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Original Research Article

Widespread Pain Hypersensitivity and Lumbopelvic Impairments in Women Diagnosed with Endometriosis

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Abstract

Objective. To explore hypersensitivity to pain and musculoskeletal impairments in the lumbopelvic area in women with and without endometriosis. **Methods**. This cross-sectional study included 66 women (41 women with endometriosis and 25 healthy women). Pain and related catastrophizing thoughts were assessed through a numeric rating scale, pressure pain thresholds (PPTs), the slump test, and the Pain Catastrophizing Scale. Lumbopelvic muscles were evaluated through ultrasound imaging, flexor/extensor resistance tests, and the lumbopelvic stability test. **Results**. Women with endometriosis showed increased self-reported intensity of current pelvic pain (CuPP), reduced local PPTs (42.8–64.7% in the affected area, *P*-value $<.001$) and higher prevalence of lumbar nerve root impingement/irritation pain and catastrophizing thoughts (*P*-value $\leq.002$). Moreover, affected women showed decreased thickness of transversus abdominis, reduced resistance of flexor and extensor trunk muscles and lower lumbopelvic stability (*P*-values $<.030$). Endometriosis stage and severity of CuPP were related to worse results in these parameters. **Conclusions**. The presence of pain sensitization signs and lumbopelvic impairments, more pronounced in patients with stage IV endometriosis and moderate/severe CuPP, warrants the development of rehabilitation interventions targeting pain and lumbopelvic impairments in women with endometriosis.

Key Words: Abdominal Muscles; Back Muscles; Endometriosis; Lumbopelvic Stability; Pelvic Pain; Pain Pressure Threshold

Introduction

Endometriosis is a heterogeneous disease characterized by the proliferation of endometrial-like tissue outside the uterus cavity (also called endometriotic lesions), with extensive variation in anatomical and clinical presentation, and symptoms do not always correspond to the disease burden [1]. It is one of the most prevalent chronic diseases in females, estimating that approximately 2–15% of women in childbearing age are affected worldwide, raising up to 20–25% among those women with chronic pelvic pain and up to 50% among infertile women [2]. Moreover, it is believed that the incidence is uprising year after year [3].

Although medical treatment (including pain killers and hormonal contraceptives), in addition to surgical ablation of endometriotic lesions in most severe cases, significantly reduces endometriosis-related burden of symptoms, treatment options are currently a palliative approach, that usually fail to completely manage symptoms [4]. In this regard, pain is considered the most common, relevant and debilitating symptom in women with endometriosis [5]. These patients often report chronic pain in the pelvis, even more pronounced during menstruation (dysmenorrea) or during daily life activities such as sexual relationships (dyspareunia), defecation (dyschezia), or urination (dysuria) [6]. Indeed, histopathological studies have revealed that endometriotic lesions are often innervated, which may be related to the increased pain reported by these patients [7]. Moreover, chronic pain may lead to a local sensitization of the affected area, as well as to a central sensitization, as recently reported for patients with intense pelvic pain [8] when compared with healthy women. Additionally, nonspecific long-term health effects on affected women have been recently reported, such as digestive complaints, psychosocial impairments, sexual functioning, or infertility [9–12], leading to a significant reduction in work productivity [13] and quality of life [14]. It is also worth mentioning that endometriosis has also been linked to two- to threefold increased risk for ovarian cancer [15].

Contrary to this well-documented array of symptoms, to the best of our knowledge, there is no available data regarding the musculoskeletal consequences of endometriosis in the affected area. In this regard, chronic pain may lead to decreased activity and, thus, to physical deconditioning, which in turn may cause lumbopelvic instability, generating a vicious cycle, as suggested in different pathologies characterized by chronic pain in the lumbopelvic area [16]. In fact, lumbopelvic stability exercises have been demonstrated to be a crucial factor to improve efficacy during daily life activities involving upper and/or lower extremities [17], ensuring the proper activation of the kinetic chain through pre-/coactivation of deep abdominal and lumbar muscles during shoulder and leg movements [18, 19]. Thus, in order to identify potential targets for rehabilitation interventions, the aim of this preliminary study was to explore pain (self-reported, nociceptive and lumbar nerve root impingement/irritation) and the presence of impairments in the lumbopelvic area in women with endometriosis and healthy unaffected women, and analyze how endometriosis stage and pain severity related to the presence of lumbopelvic impairments.

Methods

Design, Setting, and Participants

This descriptive cross-sectional study was conducted between January 2018 and January 2019. Eligible for the study were women 25–50 years of age who had a clinical diagnosis of endometriosis and had been admitted to the Obstetrics and Gynecology Units of both University Hospitals (San Cecilio and Virgen de las Nieves), Granada, Spain. Moreover, women had to be experiencing endometriosis-related symptoms and having passed a period equal to or greater than 3 months since the last surgery. The exclusion criteria included a diagnosis of any concomitant condition such as musculoskeletal conditions (e.g., knee and/or hip osteoarthritis) or any other diagnosed chronic pain syndrome such as fibromyalgia, chronic headache, arthritis or other joint problems, severe previous comorbidities (cardiovascular, respiratory, renal, hematological, endocrine, hepatic, gastrointestinal, or diagnosis of oncological pathology), damaged nerves or rhizopathia. Patients with mental illness with antidepressive medication or mental disability or other conditions that did not allow them to read or perform the assessment were also excluded. The presence or absence of these comorbidities was consulted in the clinical records of the participating hospitals, with full access to the complete previous medical history of the participants.

A group of 25 healthy women aged 25–50 years without a history of pelvic pain or other symptoms that might indicate endometriosis served as a reference group. They were recruited from the general community through announcements at the University of Granada, Spain. They were excluded if they presented history of infertility or any concomitant conditions considered as exclusion criteria for patients with endometriosis, as well as if they had undergone surgery in the last three months. Given the plausibility of nonsymptomatic endometriosis cases, healthy controls additionally underwent a gynecological examination and a transvaginal ultrasonography performed by a trained gynecologist to ensure that women in the reference group were asymptomatic and without ultrasound-visible endometrial lesions.

Participants who were interested in joining the study were summoned by telephone to receive detailed information. Subsequently, they were welcomed for an on-site assessment by a physiotherapist and signed written informed consent. The evaluations were carried out with a duration of approximately 90 minutes and, in order to

minimize the influence of menstrual cycle variability on the study results, all the evaluations took place between the 2nd and the 10th day after menstruation in women who were not using oral contraceptives. Sociodemographic and endometriosis-related information was gathered, including the clinical staging according to the ASRM criteria [20, 21], the location of the endometriotic lesions, the number of endometriosis-related surgical interventions, the use of oral contraceptives, and the endometriosis diagnosis.

Sample size was calculated with Epidat 3.4 (Xunta de Galicia, Spain) and PPTs served as primary outcome. Hence, to detect a minimal difference of 20% in the PPTs between groups [8] with an α-level of 0.05, a desired power of 80% and an estimated interindividual coefficient of variation for PPT measures of 18%, Epidat software revealed a required sample size of at least 21 participants per group.

The Helsinki Declaration for biomedical research was followed, and the study was approved by the Biomedical Research Ethics Committee of Granada (CEIm) (0792-N-18).

Variables

Pain

Self-Reported Pain Intensity.. The numeric rating scale (NRS) is a 11-point scale to assess self-reported pain intensity. It ranges from 0 at one end (no pain) to 10 at the other end of the scale (the worst possible pain imaginable). Participants were instructed to choose a whole number from the scale that best indicated the level of current pelvic pain (CuPP) that they felt, and then it was categorized as no pain (0), mild [1–3], moderate [4–7], and severe [8–10, 22]. The NRS has been widely used and has previously shown to be a reliable and valid instrument for assessing pain with an intraclass correlation coefficient (ICC) 0.95 [23], and it has been identified as the most appropriate tool for self-reported pain intensity assessment in endometriosis patients [24].

Nociceptive Pain.. The measurements of pressure pain thresholds (PPTs) were determined by using an electronic algometer (SENSEBox System, Somedic AB, Hörby, Sweden) which were defined as the lowest pressure able to elicit a sensation of pain after pressure [25]. The pressure applied was at an approximate rate of 30 kPa/s with a 1-cm^2 probe. The mean of three trials, with a 30-second resting period between trials, was used for the main analysis. The pressure algometry showed a 0.91 intraclass correlation coefficient (ICC) and a minimum clinically important difference of ≈ 174 kPa [26].

The abdominal wall was evaluated using four points marked bilaterally as reported elsewhere [27]. The supraumbilical point was assessed 3 cm above the umbilical point inside the hemiclavicular line (the lateral border of each rectus muscle). The infraumbilical point was assessed 3 cm below the umbilical point inside the hemiclavicular line. The pelvic region was assessed through three additional points: the pubic symphysis and both inguinal ligaments, tested at its midpoint [27]. The lower back area was evaluated bilaterally, using as a reference the spinous process of the fifth lumbar vertebrae, verified by ultrasound imaging, and the algometer will be placed in the paraspinal area, in the middle of the erector spinae muscle belly (i.e., approximately 3 cm to the right or left of the marked spinae) (Figure 1). Finally, the second metacarpals of both sides were assessed as a distant point to the affected area [28].

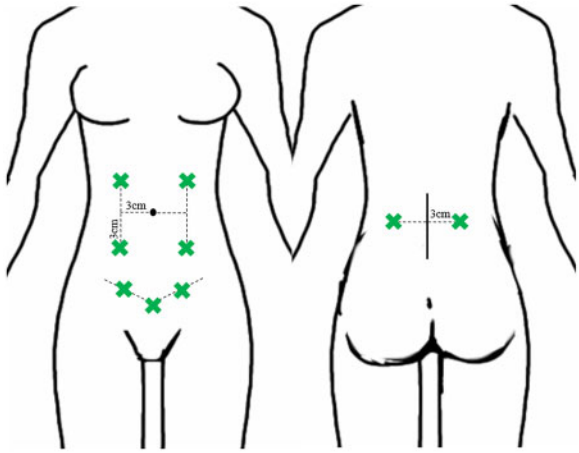

Figure 1. Locations of pressure pain threshold measurements in the abdominal and lumbopelvic area.

Additionally, a "PPT index" was calculated as previously suggested [29]. Briefly, PPTs of each patient were divided by the mean score for the same anatomical point in the control group, and finally multiplied by 100. A greater PPT index (%) indicates a lower degree of sensitization. Moreover, the mean PPT index for the lumbopelvic area was estimated as the mean PPT index of the nine tested points.

Lumbar Nerve Root Impingement/Irritation Pain.. It was bilaterally explored through the slump test. It was performed with participants placed in a sitting position with the popliteal creases flushed against the edge of the plinth, and their hands behind their backs. Before performing the test, the participants were instructed to communicate the onset of any sensation (e.g., stretch, tingling, pain). The movements were performed until the end of the range of motion or until the start of specific symptoms. The sequence of movements included flexion of the thoracic and lumbar spine, head and neck flexion, ankle dorsiflexion, and knee extension. If neural symptoms were experienced during knee extension, the motion was halted, and the participants were asked to actively extend the cervical spine to determine structural differentiation. The test was only classified as positive if the participants experienced relief of the peripheral symptoms with active cervical extension [30].

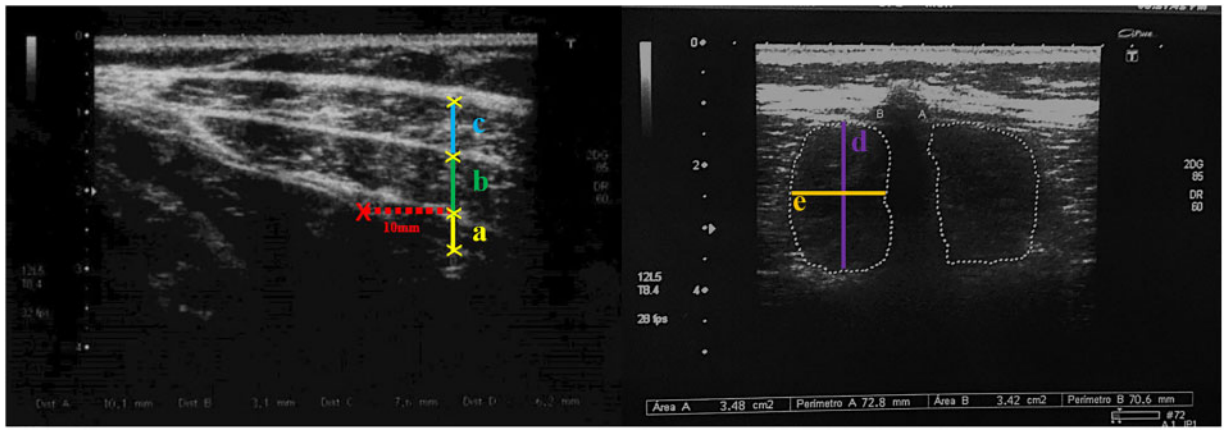

Figure 2. Ultrasound measurements of the abdominal wall (*A*) and the lumbar multifidus (*B*).

Catastrophizing Thoughts.. The Pain Catastrophizing Scale (PCS) is a validated scale to assess catastrophic thoughts. This 13-item tool consists of three subscales (rumination, magnification, and helplessness) that are scored from 0 (not at all) to 4 (all the time), resulting in a total possible score of 52. The higher the score, the more catastrophizing thoughts are present. The PCS has shown good reliability (Cronbach's alpha 0.95) [31].

Lumbopelvic Muscle Evaluation

2.2.2.1 Ultrasound imaging evaluation. All measurements were taken bilaterally following previously described methodologies [16], and all images were captured when the patient was relaxed at the end of the expiration movement with an ultrasound device (Samsung Medisom—Diagnostic Ultrasound System, Model: HM70A, Gangnam-gu, Seoul, Korea) with a 16 MHz linear probe and a depth of 5 cm.

The thickness of internal and external obliques (IOb and EOb, respectively) and transversus abdominis (TrA) were evaluated with the participant placed in a supine position with a bolster under the legs. The ultrasound probe was placed in the abdomen midway between the inferior border of the rib cage and the iliac crest on the medial axillary line. Once the muscles were identified, the probe had to be adjusted to ensure that the anterior medial edge of the transversus abdominis was 2 cm from the medial edge of the ultrasound image. When the image was captured, the distance from the most superficial to the deepest hypoechoic portion of the TrA, IOb, and EOb were measured using ultrasound's calipers (Figure 2).

The thickness of the lumbar multifidus was assessed with the participant in a prone position and correcting the lordosis with a pillow below the abdominal area. To ensure an appropriate spinal level measurement, the fifth lumbar vertebra was marked on the patient's skin. The measurement was taken at the greatest perpendicular anteroposterior distance from the processus transversus to the posterior layer of the lumbar fascia. As for the width of the lumbar multifidus, a position similar to the previous exploration was used. The multifidus was encapsulated by the spinous process medially and the lamina anteriorly. The fascial layer delineated the multifidus from the longissimus laterally and from the subcutaneous tissue posteriorly. The greatest horizontal distance between the lateral aspects of the spinous process to the fascial boundary of the longissimus muscle was taken using the ultrasound's calipers (Figure 2).

Muscle Strength.. The isometric resistance of abdominal muscles was evaluated with the trunk curl test, which showed an intraclass correlation coefficient (ICC) <0.97 [32]. Placed in a supine position with a 90° flexion of both knees and hips and arms extended without touching their knees, the participants had to perform a trunk curl and maintain an isometric position that separated the inferior angle of the scapulae from the stretcher for as long as possible up to a maximum of 90 s.

The isometric resistance of back extensors was evaluated with the muscle trunk extensor resistance test. Participants were placed in a prone position with the lower extremities standing on the stretcher and fixed with a strap, and the trunk and upper extremities hanging in a horizontal position with arms folded and the hands in touch with the contralateral shoulders. The stretcher border coincides with the anterior superior iliac spines. Participants were asked to maintain this position as long as possible. Time in seconds was measured, and higher scores reflect better performance. This test has shown high reliability with an ICC = 0.77 [33].

Lumbopelvic Stability.. The Sahrmann core stability test was performed using the Stabilizer Pressure Bio-Feedback (Chattanooga, California, USA), with the participants in a supine position and with the biofeedback unit under the lumbar spine. The pressure gauge is inflated to 40 mmHg, and the participants were asked to perform abdominal wall hollowing. There should be no change in pressure if this is performed correctly. After

abdominal wall hollowing, participants were instructed to perform 5 different leg movements corresponding to the five levels of the Sahrmann test. To progress through the levels, core stability must be maintained, with no more than a 10 mmHg increase or decrease in pressure. Participants received a score from 0 to 5 depending on the level they could complete [34]. Lumbopelvic stability level was categorized in two groups (0–1, 2–5).

Statistical Analyses

For descriptive analyses, continuous variables were summarized as mean±standard deviation and 95% confidence intervals of the mean, while categorical variables were shown as percentages. In tables, the dominant and nondominant sides reflect the women's pattern for handedness. Given the absence of normality in study outcomes, the nonparametrical Mann-Whitney *U* test was accomplished for continuous variables, while the χ^2 test was chosen for categorical variables. None of the categorical variables fulfilled the criteria for Fisher's exact test.

For all statistical analyses, the presence or absence of endometriosis diagnosis served as independent variable, and self-reported pain, PPTs, mechanosensitivity of the neural tissue, ultrasound imaging, trunk muscle endurance, and core stability were used as dependent variables. Differences in dependent outcomes were also examined between subgroups (according to the endometriosis stage and the CuPP severity [mild and moderate/severe CuPP]) through the Jonckheere's trend test. Given the reduced sample size, ASRM stratified analyses were conducted by grouping cases in similar groups in order to maximize the statistical power (stages I, II, and III [n = 15] vs stage IV [n = 26]), although additional analyses were carried out following a clinical criterion (stages I and II [n = 11] and stages III and IV [n = 30]). No imputation techniques were necessary given the absence of missing values. All statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS Statistic for Windows, Armonk, New York, USA version 23.0), while figures were designed with Graphad Prism 5.0 software (San Diego, California, USA). *P* values <.05 were considered to indicate statistical significance with a 95% confidence interval (CI), although results with *P* values between .10 and .05 were also cautiously discussed.

Results

From 50 women with endometriosis and 25 healthy women invited to this study, nine affected women (12.0%) refused to participate due to limited time availability. Results from 66 participants (41 women with endometriosis and 25 healthy women) are summarized. No differences were observed in the baseline characteristics of the 66 participants except for employment status and the use of hormonal contraceptives, with higher prevalence of unemployment and use of oral contraceptives in the endometriosis group (*P* values ≤ .001) (Table 1). Two-thirds of affected women had undergone laparoscopy (80.5%) or laparotomy (19.5%) for endometriosis-related pain relief (in most cases) or endometriotic lesion removal ≥1 year before evaluation. A total of 26 (63.4%) out of 41 of them were diagnosed with stage IV endometriosis. All women with endometriosis declared to be fully adhered to the medication (oral contraceptives and/or anti-inflammatories in all cases). The type of oral contraceptive prescribed were desogestrel, dienogest, or levonorgestrel (on continued use) for patients at risk for thrombosis or the combination of ethinylestradiol/dienogest for the others. The use of this medication served as menses suppressor in 34.1% of patients.

Pain

Using the NRS, women with endometriosis reported significantly higher pain levels compared with women from the reference group. As expected, compared with healthy women, those with endometriosis exhibited higher levels of current pelvic pain (CuPP) (4.85 ± 2.76 vs 0.46 ± 1.67, *P* values <0.001). All affected women reported any level of CuPP. A total of 9 women with stage I, II, or III endometriosis, and 14 women with stage IV endometriosis reported moderate/severe CuPP. As shown in Table 2, algometry revealed significant differences between groups in PPTs. Women with endometriosis showed lower PPT levels with respect to the reference group in all the selected points of the abdominal wall, the pelvic region and the lower back area (*P* values ranged from <.001 to .003). Moreover, PPT indexes ranged between 42.8% and 64.7% for all tested points. Moreover, we also observed a reduction in PPTs between groups for distant points to the affected area, although it did not reach the statistical significance. When women with endometriosis were stratified by ASRM staging, compared with the reference group, patients with stages I–III and those with stage IV endometriosis showed a sequential reduction in PPTs, as well as in those patients with moderate/severe CuPP compared to women with mild CuPP (Supplementary Data 1 and Supplementary Figure 1). Similarly, considering only the subset of women with stage IV endometriosis, PPTs were even lower in the subset of women with moderate/severe CuPP in comparison with those with mild CuPP (Supplementary Data 2).

Prevalence of lumbar nerve root impingement/irritation pain, assessed through the slump test, was significantly higher in affected women. Thus, 14 (34.1%) women with endometriosis showed lumbar nerve root impingement/irritation pain whilst none of the women without endometriosis yielded a positive result in this test (*P* values = .001), with a higher prevalence of lumbar nerve root impingement/irritation pain in women with

Table 1. Characteristics of the study population (N = 66)

	Without Endometriosis (n = 25) n (%)	With Endometriosis (n = 41) n (%)	*P*-value
Age (yrs)*	34.5 ± 5.2	36.7 ± 6.3	.100
Height (cm)*	164.0 ± 7.9	163.4 ± 5.9	.695
Weight (Kg)*	62.4 ± 9.0	64.2 ± 7.0	.200
Body mass index (Kg/m^2)	22.8 ± 2.7	24.1 ± 3.1	.115
Schooling			.495
University	21 (84.0)	33 (80.5)	
Up to high school	4 (16.0)	8 (19.5)	
Cohabitation			.595
Living alone	8 (32.0)	13 (31.7)	
Living as a couple	17 (68.0)	28 (68.3)	
Employment			.001
In employment	23 (92.0)	22 (53.7)	
Unemployed	2 (8.0)	19 (46.3)	
Oral contraceptives			<.001
Yes	2 (8.0)	35 (85.4)	
Endometriosis diagnosis			...
Surgery	...	28 (68.3)	
MRI	...	13 (31.7)	
ASRM staging			...
I–III	...	15 (36.6)	
IV	...	26 (63.4)	
Endometriotic lesion location			...
Deep infiltrating endometriosis	...	19 (46.3)	
Ovarian/peritoneal endometriosis	...	22 (53.7)	
Endometriosis surgical interventions			...
None	...	14 (34.1)	
One	...	17 (41.5)	
Two or more	...	10 (24.4)	
Route of surgical access			...
Laprasocopy	...	33 (80.5)	
Laparotomy	...	8 (19.5)	

*Mean±standard deviation; MRI = magnetic resonance imaging; BMI = body mass index.

stages III–IV endometriosis than in those with stages I–II, although it did not reach the statistical significance (43.3% vs 9.1%, *P* values = .064).

Similarly, higher levels of pain-related catastrophizing thoughts were found in women with endometriosis compared to controls (36.88 vs 19.80, *P* values <.001). No differences were observed in the PCS score between stages I–III and stage IV patients (37.62 ± 10.11 vs 35.60 ± 4.70; *P* values > .050) nor between stages I–II and III–IV patients (37.63 ± 9.70 vs 34.82 ± 3.31; *P* values > .050).

Lumbopelvic Muscle Evaluation

The thickness of TrA was significantly lower in the dominant side of women with endometriosis when compared with the reference group, with a significant decrease according to ASRM stages (Table 3 and Supplementary Data 3). A similar trend was also observed for EOb, although it did not reach the statistical significance (*P*-trends > .052). Additionally, an inverse trend in the thickness of TrA and EOb at both sides were observed when women with endometriosis were grouped according to the CuPP severity, although the differences in the thickness of TrA in the non-dominant side did not reach the statistical significance (*P*-trend = .086). The thickness of TrA at both sides were even lower in affected women with stage IV endometriosis and moderate/severe CuPP than in those women with stage IV endometriosis and mild CuPP, reaching the statistical significance in the nondominant side (Figure 3A).

Regarding trunk muscle resistance, affected women showed significantly reduced resistance of abdominal and back muscles than the reference group, with a negative trend according to the ASRM stage (Table 4 and Supplementary Data 4). Moreover, women with stage IV endometriosis and moderate/severe CuPP, compared to those with mild CuPP, showed lower resistance in both abdominal and back muscles (Figure 3B). Similarly, a positive correlation between the mean PPT of the abdominal and lumbopelvic region and the resistance of both abdominal and back muscles (ρ coefficients = 0.396 and 0.539, *P* values < .050). Sensitivity analyses stratifying by employment status yielded similar differences in ultrasound measurements nor trunk endurance between employed women with and without endometriosis (data not shown in tables).

Table 2. Pressure pain thresholds (kPa) in healthy women and affected women with mild and moderate/severe chronic pelvic pain

	Without Endometriosis (n = 25)	With Endometriosis						*P*-value*	*P*-trend†
		Entire Group (n = 41)		Stage I, II, and III (n = 15)		Stage IV (n = 26)			
	PPT	PPT	PPT Index (%)	PPT	PPT Index (%)	PPT	PPT Index (%)		
Supraumbilical									
Dominant side	486.37 ± 219.88 (395.61 – 577.13)	300.08 ± 187.66 (240.07 – 360.10)	61.70 ± 38.58 (49.36 – 74.04)	358.54 ± 200.67 (242.68 – 474.41)	73.72 ± 41.26 (49.90 – 97.54)	268.60 ± 176.21 (197.43 – 339.77)	55.23 ± 36.23 (40.59 – 69.86)	.002	<.001
Nondominant side	483.60 ± 223.74 (391.24 – 575.96)	313.78 ± 215.22 (244.95 – 382.61)	64.88 ± 44.50 (50.65 – 79.12)	349.05 ± 210.86 (227.30 – 470.79)	72.18 ± 43.60 (47.00 – 97.35)	294.79 ± 219.25 (206.23 – 383.34)	60.96 ± 45.34 (42.64 – 79.27)	.002	.001
Infraumbilical									
Dominant side	497.98 ± 244.21 (397.18 – 598.79)	322.26 ± 226.89 (249.70 – 394.82)	64.71 ± 45.56 (50.14 – 79.29)	374.64 ± 208.47 (254.27 – 495.00)	75.23 ± 41.86 (51.06 – 99.40)	294.06 ± 235.25 (199.04 – 389.08)	59.05 ± 47.24 (39.97 – 78.13)	.003	<.001
Nondominant side	504.26 ± 246.81 (402.38 – 606.14)	325.40 ± 225.24 (253.40 – 397.47)	64.54 ± 44.67 (50.25 – 78.82)	365.14 ± 226.97 (234.10 – 496.19)	72.41 ± 45.01 (46.42 – 98.40)	304.05 ± 225.82 (212.84 – 395.26)	60.30 ± 44.78 (42.21 – 78.38)	.002	.001
Pubis symphisis									
	567.82 ± 343.79 (425.91 – 709.73)	321.64 ± 227.14 (248.00 – 394.28)	56.65 ± 40.00 (43.85 – 69.44)	369.75 ± 260.18 (219.52 – 519.97)	65.12 ± 45.82 (38.66 – 91.57)	295.74 ± 208.06 (211.70 – 379.77)	52.08 ± 36.64 (37.28 – 66.88)	.001	<.001
Inguinal ligament									
Dominant side	492.79 ± 248.35 (390.28 – 595.30)	279.85 ± 198.04 (216.51 – 343.18)	56.79 ± 40.19 (43.94 – 69.64)	323.32 ± 232.07 (189.33 – 457.31)	65.61 ± 47.09 (38.42 – 92.80)	256.44 ± 177.62 (184.70 – 328.19)	52.04 ± 36.04 (37.48 – 66.60)	<.001	<.001
Nondominant side	459.46 ± 218.70 (369.19 – 549.74)	280.61 ± 194.73 (218.33 – 342.89)	61.07 ± 42.38 (47.52 – 74.63)	317.26 ± 199.02 (202.35 – 432.17)	69.05 ± 43.32 (44.04 – 94.06)	260.87 ± 193.39 (182.76 – 338.98)	56.78 ± 42.09 (39.78 – 73.78)	.001	<.001
Lumbar									
Dominant side	843.73 ± 302.36 (718.93 – 968.54)	446.01 ± 330.65 (340.26 – 551.75)	52.86 ± 39.19 (40.33 – 65.39)	507.76 ± 326.61 (319.17 – 696.34)	60.18 ± 38.71 (37.83 – 82.53)	412.76 ± 334.37 (277.70 – 547.81)	48.92 ± 39.63 (32.91 – 64.93)	<.001	<.001
Nondominant side	1093.41 ± 1377.59 (524.76 – 1662.05)	467.74 ± 387.33 (343.87 – 591.62)	42.78 ± 35.42 (31.45 – 54.11)	566.39 ± 421.18 (323.21 – 809.57)	51.80 ± 38.52 (29.56 – 74.04)	414.63 ± 365.26 (267.10 – 562.16)	37.92 ± 33.41 (24.43 – 51.41)	<.001	<.001
Second metacarpal									
Dominant side	488.61 ± 174.75 (416.48 – 560.74)	415.67 ± 248.65 (336.14 – 495.19)	85.07 ± 50.89 (68.80 – 101.35)	462.64 ± 250.77 (317.84 – 607.43)	94.68 ± 51.32 (65.05 – 124.32)	390.37 ± 248.69 (289.93 – 490.82)	79.89 ± 50.90 (59.34 – 100.45)	.089	.040
Nondominant side	449.69 ± 179.00 (375.81 – 523.58)	396.98 ± 215.25 (328.14 – 465.82)	88.28 ± 47.87 (72.97 – 103.59)	397.89 ± 207.99 (277.81 – 517.98)	88.48 ± 46.25 (61.78 – 115.19)	396.36 ± 223.13 (306.36 – 486.61)	88.17 ± 49.62 (68.13 – 108.21)	.197	.202

Values are expressed as mean±standard deviation.

*Differences between the reference group and women with endometriosis (Mann-Whitney *U* test).

†Differences between the reference group, affected women with stages I, II, and III and affected women with stage IV endometriosis (Jonckheere's trend test).

Table 3. Ultrasound evaluation of abdominal wall muscles and lumbar multifidus in women with and without endometriosis

		With Endometriosis				
	Without Endometriosis (n = 25)	Entire Group (n = 41)	Stage I, II, and III (n = 15)	Stage IV (n = 26)	*P*-value*	*P*-trend†
Thickness transversus abdominis						
Dominant side	0.34 ± 0.10 (0.30 – 0.38)	0.30 ± 0.09 (0.27 – 0.33)	0.30 ± 0.08 (0.25 – 0.34)	0.30 ± 0.10 (0.26 – 0.34)	.031	.038
Nondominant side	0.36 ± 0.16 (0.30 – 0.43)	0.32 ± 0.10 (0.29 – 0.35)	0.30 ± 0.04 (0.28 – 0.33)	0.33 ± 0.11 (0.29 – 0.38)	.397	.638
Thickness internal oblique						
Dominant side	0.65 ± 0.17 (0.58 – 0.72)	0.60 ± 0.19 (0.55 – 0.66)	0.59 ± 0.19 (0.48 – 0.69)	0.61 ± 0.19 (0.54 – 0.69)	.416	.552
Nondominant side	0.73 ± 0.52 (0.52 – 0.95)	0.59 ± 0.18 (0.53 – 0.64)	0.58 ± 0.17 (0.49 – 0.68)	0.59 ± 0.18 (0.52 – 0.66)	.293	.389
Thickness external oblique						
Dominant side	0.47 ± 0.20 (0.39 – 0.55)	0.42 ± 0.23 (0.34 – 0.49)	0.40 ± 0.20 (0.29 – 0.51)	0.42 ± 0.25 (0.32 – 0.52)	.107	.152
Nondominant side	0.59 ± 0.62 (0.34 – 0.85)	0.40 ± 0.22 (0.33 – 0.47)	0.43 ± 0.22 (0.30 – 0.55)	0.39 ± 0.22 (0.30 – 0.48)	.059	.052
Thickness lumbar multifidus						
Dominant side	2.33 ± 0.59 (2.08 – 2.58)	2.38 ± 0.48 (2.20 – 2.55)	2.33 ± 0.44 (2.01 – 2.65)	2.40 ± 0.50 (2.17 – 2.63)	.825	.771
Nondominant side	2.38 ± 0.48 (2.18 – 2.58)	2.45 ± 0.48 (2.28 – 2.63)	2.46 ± 0.44 (2.14 – 2.78)	2.45 ± 0.51 (2.22 – 2.68)	.541	.631
Width lumbar multifidus						
Dominant side	2.71 ± 0.71 (2.41 – 3.02)	2.47 ± 0.53 (2.28 – 2.66)	2.59 ± 0.60 (2.16 – 3.02)	2.42 ± 0.48 (2.20 – 2.64)	.071	.095
Nondominant side	2.76 ± 0.49 (2.55 – 2.97)	2.64 ± 0.51 (2.46 – 2.83)	2.90 ± 0.61 (2.46 – 3.33)	2.52 ± 0.42 (2.33 – 2.72)	.275	.146

Values are expressed as mean±standard deviation (95% confidence interval).

*Differences between the reference group and women with endometriosis (Mann-Whitney *U* test).

†Differences between the reference group, affected women with stages I, II, and III and affected women with stage IV endometriosis (Jonckheere's trend test).

Considering the lumbopelvic stability, there were significant differences between groups in the Sahrmann core stability test. While 20 (48.8%) of affected women had a lumbopelvic stability level ≤1, only four (16.0%) women from the reference group had this lumbopelvic stability level (*P* values 0.007) (Table 4). Despite a lack of statistical difference observed according to ASRM classification, a trend towards greater lumbopelvic instability in those patients with stage IV endometriosis and moderate/severe CuPP than in those with stage IV endometriosis and mild CuPP was observed (71.4% vs 33.3%, *P* values 0.052) (Supplementary Data 5). Moreover, significantly reduced PPTs were observed in affected women with lumbopelvic instability (Supplementary Data 6).

Discussion

To date, this study reveals for the first time the presence of local musculoskeletal impairments in the lumbopelvic area of women with endometriosis. This study not only corroborates previous findings of increased self-reported pain hypersensitivity in the affected area and the presence of lumbar nerve root impingement/irritation pain and catastrophizing thoughts related to pain, but also revealed (i) reduced thickness and resistance of lumbar and abdominal muscles and (ii) a lower lumbopelvic stability in women with endometriosis in comparison with healthy women. Finally, we have also detected (iii) increased musculoskeletal impairments in those affected women with more severe endometriosis, even more pronounced in those with moderate/severe CuPP.

Reduced PPTs were detected in the lumbopelvic and abdominal areas in women with endometriosis compared to healthy women, as previously reported [8, 35, 36]. Interestingly, we have also detected ASRM stage- and CuPP severity-dependent reductions of PPTs. We found that PPTs in the lumbopelvic and abdominal area in endometriosis were decreased (ranging from 42.8% and 64.7%) in comparison with healthy women. In this regard, some pelvic factors such as nerve fiber growth in endometriotic lesions or inflammatory milieu have been proposed as potential contributors to peripheral sensitization in women with endometriosis. Hence, endometriotic lesions themselves are innervated [7], and the nerve growth factor has been postulated as a crucial regulator of this process [37]. In this regard, previous research has pointed out the presence of myofascial dysfunction, in addition to regional allodynia and hyperalgesia and reduced PPTs of abdominal muscles and lumbar supraspinous ligaments in women with endometriosis [36].

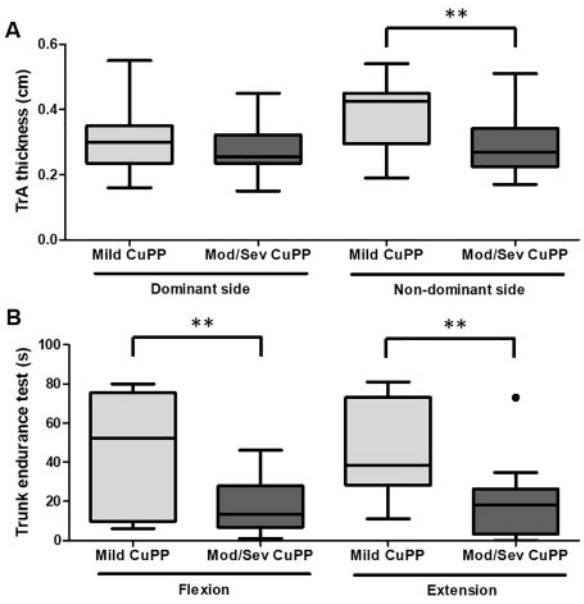

Figure 3. Lumbopelvic impairments in women with stage IV endometriosis grouped by current pelvic pain (CuPP) severity. *A*) Thickness of transversus abdominis (TrA). *B*) Trunk endurance. Differences were explored with the Mann-Whitney *U* test. ***P* values <.050.

Interestingly, they observed that women with any history of endometriosis and those with myofascial trigger points were most likely to have sensitization, suggesting that long-term remodeling of the central nervous system may persist after lesions are treated [36]. Moreover, pain chronification has been demonstrated to induce changes in the central nervous system structure and function, frequently leading to "central sensitization" [5, 38]. Thus, contrary to a previous study suggesting peripheral but not central sensitization in endometriosis patients [35], significant differences were observed in PPTs at distant points to the affected area between women with stage IV endometriosis in comparison with the reference group. Moreover, reduced PPTs were observed at the second metacarpals in women with stage IV endometriosis and moderate/severe CuPP. Our results are in accordance to those reported by Grundström et al. [8] and As-Saine et al. [39] that found lower PPTs below the tuberositas tibiae and at the thumbnail, respectively, in women with endometriosis and chronic pelvic pain in comparison with healthy women and patients without chronic pelvic pain. In this regard, in addition to potential changes in specific brain areas, psychological factors such as depressed mood, anxiety or the presence of catastrophizing thoughts may also contribute to central sensitization thorough disruption of emotion regulatory circuitry, the hippocampal network or descending inhibitory pathways (reviewed in [6]). Regarding lumbar nerve root impingement/irritation pain, we have found higher prevalence of lower limb neural tissue excitability in affected women in comparison with healthy controls. Hence, as described for other conditions, peripheral sensitization, probably through the inflammatory response, might contribute to the peripheral nerve fiber damage, leading to the development of lumbar nerve root impingement/irritation pain [5]. Moreover, our results are in accordance to a recently published case-control study that showed limb nerve excitability with lower range of motion values in women with chronic pelvic pain when compared with healthy controls [40].

To the best of our knowledge, no attention has been paid yet to musculoskeletal impairments in women with endometriosis. For the first time, we have revealed ASRM stage-dependent and CuPP-dependent reductions in the thickness of TrA in women with endometriosis. Thus, our results indicate that the stabilization effect of the lumbopelvic area that TrA usually exerts through a creation of a trunk 'rigid cylinder' might be impaired, that might difficult specific loads and the performance of daily activities [41]. The thickness of the EOb was also lower in those affected women with moderate/severe CuPP. These results are in line with previous findings of a lower thickness of muscles from the abdominal wall in patients with chronic pain in the affected area [16]. Similarly, trunk resistance was significantly decreased in women with endometriosis than in healthy women, with significant reductions according to ASRM stages and CuPP severity. Moreover, we have found a reduced lumbopelvic stability in women with endometriosis, more prevalent in those affected women with moderate/severe CuPP. Although the hypothesis of the fact that changes in the control of trunk muscles may lead to pain cannot be ruled out, these results are in agreement with the most supported by experimental and clinical evidence hypothesis that consider pain as responsible of changes in trunk muscle control (reviewed in [19]). There are many possible mechanisms described in the literature, including changes in the excitability in the motor pathway, changes in the sensory system and factors associated with the attention demanding, stressful and fearful aspects of pain [19]. In fact, we have also found higher catastrophizing thoughts in women with lower lumbopelvic stability. Moreover, it is worth to mention that the experienced pelvic pain, in addition to the lower thickness detected in abdominal muscles, may be responsible of the observed poorer scores obtained on the trunk endurance and lumbopelvic stability tests in women with endometriosis.

Some limitations need to be taken into account for the interpretation of these results. Firstly, the use of a cross-sectional design hampers the elucidation of causal effects. Given that PPTs served as primary outcome for sample size calculation, the limited sample size might hamper the identification of significant differences between groups in some outcomes. Similarly, despite the confirmation of the absence of a history of endometriosis-related symptoms and ultrasound-visible endometrial lesions by a trained gynecologist in the reference group before examination, we cannot fully rule out the presence of any ultrasound-invisible endometrial lesion in any control

Table 4. Trunk muscle endurance and lumbopelvic stability in women with and without endometriosis

		With Endometriosis				
	Without Endometriosis (n = 25)	Entire Group (n = 41)	Stage I, II, and III (n = 15)	Stage IV (n = 26)	*P*-value‡	*P*-trend§
Trunk endurance test (s)*						
Flexion	57.66 ± 24.00 (47.75 – 67.57)	31.13 ± 23.72 (23.64 – 38.62)	34.55 ± 20.25 (23.33 – 45.76)	29.16 ± 25.69 (18.79 – 39.54)	<.001	<.001
Extension	102.34 ± 54.17 (79.98 – 124.70)	38.92 ± 38.80 (26.67 – 51.16)	53.27 ± 52.82 (24.02 – 82.53)	30.63 ± 25.51 (20.33 – 40.94)	<.001	<.001
Lumbopelvic stability†					.007¶	
0–1	4 (16.0%)	20 (48.8%)	6 (40.0%)	14 (53.8%)		
2–5	21 (84.0%)	21 (51.2%)	9 (60.0%)	12 (46.2%)		

*Values are expressed as mean±standard deviation (95% confidence interval).
†Values are expressed as n (%).
‡Differences between the reference group and women with endometriosis (Mann-Whitney *U* test for trunk endurance test and χ^2 test for lumbopelvic stability).
§Differences between the reference group, affected women with stages I, II, and III and affected women with stage IV endometriosis (Jonckheere's trend test).
¶Differences between affected women with stages I, II, and III and affected women with stage IV endometriosis (χ^2 test).

women. Moreover, the exclusion of patients with any other chronic overlapping pain condition may reduce the generalizability of the results found. Despite self-reported pelvic pain intensity was recorded, associations between abdominal and lower back pain and lumbopelvic impairments were not explored. Moreover, other parameters not considered in this study, such as the type and number of surgical interventions or the route of surgical access might be involved in the associations found. However, the fact that included women did not undergone surgery in the last 12 months before examination has considerably reduced the potential influence that surgery may have on the main outcomes. Similarly, despite the fact that all participants with endometriosis declared the full adherence to their prescribed endometriosis treatment, subtle differences in the current treatment of each patient might also influence the results found. Given that significant differences have been observed according to ASRM stages, further studies exploring differences in women with different clinical presentations of endometriosis should be carried out. Additionally, muscle architecture was only assessed through muscle thickness. It might be possible that assessment of muscle quality based on echogenicity might increase our understanding of the changes that occur in the trunk muscles of women with endometriosis. Finally, more comprehensive studies assessing motor control impairments in these patients need to be accomplished, given that we have been limited to an indirect evaluation of the lumbopelvic stability. In this regard, additional tests, such as superficial electromyography that addresses the activation of trunk and extremity muscles over time, should be accomplished in order to obtain a better overview of lumbopelvic dysfunction during loads in these patients.

Taken together, the findings of this study have direct clinical implications. Endometriosis patients, that are currently treated with surgical and medical treatments (in absence of evidence for rehabilitative therapies), develop lumbopelvic impairments that may determine or aggravate endometriosis burden of symptoms, leading to increased economic costs for health systems. Therefore, effectiveness of rehabilitation programs, such as lumbopelvic stabilization interventions, targeting these musculoskeletal impairments should be evaluated in the close future in order to offer additional therapeutic tools for this subset of patients.

In summary, endometriosis patients suffer increased pain in the lumbopelvic area, as well as both central and peripheral sensitization and lumbar nerve root impingement/irritation pain. Additionally, they have decreased thickness of abdominal wall muscles, reduced resistance of both trunk flexor and extensor muscles and decreased lumbopelvic stability with respect to healthy women. Moreover, these musculoskeletal impairments were aggravated in those patients with stage IV endometriosis and moderate/severe CuPP.

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Supplementary Data

Supplementary data are available at *Pain Medicine* online.

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