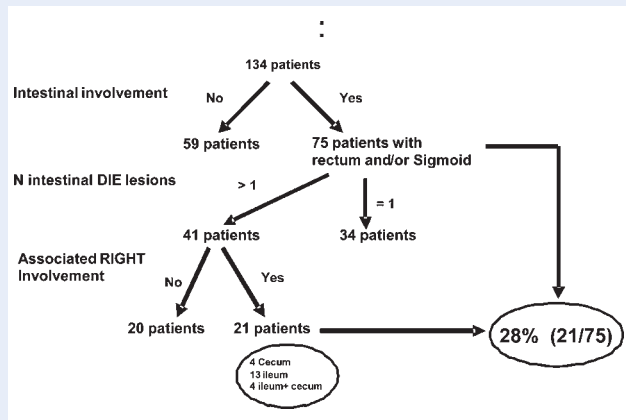


Figure 1 Intestinal endometriosis: the anatomic distribution of lesions in 134 patients with DIE.

means an innocuous surgical procedure and presents a real risk of complications (Darai *et al.*, 2007). This point is essential insofar as the patients concerned are young (32.1 ± 5.0 years in this study) and present painful functional symptoms without any question of malignancy. Preoperative knowledge of the existence of intestinal infiltration is important in order to be able to inform the patient about the various treatment possibilities together with their respective risks and

to establish a good basis for deciding on the treatment strategy in agreement with her.

Apart from its excellent diagnostic efficiency, TVUS has important advantages compared with TRUS. It is a less invasive means of investigation than TRUS, is cost-effective, familiar and well accepted by patients in obstetrics and gynecology, and can be used in all cases without anesthesia. Unlike TRUS, TVUS performs well for diagnosis of ovarian endometriomas (Bazot *et al.*, 2007b), which are often associated with DIE lesions and must be considered as a marker for severity of the disease (Chapron *et al.*, 2008). Furthermore, DIE lesions are frequently multifocal (Chapron *et al.*, 2003b). In our experience, intestinal DIE lesions are associated with other DIE locations (USL, vagina, bladder, ureter) in 93% of cases. TVUS gives better results than TRUS for the diagnosis of these associated DIE lesions, notably when there is infiltration of the USL and bladder (Bazot *et al.*, 2007b). Further work is required to establish whether TVUS should be systematically combined in the future with water-contrast in the rectal lumen (Valenzano Menada *et al.*, 2008) or saline solution in the vagina (Dessole *et al.*, 2003) and whether the use of ultrasound transmission gel improves the diagnosis accuracy (Guerriero *et al.*, 2007). While, like others (Bazot *et al.*, 2007b), we performed TVUS without bowel preparation, further studies will be necessary to find out if mechanical lower bowel cleansing using a rectal enema prior to the examination (Abrao *et al.*, 2007) will improve TVUS accuracy.

Although TVUS is efficient for the diagnosis of rectal involvement, this technique raises two controversial points. First, TVUS is an operator-dependent procedure. Specific training for the practitioners is essential to understand the DIE TVUS imaging semiology. Since our radiologists came to the operating room to find out for themselves what the problems facing us are and to understand the anatomy of the posterior pelvic compartment, we have seen better accuracy for the imaging results. Second, intestinal DIE lesions are multifocal in the digestive wall in almost one case out of two (Chapron *et al.*, 2003b). In our experience, rectal lesions are associated with a second intestinal lesion in 54.6% of cases (41/75) (Fig. 1). Similarly, rectosigmoid lesions are associated with ileo-cecum DIE lesions (cecum and/or terminal ileum) in 28% of cases (Fig. 1). These 'high sigmoid' and/or 'right bowel lesions' (cecum and/[EI] or ileum) will be more difficult to diagnose with TVUS. Their frequency justifies carrying out a systematic complete intestinal work-up, since the number and location of intestinal lesions governs the choice of surgical procedure. In case of a single intestinal lesion, and especially when it is isolated (without other associated DIE lesions in the bladder, the

Table IV Sensitivity, specificity, positive and negative predictive value of TVUS and TRUS in the diagnosis of rectal involvement for patients presenting with DIE (n = 134)

	TVUS		TRUS	
	% (n)	95% CI	% (n)	95% CI
Sensitivity	90.7% (68/75)	0.84/0.97	96.0% (72/75)	0.92/1.00
Specificity	96.5% (56/58)	0.92/1.01	100% (59/59)	1.00/1.00
PPV	97.1% (68/70)	0.93/1.01	100% (72/72)	1.00/1.00
NPV	88.9% (56/63)	0.81/0.97	95.2% (59/62)	0.90/1.01

PPV, positive predictive value; NPV, negative predictive value.

vagina or the ureter), laparoscopic surgery is the preferred operating technique (Possover et al., 2000; Duepree et al., 2002; Darai et al., 2005; Jatan et al., 2006; Ribeiro et al., 2006). In case of multiple intestinal lesions, and especially when a 'right bowel lesion' (cecum and/or terminal ileum) is associated with the rectal lesion, laparotomy may be required given that in these situations, two bowel resections will be necessary to carry out complete exeresis during the same operation. To the best of our knowledge, our study is the first to underline the frequency and insist on the importance of diagnosing 'right bowel involvement' in the diagnostic and treatment strategy for patients presenting intestinal DIE lesions.

The multifocality of DIE lesions (Chapron et al., 2006) justifies a multidisciplinary diagnostic and treatment management. The possibility of intestinal lesions associated with gynecologic DIE requires close collaboration with gastrointestinal tract surgeons, and also urologists in the event of ureter involvement. Concerning the diagnosis, collaboration with radiologists is essential in order to establish a precise pre-operative map of the DIE lesions. In practice, the main question is to identify which is the best radiological examination to associate with TVUS to diagnose these DIE lesions. TRUS presents the same limitations as TVUS in the case of 'high' or 'right' (cecum and/or ileum) bowel lesions. Although MRI is an efficient means of examination allowing a complete pelvic work-up to be established (Kinkel et al., 1999), bowel movements, notably in the sigmoid and ileo-cecal junction areas, may generate artifacts (Abrao et al., 2007) that will hamper the diagnosis with the risk of overlooking and under-estimating the extent of intestinal DIE lesions. Studies are needed to find out if multi-slice computerized tomography is of interest in this context (Biscaldi et al., 2007).

In view of its simplicity, good tolerance and efficiency, our results encourage us to propose TVUS as the radiological examination which must be performed systematically and at first intention. TVUS is just as accurate as TRUS for diagnosing intestinal infiltration and yields better results for associated DIE locations (notably the bladder and USL). MRI must be also proposed systematically in our opinion in order to make a complete pelvic work-up. So the basic question in daily practice is whether it is necessary to carry out TRUS systematically in a patient presenting a clinical suspicion of DIE. If intestinal infiltration is found at TVUS, we feel that TRUS is not needed, given that it will provide no further information than TVUS. However, if there is a real clinical suspicion of intestinal involvement (Chapron et al., 2002; Abrao et al., 2007) but neither TVUS nor MRI show any intestinal infiltration digestive, TRUS must be performed.

Conclusion

With experience, we have changed our radiological diagnostic approach. Initially, we felt that TRUS was a key means of investigation to be carried out systematically in order to look for intestinal involvement in patients presenting a clinical suspicion of DIE. Today, we consider that TVUS must be the first-line imaging process for these patients. The goal in the coming years is to define according to precise criteria the modalities for preoperative radiological work-up for these patients. If TVUS and MRI definitely show intestinal infiltration, we recommend in future that TRUS should not be used in addition.

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