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Assessment of levator hiatal area using 3D/4D transperineal ultrasound in women with deep infiltrating endometriosis and superficial dyspareunia treated with pelvic floor muscle physiotherapy: randomized controlled trial

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KEYWORDS: 3D/4D transperineal ultrasound; chronic pelvic pain; deep infiltrating endometriosis; dyspareunia; pelvic floor muscles; pelvic floor physiotherapy

CONTRIBUTION

What are the novel findings of this work?
Pelvic floor physiotherapy appears to be a promising new treatment to improve pelvic floor relaxation, superficial dyspareunia and chronic pelvic pain in women with deep infiltrating endometriosis (DIE).

What are the clinical implications of this work?
In the context of tailored multidisciplinary care, pelvic floor physiotherapy may represent an additional valid, minimally invasive, innovative and well-tolerated therapeutic option for women with DIE.

ABSTRACT

Objectives *Deep infiltrating endometriosis (DIE) is associated with chronic pelvic pain, dyspareunia and pelvic floor muscle hypertonia. The primary aim of this study was to evaluate the effect of pelvic floor physiotherapy (PFP) on the area of levator ani hiatus during Valsalva maneuver, assessed using transperineal ultrasound, in women with DIE suffering from superficial dyspareunia.*

Methods *This was a randomized controlled trial of 34 nulliparous women diagnosed with DIE and associated superficial dyspareunia. After an initial clinical examination, all patients underwent three-dimensional/four-dimensional (3D/4D) transperineal ultrasound to measure the levator hiatal area (LHA) at rest, on maximum pelvic floor muscle contraction and on maximum Valsalva maneuver, and were asked to rate their pain symptoms using a numerical rating scale (NRS). Eligible women were assigned randomly (1:1 ratio) to no intervention (control group, 17 women) or treatment with five individual sessions of PFP (study group, 17 women). Four months after the first examination, all women underwent a second evaluation of pain symptoms and LHA on transperineal ultrasound. The primary outcome measure was the percentage change in LHA on maximum Valsalva maneuver between the baseline and follow-up examinations. The percentage changes in pain symptoms between the two examinations, including superficial and deep dyspareunia, dysmenorrhea, chronic pelvic pain, dysuria and dyschezia, were also evaluated.*

Results *Thirty women, comprising 17 in the study group and 13 in the control group, completed the study and were included in the analysis. The percentage change in LHA on maximum Valsalva maneuver between the two examinations was higher in the study group than in the control group (20.0 ± 24.8% vs −0.5 ± 3.3%; P = 0.02), indicating better pelvic floor muscle relaxation. After PFP treatment, the NRS score for superficial dyspareunia remained almost unchanged in the control group (median change in NRS (Δ-NRS), 0 (interquartile range (IQR), 0–0)) while a marked reduction was observed in the study group (median Δ-NRS, −3 (IQR, −4 to −2); P < 0.01). Moreover, there was a significant difference between the PFP and control groups with regards to the change in*

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chronic pelvic pain (median Δ-NRS, 0 (IQR, −2 to 0) vs *0 (IQR, 0–1);* P = *0.01).*

Conclusions *In women with DIE, PFP seems to result in increased LHA on Valsalva maneuver, as observed by 3D/4D transperineal ultrasound, leading to improved superficial dyspareunia, chronic pelvic pain and pelvic floor muscle relaxation.* © *2021 International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Endometriosis, defined as the presence of endometrial glands and stroma outside the uterine cavity, is a chronic inflammatory disease. It affects 6–10% of women of reproductive age and is associated with chronic pelvic pain (CPP) and/or infertility[1,2]. Deep infiltrating endometriosis (DIE) occurs when endometriotic implants penetrate below the peritoneal surface, involving the rectovaginal septum, rectum, uterosacral ligaments, ureters and urinary bladder[3–5]. DIE is strongly associated with severe pelvic pain, including dysmenorrhea, dyspareunia, CPP, dysuria and dyschezia, as well as bladder, sexual and bowel dysfunctions[6–8]. The connection between DIE and deep dyspareunia (pain in the vagina and pelvis during sexual intercourse[9]) has been previously studied[10,11]. However, only a few studies have focused on superficial dyspareunia (pain occurring in or around the vaginal entrance[9]), which seems to be widespread in women with endometriosis and in most cases concomitant with deep dyspareunia[12,13].

CPP syndromes, such as endometriosis, can be associated with increased pelvic floor muscle tone, suggesting a role for the pelvic floor in the pathogenesis of pain[14,15]. Pelvic floor muscle contractility and relaxation can be evaluated reliably and quantitatively using three-dimensional/four-dimensional (3D/4D) transperineal ultrasound (TPU) by measuring dynamic changes in the levator ani muscle hiatal dimensions on pelvic floor contraction and during Valsalva maneuver[16–19]. Women with DIE were found to have pelvic floor muscle hypertonia, as demonstrated by a smaller levator hiatal area (LHA) at rest and reduced enlargement of the LHA on Valsalva maneuver, showing inadequate pelvic floor relaxation[20,21]. Pelvic floor physiotherapy (PFP) is a minimally invasive treatment often used to manage dysfunctions including vestibulodynia, pelvic organ prolapse, urinary and fecal incontinence, obstructed defecation and sexual dysfunction[22–25]. Moreover, PFP seems to be promising in women with DIE, leading to an improvement in dyspareunia and pelvic floor muscle relaxation[26].

The primary aim of this study was to evaluate the effect of PFP on the LHA during Valsalva maneuver in women with DIE suffering from superficial dyspareunia. Secondary outcomes included the change in LHA at rest and on pelvic floor muscle contraction (PFMC) and in pain symptoms after PFP.

METHODS

Study design and participants

This was a randomized controlled trial (RCT) conducted between June 2018 and December 2019 at our referral center for endometriosis. Women were contacted and invited to participate in accordance with the following inclusion criteria: age between 18 and 45 years, clinical and ultrasound diagnosis of DIE according to the criteria of the International Deep Endometriosis Analysis Group[27], and associated superficial dyspareunia. Exclusion criteria included previous or current genital malignancy, pelvic organ prolapse, previous surgery for DIE, current or previous pregnancy, congenital or acquired abnormalities of the pelvis or pelvic floor, history of sexual abuse, current genitourinary infection and presence of other causes of CPP; written informed consent was obtained from all participating women. The study protocol was approved by the local institutional ethics committee (345/2017/O/Sper) and the study was registered on ClinicalTrials.gov (ID NCT03572075).

First examination

During the first clinical examination, participants were asked to rank their endometriosis-related pain symptoms (CPP, dysmenorrhea, dysuria, dyschezia, dyspareunia) using a numerical rating scale (NRS) from 0 (no pain) to 10 (worst pain)[28], with a focus on dyspareunia, differentiating between deep dyspareunia (pain in the vagina and pelvis during sexual intercourse) and superficial dyspareunia (pain that occurs in or around the vaginal entrance)[9]. In addition, each woman underwent 3D/4D-TPU, to measure the LHA at rest, on maximum PFMC and on maximum Valsalva maneuver. Data on age, body mass index, medical history, current or previous hormone therapies and previous surgery were collected for each woman.

Transperineal ultrasound

3D/4D-TPU was performed by the same operator (S.D.F.) using the validated OmniView-VCI technique, as previously described[29,30]. All acquisitions were performed using a Voluson E6 ultrasound system (GE Healthcare, Zipf, Austria) with a RAB 8–4-MHz volume transducer. The acquisition angle was set at 85°, with high render quality. The convex volumetric ultrasound transducer was positioned translabially in the midsagittal plane, with the patient in the lithotomy position[31]. All volumes and LHAs were anonymized and subsequently analyzed offline by one of the investigators who was blinded to clinical and sonographic data, using dedicated software (4D View 14.4; GE Healthcare). All LHAs were measured by tracing the inner edge of the levator ani muscle, the pubic symphysis and the inferior pubic ramus (Figure 1).

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Randomization

Participants were assigned randomly to no intervention (control group) or to receive PFP sessions (study group) in a 1:1 ratio. Block randomization was computer generated and the allocation was hidden in opaque envelopes until randomized.

Physiotherapy treatment

Before the start of therapy, the participants received information on pelvic floor anatomy and function, with the help of anatomical illustrations. In addition, the physiotherapist (V.P.), experienced in pelvic floor muscle dysfunction, performed a digital evaluation of the pelvic floor muscle tone. This was performed after the TPU, given that digital examination may induce pain with consequent contraction of the pelvic floor, which could affect the LHA assessment. Pubococcygeus and ischiococcygeus muscle tone were assessed bilaterally at rest, and during pelvic floor contraction and relaxation. After the first examination, the women in the study group underwent five individual sessions of PFP, of 30 min each, on weeks 1, 3, 5, 8 and 11. In each session, the women underwent a Thiele massage, which consists of digital pressure and subsequent stretching of the muscles in order to relax them, restoring normal pelvic floor tone and the ability to coordinate muscle behavior, as previously described[12,32].

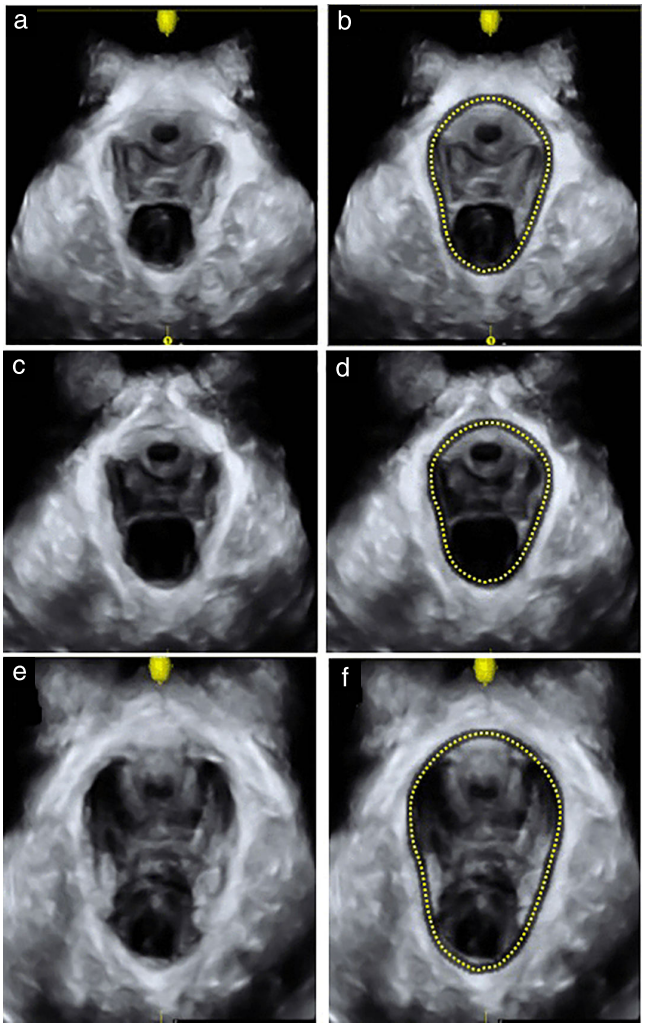


Figure 1 Three-/four-dimensional transperineal ultrasound images showing the levator hiatus at rest (a,b), on maximum pelvic floor muscle contraction (c,d) and on maximum Valsalva maneuver (e,f), and tracing of the hiatal area (b,d,f).

Second examination

Four months after randomization, all participants underwent a second examination, in which they were asked to rank again their endometriosis-related pain symptoms and underwent another 3D/4D-TPU assessment of the LHA at rest, on maximum PFMC and on maximum Valsalva maneuver. In addition, the women in the study group were asked to rate their satisfaction with their physiotherapy treatment using a 5-item scale (1, very dissatisfied; 2, dissatisfied; 3, neither satisfied nor dissatisfied; 4, satisfied; and 5, very satisfied).

Main outcome measures

The primary outcome measure of the study was the percentage change in LHA during maximum Valsalva maneuver from the first to the second examination, which was calculated using the following formula: ((LHA during Valsalva on the second examination – LHA during Valsalva on the first examination)/LHA during Valsalva on the first examination) × 100.

Secondary outcome measures included the proportional change in LHA at rest and on maximum PFMC between the first and second examinations as well as the absolute and proportional changes in pain symptoms, including superficial and deep dyspareunia, dysmenorrhea, CPP, dysuria and dyschezia in the two groups.

Statistical analysis

The sample-size estimate was based on the effect size of physiotherapy on LHA during maximum Valsalva maneuver that we considered clinically significant. Assuming a baseline LHA[20] of 14.5 cm^2, and a potential increase at the second examination of 0 ± 1 cm^2 (0%) in the control group and of 1.5 ± 1 cm^2 (10.3%) in the study group, we needed a total sample of 18 subjects, nine per group, to detect the specified mean difference between the groups with 80% power using a two-sided 5%-level test. Comparisons between the groups were performed using the Wilcoxon–Mann–Whitney test for continuous variables, and the Fisher exact test or χ^2 test, when appropriate, for categorical variables. All randomized patients were analyzed, regardless of adherence to the allocated treatment and without imputation for missing data. Continuous data are expressed as mean ± SD or median (interquartile range (IQR)), and categorical variables as *n* (%). Data analysis was carried out using Stata Software, version 15 (StataCorp., 2017; Stata Statistical Software, College Station, TX, USA), and the statistical significance level was set at 5%.

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RESULTS

Between June 2018 and December 2019, 34 women were enrolled and randomly assigned to the two groups: 17 were assigned to the study group and underwent PFP and 17 were assigned to no intervention (control group). Four patients in the control group dropped out and did not participate in the second examination. The data of the remaining 30 women (17 in the study group and 13 in the control group) were included in the final analysis. All patients in the PFP group attended all five physiotherapy sessions.

The baseline characteristics of the women at first examination are reported in Table 1. Among the 30 participants, 11 did not take any medical therapy for endometriosis (five in the control group and six in the study group), while 19 took estroprogestin or progestin therapy (eight in the control group and 11 in the study group). No differences were noted between the two groups with respect to medical therapy ($P = 0.86$), which was not modified during the study period. As regards the location of endometriosis, all women had posterior DIE (in the rectum, rectovaginal septum, vagina, uterosacral ligaments), 18 had adenomyosis (60%) and 13 had ovarian endometriomas (43%). None of the patients had anterior DIE. All women had superficial dyspareunia, while 24 (80%) also reported deep dyspareunia. No significant differences were found between the two groups regarding the intensity of symptoms and LHA measurements.

Table 1 Baseline characteristics, symptoms and ultrasound findings of 30 women with deep infiltrating endometriosis (DIE) and superficial dyspareunia who completed the study, according to whether they were randomized to pelvic floor physiotherapy (PFP) or no intervention (controls)

Characteristic	*Controls (n = 13)*	*PFP (n = 17)*	P
Age (years)	32.8 ± 6.7	32.5 ± 7.6	1.0
BMI (kg/m^2)	21.7 ± 4.4	22.1 ± 3.5	0.48
Adenomyosis	7 (54)	11 (65)	0.55
Ovarian cyst	4 (31)	9 (53)	0.23
Anterior DIE	0 (0)	0 (0)	1.0
Location of posterior DIE			
Left USL	8 (62)	7 (41)	0.27
Right USL	3 (23)	5 (29)	1.0
Rectum	4 (31)	5 (29)	1.0
RVS	1 (8)	3 (18)	0.61
Vagina	0 (0)	1 (6)	1.0
Superficial dyspareunia*	8 (7–10)	8 (6–10)	0.78
Deep dyspareunia*	7 (6–8)	7 (4–9)	0.72
Dysmenorrhea*	3 (0–6)	4 (0–8)	0.52
Chronic pelvic pain*	3 (0–5)	5 (0–6)	0.32
Dysuria*	0 (0–0)	0 (0–0)	0.66
Dyschezia*	0 (0–4)	0 (0–6)	0.94
LHA at rest (cm^2)	10.8 ± 2.1	10.3 ± 2.1	0.41
LHA on max PFMC (cm^2)	8.1 ± 2.2	9.0 ± 2.4	0.17
LHA on max VM (cm^2)	12.2 ± 2.2	11.4 ± 2.4	0.15

Data given as mean ± SD, *n* (%) or median (interquartile range). *Assessed with numerical rating scale. BMI, body mass index; LHA, levator hiatal area; max, maximum; PFMC, pelvic floor muscle contraction; RVS, rectovaginal septum; USL, uterosacral ligament; VM, Valsalva maneuver.

The proportional changes in LHA at rest, on maximum PFMC and on maximum Valsalva maneuver between the first and the second examinations in the two groups are shown in Figure 2. The percentage change in LHA on maximum Valsalva maneuver was higher in the study group than in the controls (20.0 ± 24.8% *vs* −0.5 ± 3.3%, respectively; $P = 0.02$), indicating better pelvic floor muscle relaxation. No significant difference was noted between the two groups with regard to the percentage change in LHA at rest and on maximum contraction between the first and second examinations.

Changes in symptoms, as evaluated by NRS scores, between the baseline and follow-up examinations in the two groups are reported in Table 2. With respect to change in dyspareunia intensity, the difference between the cases and controls failed to reach statistical significance for deep dyspareunia ($P = 0.07$), however, there was a significant reduction in the NRS scores for superficial dyspareunia in the study group compared with the control group ($P < 0.01$). In particular, the NRS score for superficial dyspareunia remained almost unchanged in the control group (median change in NRS (Δ-NRS), 0 (IQR, 0–0)) while a marked reduction was observed in the study group (median Δ-NRS, −3 (IQR, −4 to −2)). Moreover, the change in CPP was significantly different between the control and study groups (median Δ-NRS, 0 (IQR, 0–1) *vs* 0 (IQR, −2 to 0); $P = 0.01$), showing improvement of this symptom in patients who underwent PFP. There was no significant difference between the two groups in the change in other symptoms (dysmenorrhea, ovulatory pain, dyschezia, dysuria) between the first and second examinations.

At the second examination, 76% (13/17) of women in the study group reported they were 'very satisfied' and 24% (4/17) 'satisfied' with the physiotherapy treatment.

DISCUSSION

This is the first RCT to assess the benefits of PFP on pelvic floor relaxation and pain symptoms in women with DIE. Patients in the PFP arm showed a higher percentage change in LHA on maximum Valsalva maneuver than did controls, reflecting an improvement in pelvic floor relaxation after treatment. In addition, women who participated in PFP sessions showed an improvement in superficial dyspareunia and CPP in comparison with controls.

Dyspareunia frequently affects women with endometriosis, with an incidence ranging between 32% and 70%, and represents one of the most challenging symptoms of the disease[33,34]. Most studies have generally focused on dyspareunia as painful intercourse, without discriminating between deep and superficial dyspareunia[33,34]. Recent studies highlight the fact that superficial dyspareunia is frequently reported by women with endometriosis, especially with DIE, both as an isolated symptom and concurrent with deep dyspareunia[12,13]. Moreover, women with

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superficial dyspareunia seem to have pelvic floor muscle hypertonia[13]. The reduction in superficial dyspareunia in women who underwent PFP, which is in line with findings of previous studies[12,26,32], suggests that this condition is related to inadequate relaxation of the pelvic floor muscles. Conversely, the absence of an effect of PFP on deep dyspareunia confirms that the origin of this symptom is mainly related to the presence of the endometriotic lesion itself, and that pain is likely to be caused by mechanical pressure or traction exerted on rigid fibrotic tissue during sexual intercourse[21].

We also observed a subjective reduction in CPP in the study group compared with the controls, in line with previous studies conducted on women with CPP treated with physiotherapy[22–25,35]. Whether pelvic floor hypertonia is the cause or effect of CPP in women with DIE remains unclear. Potential mechanisms explaining the relationship between chronic pain and pelvic floor hypertonia in patients with endometriosis include peripheral and central sensitization to pain with lowering of nociceptive thresholds, along with abnormalities of pelvic floor relaxation and coordination[21,36,37]. Pelvic floor hypertonic disorder, either as the primary factor or as a component of pelvic pain syndrome, often represents an aggravating factor for progression and prolongation of CPP[14]. Identification and treatment of pelvic floor hypertonia may contribute to breaking this vicious circle, resulting in improvement in the pain and dysfunction associated with DIE. In particular, the Thiele massage technique was found to improve pelvic floor myalgia, reduce pain levels and improve sexual function in women with pelvic floor muscle hypertonia, CPP, interstitial cystitis and dyspareunia[32–34].

3D/4D-TPU is an objective and reproducible method for evaluating pelvic floor muscle function, including

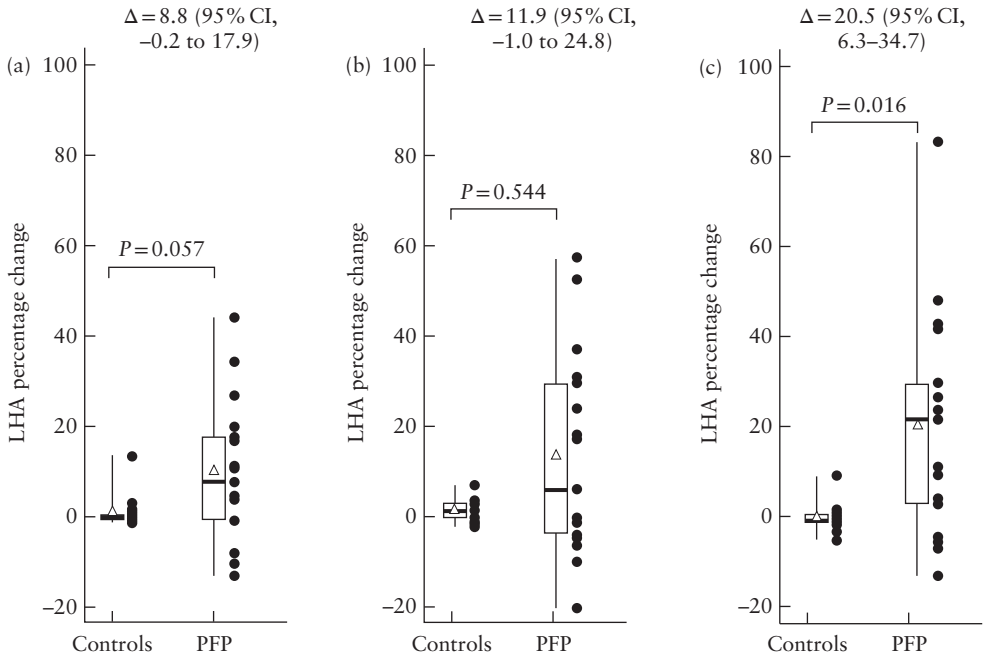


Figure 2 Dot plots combined with box-and-whiskers plots showing percentage change in levator hiatal area (LHA) at rest (a), on maximum pelvic floor muscle contraction (b) and on maximum Valsalva maneuver (c) from the first to the second examination, in women treated with pelvic floor physiotherapy (PFP) and controls. Boxes are median and interquartile range, whiskers are range and triangles indicate mean. Differences (Δ) in LHA changes and *P*-values are also shown.

Table 2 Numerical rating scale (NRS) scores for pain symptoms at the baseline and follow-up examinations and difference (Δ) in scores between the two examinations in 30 women with deep infiltrating endometriosis and superficial dyspareunia, according to whether they were randomized to pelvic floor physiotherapy (PFP) or no intervention (controls)

	Controls (n = *13*)			*PFP* (n = *17*)			
Symptom	*First examination*	*Second examination*	*Δ*	*First examination*	*Second examination*	*Δ*	P*
Superficial dyspareunia	8 (7–10)	8 (7–10)	0 (0–0)	8 (6–10)	4 (3–7)	−3 (−4 to −2)	< 0.01
Deep dyspareunia	7 (6–8)	6 (5–7)	0 (0–0)	7 (4–9)	6 (3–8)	−1 (−2 to 0)	0.07
Dysmenorrhea	3 (0–6)	3 (0–6)	0 (0–0)	4 (0–8)	0 (0–5)	0 (−1 to 0)	0.30
Chronic pelvic pain	3 (0–5)	5 (0–5)	0 (0–1)	5 (0–6)	4 (0–5)	0 (−2 to 0)	0.01
Ovulatory pain	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–5)	0 (0–0)	0 (0 to 0)	0.07
Dysuria	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0 to 0)	0.88
Dyschezia	0 (0–4)	0 (0–5)	0 (0–0)	0 (0–6)	0 (0–5)	0 (0 to 0)	0.70

Data are given as median (interquartile range). *Difference in Δ-NRS between control and PFP groups.

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contraction and relaxation. Moreover, it is a non-invasive technique, compared with traditional digital examination, well tolerated by patients and relatively easy to learn[38,39]. These features make TPU particularly useful for the assessment of women suffering from CPP and DIE[13,35]. In addition, TPU can be used to provide visual feedback during PFP to women with DIE, in order to enhance their confidence and optimize therapy[26]. Using this technique, improvements in pelvic floor relaxation capability after physiotherapy sessions can be quantified by measuring the LHA on Valsalva maneuver. Other advantages of TPU are that it is widely available to gynecologists and that it can be performed fairly quickly in a clinical setting[38].

Considering the high satisfaction rates with the PFP treatment expressed by the participants, together with the positive clinical and sonographic findings of this study, we believe that clinicians should consider the use of PFP as an additional therapeutic strategy in the multidisciplinary management of women with endometriosis, pelvic floor hypertonia and superficial dyspareunia[40].

We feel that further studies, preferably multicenter, are warranted to confirm our findings before large-scale implementation of physiotherapy protocols for the management of women with DIE suffering from superficial dyspareunia. Moreover, a long-term follow-up study to evaluate the maintenance of outcomes after PFP is warranted; this is currently under consideration.

The main strengths of this study are its originality and randomized design, and the use of a non-invasive and reliable technique to assess the pelvic floor muscles. Moreover, all sonographic data were analyzed by operators blinded to the women's clinical data. Another strength is the use of a standardized physiotherapy protocol (Thiele massage), which has previously shown good efficacy in the treatment of women with CPP, dyspareunia and pelvic floor hypertonia[41,42]. The main limitation of the study is the small study population. Moreover, women were not blinded to the intervention, therefore, it is possible that the placebo effect may have contributed to the observed improvement in dyspareunia and pelvic pain.

In conclusion PFP seems to be effective in improving pelvic floor muscle relaxation, superficial dyspareunia and CPP in women with DIE. As such, the studied physiotherapy protocol may improve patients' quality of life and sexual life, which are often compromised in women with DIE[11,43]. 3D/4D-TPU is a reliable, objective and non-invasive method for assessing the pelvic floor muscles in these women. In the current context of tailored, multidisciplinary care[40], PFP may represent an additional valid, minimally invasive, innovative and well-tolerated therapeutic option for women with DIE, particularly those with superficial dyspareunia and CPP.

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