ORIGINAL ARTICLE



Pelvic floor dysfunction at transperineal ultrasound and voiding alteration in women with posterior deep endometriosis

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Abstract

Introduction and hypothesis Posterior deep infiltrating endometriosis (DIE) has been associated with pelvic floor muscle (PFM) alteration and voiding dysfunction (VD). The aim of this study is to evaluate the correlation between the presence of VD and altered PFM morphometry, objectively evaluated using 3D/4D transperineal ultrasound at rest and during dynamic maneuvers, in patients with posterior DIE.

Methods A prospective study was conducted on 108 symptomatic women scheduled for surgical removal of posterior DIE. The study population was divided in two groups according to presence or absence of VD on the Bristol Female Lower Urinary Tract Symptoms (BFLUTS). A 3D/4D transperineal ultrasound was performed to compare the following PFM morphometric parameters: levator hiatus area (LHA), antero-posterior (AP) and left-right (LR) diameters and levator ani muscle (LAM) coactivation. LAM coactivation was defined as the paradoxical contraction of the pelvic floor muscle during the Valsalva maneuver causing a smaller LHA than in the resting state.

Results Forty-eight (45.2%) women presented VD, while 60 (54.8%) women did not report any voiding complaints. Baseline characteristics did not significantly differ between the two groups. We did not find any significant statistical differences in PFM parameters between the two groups, except for a higher rate of levator ani muscle coactivation in women with VD compared with women without VD [64.6% (31/48) versus 31.7% (19/60), respectively; p = < 0.001].

Conclusions In women affected by posterior DIE, LAM coactivation at 3D/4D transperineal ultrasound seems to be more frequent in patients with than without VD.

Keywords Transperineal ultrasound · Endometriosis · LAM coactivation · Voiding dysfunction

Introduction

Endometriosis is a chronic inflammatory condition affecting women in reproductive age, with an overall prevalence of 5-10% [1].

Endometriosis can be divided into superficial, ovarian and deep infiltrating endometriosis (DIE). In DIE, endometriotic lesions penetrate pelvic structures, causing adhesions and

Diego Raimondo die.raimondo@gmail.com anatomical distortion. In particular, posterior DIE can involve the uterosacral ligament (USL), torus uterinum, posterior vaginal wall and anterior rectal wall [2, 3]. Although the exact prevalence of posterior DIE is unknown, it affects nearly 12% of women with endometriosis [4]. Typical symptoms related to posterior DIE are chronic pelvic pain, dysmenorrhea, dyspareunia and dyschezia [5].

Recent studies showed that posterior DIE can alter voiding function [3, 6-10], probably because of the neurotropism expressed by endometriotic cells and the underlying pelvic inflammatory condition that involves nerve endings [11, 12]. Moreover, deep endometriotic lesions can also be associated with hypertonic or non-relaxing pelvic floor muscle (PFM) dysfunction [13-15].

Hypertonic or non-relaxing pelvic floor muscle (PFM) dysfunction is defined as impaired relaxation or constant contraction causing hypertone, spasm, loss of strength and coactivation of PFM. Several factors may contribute to the

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development of non-relaxing PFM dysfunction in women with chronic pelvic pain, including direct or neuropathic injury of the pelvic floor muscle, antalgic reaction to pelvic pain symptoms and inflammation. Non-relaxing PFM dysfunction has been associated with various symptoms including impaired voiding or defecation, pelvic pain and sexual dysfunction [16, 17].

Voiding dysfunction can be caused by both detrusor underactivity and mechanical or functional bladder outlet obstruction. Both external urethral sphincter and pubo-coccygeal muscles contribute to functional bladder outlet obstruction and may cause dysfunctional voiding in women [16]. Female dysfunctional voiding is defined as an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the periurethral striated or levator ani muscle during voiding in neurologically normal women [18].

Assessment of PFM using digital palpation or electromyography may be subjective and elicit pain, causing muscle contraction, which could represent a bias. Previous studies demonstrated that transperineal ultrasound can represent an objective, reliable and non-invasive diagnostic tool for PFM morphometry evaluation [19, 20].

Our group previously reported that women with DIE may have an increased PFM tone, evaluated with 3D/4D transperineal ultrasound, compared with both healthy women and women with exclusive ovarian endometriosis [13, 14].

The aim of this study is to assess a possible correlation between the presence of voiding dysfunction (VD) and altered PFM morphometry using 3D/4D transperineal ultrasound at rest and during dynamic maneuvers in patients with posterior DIE.

Materials and methods

This prospective study was conducted between January 2017 and June 2018 in a tertiary referral center for treatment of endometriosis. During the study period, consecutive symptomatic fertile women scheduled for complete laparoscopic excision of macroscopic posterior deep endometriotic lesions were enrolled in the study.

Exclusion criteria included: current or previous pregnancy, previous surgery for deep endometriosis, postmenopausal status, pelvic organ prolapse, vulvodynia, active vaginal or urinary infections, congenital or acquired abnormalities of the pelvis or pelvic floor, bladder endometriosis, use of antidepressants, history of chronic pelvic pain conditions (i.e., pelvic inflammatory disease, interstitial cystitis, irritable bowel disease), sexual abuse or vesical neurological problems. Understanding of written and spoken Italian language was required.

Prior to surgery, an accurate medical history was collected, and all patients underwent bimanual and speculum examinations as well as pelvic ultrasonography. When necessary, additional preoperative imaging methods were performed to plan surgery, including magnetic resonance imaging and multidetector computerized tomography. Data about age, body mass index (BMI), medical history, pain symptoms, and current or previous hormonal therapy (estro-progestins or progestins) were collected. Pain symptoms related to endometriosis (chronic pelvic pain, dysmenorrhea, dyspareunia, dysuria, dyschezia) were assessed using a numerical rating scale (NRS) from 0 to 10.

Patients gave written informed consent to participate in this study. The study protocol was approved by the local institutional Ethics Committee (196/2015/O/Sper).

At enrollment, patients were asked to complete the Bristol Female Lower Urinary Tract Symptoms (BFLUTS) questionnaire to evaluate and assess urinary symptoms [21]. The BFLUTS questionnaire is a validated questionnaire designed to enable the assessment and quantification of the widest range of lower urinary tracts symptoms (LUTS) in women and their impact on sexual function and quality of life. It is divided into three items to evaluate bladder filling, emptying and incontinence [22]. In particular, we analyzed VD expressed as hesitancy, slow or intermittent stream, straining or sensation of incomplete emptying. Women who answered never to all items were included in the 'non-voiding dysfunction group.' Conversely, patients with at least one voiding symptom were included in the 'voiding dysfunction group.'

Two experienced operators, blinded to group assignment, performed 3D/4D transperineal ultrasound after complete bladder emptying and before gynecological bimanual examination and transvaginal ultrasound scans in order not to evoke pain. Bladder emptying was confirmed by transabdominal ultrasound with evaluation of the post-void residual (pathological post-void residual was defined as volume > 150 ml). The evaluation of PFM with 3D/4D was performed using a Voluson E6 system (GE Healthcare, Zipf, Austria) with an RAB 8-4 MHz volume transducer, with the highest quality and 85° angle. As previously described, the convex volumetric ultrasound transducer was positioned translabially in the midsagittal plane, with patients in lithotomy position. Measurements were performed in the axial plane of minimal hiatal dimensions [20]. Youssef et al. demonstrated good testretest, intra- and inter-observer reliability for this procedure [19]. Moreover, they were comparable to different pelvic floor assessment techniques and diagnostic tools [23]. The anteroposterior (AP) diameter, left-right (LR) diameter and levator hiatus area (LHA) were recorded to evaluate PFM tone at rest, muscle strength during PFM contraction and levator ani muscle (LAM) coactivation during the Valsalva maneuver. Threedimensional volume acquisition was required for LHA, AP and LR diameter measurements at rest, while 4D acquisition was necessary for dynamic evaluations. Each difference in these parameters, during PFM contractions or the Valsalva maneuver, was calculated as percent change from baseline (i.e., levator hiatus area narrowing = (levator hiatus area at rest - levator hiatus area at contraction)/levator hiatus at rest \times 100) [14].

LAM coactivation was defined as the paradoxical contraction of the pelvic floor muscle concomitant with the abdominal wall. During ultrasound examination this condition was described as a smaller antero-posterior (AP) diameter during the Valsalva maneuver than in the resting state. LAM coactivation was considered persistent if still present after three attempts [14, 24] (Fig. 1).

All volumes, areas and diameters were subsequently evaluated by another investigator, blinded to clinical and sonographic data, using a specific software (4D View 14.4; GE Healthcare).

To determine the sample size, we performed a pilot study with 64 patients, using the presence/absence of levator ani coactivation and presence/absence of voiding dysfunction as variables. These data were used to determine the appropriate sample size for detecting a significant difference between two independent groups. A two-sided test was conducted assuming a 5% significance level and 80% test power. The sample size calculated with the input data (dichotomous data) using a prevalence of voiding dysfunction of 61% (among women with PFM dysfunction) and 34% (among women without PFM dysfunction) equaled 106.

Continuous data were expressed in terms of mean \pm SD or median (range). Categorical variables were expressed as

absolute number and percentage. Univariate comparisons of continuous data were analyzed with the two-sample *t*-test or Mann-Whitney test, while categorical data were compared using Fisher's exact test or chi-squared test as appropriate. p < 0.05 was considered significant for all tests. Statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS) software, version 24.0 (IBM Corp., Armonk, NY, USA).

Results

One hundred eight women with posterior DIE were included in the study. In all patients, pathological examination confirmed the diagnosis of endometriosis. According to the results of the BFLUTS questionnaire, patients enrolled were divided into two different groups: 48 (45.2%) women with VD and 60 (54.8%) women without VD. Baseline characteristics did not significantly differ between the two groups for either preoperative data or disease localizations (Tables 1 and 2).

The most frequent VD symptom detected in the 'voiding dysfunction group' was 'slow or intermittent stream' in 38/48 (79.2%), while 'hesitancy' and 'straining or sensation of incomplete emptying' were reported in 37/48 (77.1%).

After bladder emptying, no patient presented a pathological post-void residual at transabdominal ultrasound. Transperineal ultrasound was successfully performed in all

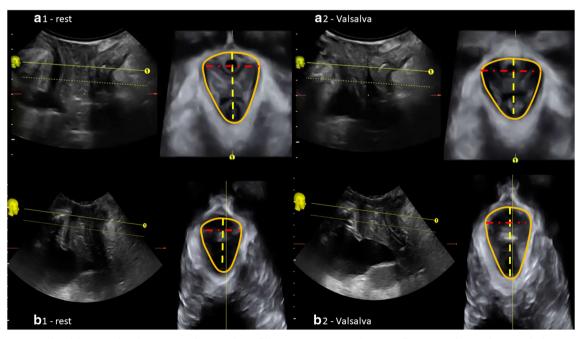


Fig. 1 A: Transperineal images showing a normal expansion of the antero-posterior (AP) diameter under maximum Valsalva maeuver. A1 and A2 show the midsagittal plane and the 3D reconstruction of the levator hiatus area (LHA) at rest and at maximum Valsalva maneuver, respectively. B: Transperineal images showing abnormal reduction of the

antero-posterior (AP) diameter under maximum Valsalva maneuver (levator ani coactivation). B1 and B2 show the midsagittal plane and the 3D reconstruction of the levator hiatus area (LHA) at rest and at maximum Valsalva maneuver, respectively

	VD group (n.48)	Non-VD group (n. 60)	<i>p</i> value
Age (years), mean ± DS	37±6.9	36±7.1	0.7 ^a
Body mass index (kg/m ²), mean \pm DS	23.5 ± 5.3	22.6 ± 3.6	0.5^{a}
Hormonal therapy, <i>n</i> (%)	43 (89.6%)	49 (81.7%)	0.2 ^b
Current smoker, n (%)	9 (18.7%)	11 (18.3%)	1.0 ^b
Preoperative pain symptoms assessed through nur	nerical rating scale (NRS), median (range)	
Dysmenorrhea	8 (0–10)	9 (0–10)	0.2^{a}
Dyschezia	5 (0-10)	5 (0–10)	0.4^{a}
Dysuria	0 (0–10)	0 (0–10)	1 ^a
Dyspareunia	6 (0–10)	7 (0–10)	0.2^{a}
Chronic pelvic pain	5 (0-10)	0 (0–10)	0.2^{a}

Table 1	Preoperative data	of the voiding	dysfunction	(VD) g	group and nor	1-VD group
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^a Student's t-test or Mann-Whitney test, as appropriate

^b Chi-squared test or Fisher's exact test, as appropriate

patients, and no patients were excluded because of discomfort related to this examination. The outcomes of static and dynamic pelvic floor muscle examinations are shown in Table 3. Persistent LAM coactivation was detected in 31/48 (64.6%) of women with VD compared with 19/60 (31.7%) of patients without VD (p = < 0.001).

Transperineal measures of LHA at rest and during contraction did not have significant statistical differences between the two groups.

Discussion

In this study we did not find any significant statistical difference in PFM evaluation between the two groups, except for AP diameters during the Valsalva maneuver. Women with posterior DIE and voiding symptoms presented a higher rate of LAM coactivation compared with women without VD, indicating a possible impact of loss of muscle coordination on VD.

 Table 2
 Endometriotic localizations in the voiding dysfunction (VD) group and non-VD group

Localization, n (%)	VD group (n.48)	Non-VD group (n. 60)	<i>P</i> value (< 0.05)
Rectum	31 (64.6%)	35 (58.3%)	0.5
Recto-vaginal septum	14 (29.2%)	15 (25%)	0.6
Utero-sacral ligaments	13 (27.1%)	17 (28.3%)	0.9
Parametrium	5 (10.4%)	2 (3.3%)	0.1
Sigmoid	7 (14.6%)	13(21.7%)	0.3
Vagina	0 (0%)	2 (3.3%)	-

Chi-squared test or Fisher's exact test, as appropriate

Voiding dysfunctions are among the most studied postoperative functional complications of surgical treatment for posterior DIE, affecting 5-20% of patients [9]. To differentiate preoperative urinary symptoms from those arising de novo, attention has recently been focused on the evaluation of urinary dysfunction related to posterior DIE per se [3, 9, 10, 25–27]. After the main confounding factors (such as previous surgery, pelvic pain syndromes and concomitant bladder endometriosis) had been excluded, 45.2% of the women in this study had VD at the BFLUTS questionnaire. These data are consistent with the evidence gathered from previous studies. Using an informal questionnaire, De Lapasse et al. prospectively observed that 5 (42%) of 12 patients with posterior DIE complained of straining to void [8]. Panel et al. (2016) in a prospective study on 20 patients with posterior DIE reported voiding symptoms in 11 cases (55%) on the Pelvic Floor Distress Inventory [25]. De Resende et al. (2018) in a recent prospective study assessing urinary alterations in women with DIE using the International Prostate Symptom Score (IPSS) found high rates of VD (from 28 to 43%) and a strong association between VD and parametrial infiltration by the disease. The authors hypothesized that parametrial lesions can irritate sympathetic fibers, thus leading to urethral sphincter hypertone and causing outlet obstruction [26].

Chronic pelvic pain syndromes including DIE are usually associated with pelvic floor muscle hypertone and spasms, muscular weakness, loss of coordination and relaxation negatively affecting micturition [15, 28]. Dysfunctional voiding could also be explained by a learned behavioral disturbance, in which the patient attempts to inhibit micturition by contracting the levator ani muscle during emptying [29].

Loss of muscle coordination, including learned behavioral disturbance, could be reversed by conservative measures including patient education, behavioral modifications, lifestyle

Transperineal measures, mean \pm SD		VD group $(n = 48)$	Non-VD group ($n = 60$)	p value
At rest (3D)	LHA (cm ²)	11.4 ± 2.8	11.6 ± 3.2	0.8 ^a
	AP diameter (cm)	4.8 ± 0.7	4.6 ± 0.6	0.3 ^a
	LR diameter (cm)	3.3 ± 0.5	3.2 ± 0.5	0.7^{a}
During PFM contraction (4D)	LHA (cm ²)	9.8 ± 2.2	9.6 ± 2.2	0.8^{a}
	Narrowing from baseline (%)	13.6 ± 11.8	15.3 ± 12.0	0.6^{a}
	AP diameter (cm)	4.0 ± 0.8	3.8 ± 0.6	0.5^{a}
	Reduction from baseline (%)	16.7 ± 15.8	16.1 ± 12.1	0.9^{a}
	LR diameter (cm)	3.0 ± 0.4	3.1 ± 0.4	0.8^{a}
	Reduction from baseline (%)	10.2 ± 15.5	5.1 ± 12.4	0.2^{a}
During Valsalva maneuver (4D)	LHA (cm ²)	12.3 ± 3.1	13.1 ± 4.0	0.4^{a}
	Enlargement from baseline (%)	9.3 ± 22.4	14.4 ± 24.6	0.4^{a}
	AP diameter (cm)	4.7 ± 0.7	5.0 ± 0.8	0.1^{a}
	Increase from baseline (%)	-0.2 ± 17.9	10.5 ± 20.5	0.03 ^a
	LR diameter (cm)	3.5 ± 0.5	3.6 ± 0.5	0.5^{a}
	Increase from baseline (%)	6.9 ± 18.3	11.0 ± 14.8	0.3 ^a
LAM coactivation		31 (64.6%)	19 (31.7%)	<0.001 ^b

 Table 3
 Pelvic floor muscle morphometry at three- (3D) and four-dimensional (4D) transperineal ultrasound in the voiding dysfunction (VD) group and non-VD group

LHA levator hiatus area, AP antero-posterio diameter, LR left-right diameter

^a Student's *t*-test

^b Fisher's exact test

changes, and pelvic floor rehabilitation/physical therapy through pelvic floor exercises and bio-feedback [30].

Even if it is possible to assess muscular disturbances with digital palpation or electromyography, these evaluations could be subjective or evoke pain and consequent muscular contractions, altering results [3, 15]. Our group previously demonstrated that 3D/4D transperineal ultrasound might provide an objective and non-invasive method to evaluate the presence of pelvic floor dysfunction in patients with DIE [13, 14].

Strengths of our study include its prospective design, sample size calculation, sonographer investigator blinded to clinical data, the use of an objective ultrasound evaluation to assess PFM and a specific questionnaire to assess voiding function. Our results, however, cannot be generalized because of the selective inclusion of women with symptomatic DIE scheduled for surgery and the exclusion criteria adopted to have a histological confirmation of endometriosis and to reduce potential biases, respectively. The sample size (n = 106) of the study was calculated for equal and balanced groups. In this study, we did not reach the number required for both groups, and this could be a limitation of our study. However, the re-calculated power for unequal sample sizes was 80.7%, using the number of the enrolled patients for each group. Another possible limit of our study was the lack of urodynamic evaluation for the assessment of voiding disturbances. Nevertheless, voiding symptoms were self-reported by the patients using a validated questionnaire. Lastly, an Italian translation of the BFLUTS questionnaire used in this study has not yet been validated.

In conclusion, in women affected by posterior deep infiltrating endometriosis, LAM coactivation seems to be more frequent in patients with voiding dysfunction than in patients without impaired voiding phase. In women affected by posterior DIE and VD, 3D/4D transperineal ultrasound may be an objective and non-invasive tool for the assessment of PFM dysfunction. Other studies are needed to justify a causative connection between these two factors.

Compliance with ethical standards

Conflicts of interest None.

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