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Widespread myofascial dysfunction and sensitization in women with endometriosis-associated chronic pelvic pain: A cross-sectional study

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Abstract

Background: Chronic pelvic pain persists in some women with endometriosis even after lesion removal and optimized hormonal treatment.

Objective: Characterize the presence and distribution of pain, myofascial dysfunction, and sensitization beyond the pelvis in women with endometriosis-associated chronic pelvic pain.

Methods: Cross-sectional study of 30 women prior to participation in a clinical trial. Evaluation included pain-focused abdominopelvic gynecologic examination with identification of pelvic floor muscle spasm. Neuro-musculoskeletal examination assessed paraspinal allodynia and hyperalgesia bilaterally and myofascial trigger points in 13 paired muscles. Pressure-pain thresholds were measured over interspinous ligaments and trigger-points. Women completed the body territories element of the Body Pain Index.

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Results: All women had pelvic floor muscle spasm that they self-identified as a major focus of pain. Twenty of 30 women described their pelvic pain as focal. However, all demonstrated widespread myofascial dysfunction with low pressure-pain thresholds and trigger-points in over two-thirds of 26 assessed regions. Widespread spinal segmental sensitization was present in 17/30, thoracic in 21/30, and lumbosacral/pelvic in 18/30. Cervical sensitization manifested as low pressure-pain thresholds with 23/30 also reporting recurrent, severe headaches and 21/30 experiencing orofacial pain. Those reporting diffuse pelvic pain were more likely to have widespread (p=.024) and lumbosacral/pelvic (p=.036) sensitization and report over 10 painful body areas (p=.009).

Conclusions: Women with endometriosis-associated chronic pelvic pain often have myofascial dysfunction and sensitization beyond the pelvic region that may be initiated or maintained by on-going pelvic floor spasm. These myofascial and nervous system manifestations warrant consideration when managing pain in this population.

Clinicaltrials.gov identifier: NCT01553201

1. Introduction:

In endometriosis, an inflammatory disease affecting reproductive-aged women associated with infertility and pain, endometrial tissue grows outside the uterus as estrogen-dependent/progesterone-resistant pelvic lesions with their own blood supply and innervation (Al-Sabbagh et al., 2012;Berkley et al., 2004;McKinnon et al., 2015;Zondervan et al., 2020). Endometriosis-associated pain, usually a triad of dysmenorrhea, non-menstrual pelvic pain, and dyspareunia, begins early in reproductive life and persists, imposing a significant burden (Schliep et al., 2015;Stratton and Berkley 2011). Gynecologists have attributed the pain to endometriosis lesions(Fauconnier and Chapron 2005). Thus, standard treatment focuses on surgery to remove lesions and hormone administration to prevent lesion growth.

Clinical and animal studies illustrate that neither the extent nor location of endometriosis relates to the severity or location of pelvic pain (As-Sanie et al., 2012;Bajaj et al., 2003;Stratton et al., 2015). By contrast, lesion type does matter. Removal of deep infiltrating lesions—the type most often innervated—is frequently associated with improvement in pelvic pain (Chapron et al., 2012;Wang et al., 2009). Additionally, women with deep lesions and endometriomas (endometriotic ovarian cysts) experience greater pain than those with endometriomas only (Chapron et al., 2012).

Unfortunately, the lack of correlation between lesions and pain is supported by return of pain after surgery in many women without new lesions(Vercellini et al., 2009). Similarly, hormonal management often provides insufficient pain relief even if menses and new lesion growth are suppressed (Stratton and Berkley 2011).

Thus, persistent endometriosis-related pelvic pain cannot be explained by the presence of lesions. It may be, rather, that bidirectional communication between central and peripheral pain processes initiates and maintains pathologic neuroplastic changes, perpetuating pain (Aredo et al., 2017;Berkley et al., 2005;Stratton et al., 2015). Sensitization manifests as regional allodynia, hyperalgesia, and pain beyond the visceral pathology(Latremoliere and

Woolf 2009). Sensitization is commonly assessed by quantitative cutaneous sensory testing of peripheral areas using thermal or mechanical stimulation modalities (Arendt-Nielsen and Yarnitsky 2009). However, such limited testing inadequately illustrates the association between sensitization and myofascial dysfunction, which often independently contribute to pain persistence. Fundamental to myofascial dysfunction are myofascial trigger points–hard, tender nodules in a taut band of skeletal muscle that, when palpated, often reproduce a person's pain(Simons 1999). In endometriosis-associated pain, palpation of pelvic floor muscles in spasm may reproduce a woman's pelvic pain (Langford et al., 2007). The presence of co-morbid non-pelvic pain, sensitization and myofascial trigger points have rarely been studied in the endometriosis population (As-Sanie et al., 2013;Bajaj et al., 2003;Grundstrom et al., 2019;Yosef et al., 2016).

We previously reported that women with pelvic pain and any history of endometriosis have higher rates of pelvic sensitization and myofascial dysfunction than healthy pain-free women and those with pain but no endometriosis history (Stratton et al., 2015). In the present study of women with treated endometriosis and persistent pain, we performed a pain-focused abdominopelvic gynecologic examination to identify the pattern of pelvic pain and a detailed neuro-musculoskeletal assessment to determine the distribution of myofascial trigger points and cutaneous sensitization. These comprehensive assessments offer a novel approach to characterizing the pain phenotype of women with endometriosis-associated pain.

2. Materials and methods

2.1 Participants:

The cross-sectional baseline assessment of women with endometriosis enrolled at the National Institutes of Health Clinical Center in a clinical trial for endometriosis-associated chronic pelvic pain and pelvic floor spasm is presented. The study was approved by the National Institute of Child Health and Human Development Institutional Review Board (Clinicaltrials.gov identifier: NCT01553201). All participants gave written informed consent.

Eligible participants were aged 18–50 years, with a history of surgically-diagnosed endometriosis and at least three months of chronic pelvic pain. At study enrollment, no participant had any clinical indication for further endometriosis-directed surgery. Women had also optimized hormonal and pain treatments for endometriosis-associated pain with their gynecologists and pain specialists in accordance with standard care. Only those women who could distinguish their endometriosis-associated pelvic pain from other concurrent pain syndromes were included; women with chronic pelvic pain symptoms attributable to other identifiable causes were excluded. Women with a history of urinary or fecal incontinence, known pelvic prolapse, or hysterectomy with bilateral salpingo-oophorectomy, current pregnancy or lactation, or known neuromuscular junction disorders were excluded.

The sample size of 30 was calculated for the parent clinical trial. All women participating in the clinical trial were included in the collection of baseline clinical characteristics reported in this cross-sectional analysis.

2.2 Abdominopelvic examination:

Participants underwent a baseline evaluation that included an abdominopelvic pain-focused examination by a gynecologist and a comprehensive neuro-musculoskeletal examination by a physiatrist. The abdominal and low-back examination assessed sacroiliac joint and abdominopelvic pain, allodynia, and the number and associated pain level of abdominal myofascial trigger points. A single-digit pelvic examination assessed tenderness and spasm in bilateral pubococcygeus, iliococcygeus, and obturator internus muscles (Figure 1) and bladder, urethral, uterosacral ligament, forniceal and vaginal wall pain, as well as uterine and adnexal size, pain, and mobility. Patients rated the pain intensity associated with palpation at each site using a visual analogue scale (VAS) or verbal report from 0–10 (no pain-worst possible pain). Participants indicated the location of their most intense pain and described the overall pattern of pelvic tenderness/pain as “diffuse” or “focal.”

2.3 Neuro-musculoskeletal examination:

The neuro-musculoskeletal examination assessed dermatomes, sclerotomes, and myotomes to identify sites of widespread pain, sensitization, and myofascial dysfunction (Aredo et al., 2017). The spinal segment cervical-2 through sacral-2 dermatomes were assessed from cephalad to caudad for allodynia and hyperalgesia bilaterally, approximately 2.5 cm lateral to the spinous process (Figure 2). Allodynia and hyperalgesia were determined using a 300-g Semmes-Weinstein monofilament (Touch Test Sensory Evaluator, North Coast Medical Inc, Morgan Hill, California) and a Wartenberg pinwheel, respectively.

The pressure-pain threshold, the minimum amount of pressure eliciting pain (Fischer 1998), was measured over the interspinous ligaments from cervical-1 to sacral-1 using a Fischer’s pressure algometer (Figure 2). A low pressure-pain threshold for interspinous ligaments was defined as less than 4 kg/cm^2 (Giesecke et al., 2003;Wolfe et al., 1990). The myotome was examined for myofascial trigger points in the thirteen paired muscles (26 assessed regions) routinely evaluated in patients undergoing assessment for fibromyalgia (Figure 2). The criteria used to identify myofascial trigger points were palpable, discrete, hyper-irritable loci within a taut band of skeletal muscle (Fernandez-de-Las-Penas and Dommerholt 2018;Simons 1999).

The pressure-pain threshold over each myofascial trigger point was measured, with low threshold defined as less than 4 kg/cm^2 (Giesecke et al., 2003;Granges and Littlejohn 1993). If more than half of the examined dermatomal segments (C2-S2) on either side (12 or more of 23 segments) evoked pain during the allodynia or hyperalgesia assessment, the subject was classified as having regional allodynia or regional hyperalgesia, respectively(Fischer 2002;Haanpaa et al., 2011). Sensitization was then categorized by region (cervical, thoracic, or lumbosacral/pelvic) or as widespread based on the presence and location of findings of regional allodynia or hyperalgesia. Subjects were classified as having myofascial dysfunction if myofascial trigger points were present in seven or more muscles on each side.

2.4 Baseline questionnaires and medical history:

A pelvic pain questionnaire was used to assess dysmenorrhea, dyspareunia, or non-menstrual pelvic pain and their respective severity. Using the Brief Pain Inventory (BPI)

map, subjects indicated which of the 71 body territories were painful (Melzack 1975). Participants reporting 10 or more painful body territories were considered to have widespread pain. Orofacial pain was defined as reporting at least one painful territory in the head, neck or jaw region on the body territories map. A history of recurrent severe headaches and migraine headaches was obtained as part of the medical history.

2.5 Statistical Analysis:

Demographic data, including duration of chronic pelvic pain and hormone use at study entry, were tabulated and are described as frequency (percentage), mean (standard deviation), or median (inter-quartile range). Continuous data were checked for distributional assumptions. The findings on gynecologic examination relating to the pain phenotype included the presence of pelvic floor spasm, other sites of pelvic pain, abdominopelvic wall and sacroiliac joint tenderness, and whether the abdominopelvic or pelvic pain was focal or diffuse. With regard to the neuro-musculoskeletal assessment, the proportion of women with regional or widespread sensitization and widespread myofascial dysfunction were determined.

We evaluated the association among physical findings in the gynecologic and physiatry examinations and the patient-reported symptoms described above. We assessed whether reporting diffuse pelvic pain was associated with widespread pain on the BPI, lumbosacral spinal segmental sensitization, or widespread spinal segmental sensitization and whether widespread pain on the BPI was associated with widespread spinal segmental sensitization. Complete information was obtained on each participant; there were no missing data points. Potential confounders were not assessed in this analysis of baseline data.

Statistical analyses were conducted using SAS v. 9.4 (SAS Institute, Inc, Cary, NC). Chi-square and Fisher's exact test were used for the analyses of potential associations between binary variables. Logistic regression analysis computed the odds ratios and 95% Confidence Intervals (CI), which are reported along with p values.

3. Results

Thirty women with a median age of 30 years (range 18–50) and endometriosis-associated chronic pelvic pain duration ranging from 2 to 25 years [mean 11.5 (6.5)] were enrolled. Women were racially diverse; most were employed and college-educated (Table 1). At enrollment, twenty-three (77%) of 30 subjects were using some form of hormonal treatment, most of which suppressed menses. Twenty-nine (97%) of 30 women reported non-menstrual pelvic pain and 27 (90%) reported dysmenorrhea at their last menses. Of the 15 women who had sexual intercourse in the last month, 14 (93%) reported dyspareunia. Seven others avoided intercourse because of pain.

During the abdominopelvic examination, all participants were found to have pelvic floor muscle spasm. Of those, 23/30 (77%) had spasm in at least 4 of 6 pelvic floor muscles examined. All acknowledged the pelvic floor as a major focus of their pelvic pain. Twenty (67%) of 30 women described their pelvic pain as focal while 10 (33%) described it as diffuse and not localized. Across the abdominopelvic region, most participants (17/30, 57%)

had abdominal pain only in the pelvic region, 12 (40%) experienced no pain on abdominal palpation and one (3%) had diffuse abdominal pain. Nine (30%) women had sacroiliac joint pain.

On the neuro-musculoskeletal exam, all women had widespread myofascial dysfunction as evidenced by myofascial trigger points in more than two-thirds of assessed regions. Fourteen (47%) of 30 women had myofascial trigger points in all 26 assessed regions. A low pressure-pain threshold was observed in all of the assessed myofascial trigger points (Figure 3). Most women had widespread (17/30, 57%), thoracic (21/30, 70%), and lumbosacral/pelvic (18/30, 60%) spinal segment sensitization. Cervical spinal segment sensitization was manifested as low pressure-pain thresholds; in addition, orofacial pain was reported in 21/30 (70%) or recurrent severe headaches in 23/30 (77%). The pressure-pain thresholds over the interspinous ligaments were generally low within the cervical, thoracic, and lumbosacral/pelvic regions (Figure 4). Overall, sixteen (53%) of 30 women had low pressure-pain thresholds over all interspinous ligaments.

Participants reporting diffuse pelvic pain rather than focal pelvic pain were more likely to indicate having at least 10 painful body territories (80% vs 25%; OR=12.0; 95% CI: 1.89–76.37; p=.009) and were more likely to have lumbosacral spinal segmental sensitization (90% vs 45%; OR=11.0; 95% CI: 1.16–103.94; p=.036) or widespread spinal segmental sensitization (90% vs 40%; OR=13.5; 95% CI: 1.42–128.26; p=.024) on the physiatry examination. In addition, those indicating more than 10 painful body territories were more likely to have widespread sensitization (92% vs 8%; OR=28.8; 95% CI: 2.91–284.72; p=.004).

4. Discussion

In this baseline assessment of women with endometriosis-associated persistent pelvic pain, we explored the relationship between the pattern and distribution of pain in a pain-focused abdominopelvic gynecologic examination and the neuro-musculoskeletal findings of sensitization and myofascial dysfunction at baseline. Notably, the gynecological examination showed that these women all had pelvic floor muscle spasm, frequently encompassing at least four of six pelvic floor muscles, that, when palpated, evoked their typical pelvic pain. Importantly, the neuro-musculoskeletal examination revealed that all women also had widespread myofascial dysfunction with palpable myofascial trigger points and low pressure-pain thresholds in nearly all muscles tested. Similarly, widespread and regional sensitization were observed in most women in addition to low pressure-pain thresholds over the interspinous ligaments. Our findings demonstrate that women with endometriosis-associated chronic pelvic pain may have widespread myofascial dysfunction and sensitization beyond the pelvic focus of pain. Previous studies have provided translational evidence of ways in which endometriosis lesions can engage the nervous system and contribute to sensitization that sustains persistent pain. Endometriosis-associated chronic pelvic pain may develop and be maintained by compression or infiltration of nerves near the lesions, innervation of blood vessels vascularizing developing lesions, and innervation of endometrial lesions by sensory and sympathetic nerve fibers (Anaf et al., 2000;Berkley et al., 2004;Ramer and Bisby 1999;Stratton and Berkley 2011;Woolf 1996). In

animal models, Li et al. showed persistent pain hypersensitivity in mice with endometriosis compared with controls while Yano et al. found that non-noxious abdominal stimulation in macaques with endometriosis activated the thalamus and insula– brain regions associated with pain– to a greater degree than in healthy controls (Li et al., 2018;Yano et al., 2019). Moreover, Dodds et al. demonstrated glial adaptations – specifically increased astrocyte and microglia immunoreactivity – in animal models with endometriosis-like lesions compared to healthy controls, indicating nervous system engagement by these immune-like cells in this condition (Dodds et al., 2019). These animal studies support our clinical findings of the association between sensitization and endometriosis.

In clinical studies, women with endometriosis-associated chronic pelvic pain exhibit signs of nervous system remodeling even after surgical and hormonal treatment of the lesions, further suggesting the role of central processes and sensitization in the maintenance and amplification of the pain. Within the pelvis, cross-organ sensitization between the reproductive and urinary tract can present as severe dysmenorrhea persisting after stone elimination(Costantini et al., 2020). Interestingly, treatment of secondary trigger points in the referred pain area improved symptoms. In studies using magnetic resonance imaging, As-Sanie et al. showed decreased brain gray matter volume in central pain processing regions (left thalamus, left cingulate gyrus, right putamen, and right insula) as well as increased levels of excitatory neurotransmitters in the anterior insula in this population (As-Sanie et al., 2012;As-Sanie et al., 2016). Additionally, women with endometriosis-associated pelvic pain have reduced pain thresholds in areas of referred pain and generalized somatic hyperalgesia with applied pressure to sites beyond the pelvic region, characterizing sensitization (As-Sanie et al., 2013;Bajaj et al., 2003;Jarrell and Arendt-Nielsen 2013;Laursen et al., 2005;O'Neill et al., 2007;Stratton et al., 2015). It is important to note that chronic pelvic pain in women also develops in the absence of endometriosis and may similarly be associated with and sustained by sensitization (As-Sanie et al., 2013;Giamberardino et al., 2014;Grundstrom et al., 2019;Yosef et al., 2016).

In patients with chronic pain, central sensitization can be assessed using quantitative sensory testing. Changes in nociceptive pathways are indicated by changes in pain and tolerance thresholds, which are assessed by measuring the intensity of the stimulus needed to elicit a hyper-excitable response, such as increased pain sensitivity, at a specific body region (Arendt-Nielsen et al., 2018;Arendt-Nielsen and Yarnitsky 2009;Siao and Cros 2003;Woolf 2011). Sensory testing usually employs repetitive mechanical, thermal, or chemical cutaneous stimulation to measure pain threshold on a small region of the body, typically the hands or feet (Arendt-Nielsen et al., 2018;Rolke et al., 2006). Testing restricted to specific body territories have contributed to our understanding of how pain is initiated and maintained by sensitization. However, they provide an incomplete map of painful areas and limit the clinician's ability to determine the pattern or extent of the body regions involved in pain. These limited techniques do not convey a comprehensive pain phenotype, nor do they provide adequate insight into how myofascial dysfunction observed with sensitization can further perpetuate the pain. It is important to fully assess all body territories, as patients with sensitization often have widespread hyperalgesia, allodynia and multiple painful regions throughout the body (Maixner et al., 2016;Orr et al., 2020).

In this study, myofascial dysfunction was assessed by identifying the presence of myofascial trigger points contained within the paired muscles that are typically screened during a fibromyalgia evaluation outside of the pelvic floor. Unexpectedly, the patients were found to have widespread myofascial dysfunction, similar to that observed in women with fibromyalgia. These findings, along with our finding of spasm in pelvic floor muscles, may reflect the development of a viscerosomatic reflex, in which muscle tone increases and produces spasm in areas of referred pain (Patterson and Wurster 2003;Woolf 2011). Thus, visceral pain disorders, such as endometriosis or migraine headache, may act as triggering factors for fibromyalgia-like symptoms (Costantini et al., 2017;Giamberardino et al., 2015). Somatic structures innervated by the same spinal segment as the visceral pathology can contribute to associated allodynia, hyperalgesia, and myofascial trigger points (Stratton et al., 2015). In addition, through viscerosomatic convergence, ongoing noxious visceral input can sensitize various areas of the spinal cord as visceral afferent fibers extend over multiple spinal segments, leading to widespread sensitization (Aredo et al., 2017).

Our findings suggest that women with endometriosis-associated chronic pelvic pain experience widespread myofascial dysfunction as well as generalized and regional sensitization, often unevaluated and unrecognized by the clinician. Moreover, we found that patients reporting diffuse pain on pelvic exam were more likely to have lumbosacral and widespread sensitization. Clinicians should elicit and use such patient-reported descriptions to signal the need to evaluate pain symptomatology and signs of sensitization beyond the pelvic region. Importantly, given that palpation of the pelvic floor spasm recreated these patients' chronic pelvic pain, this area might be considered a "pain generator." As a pain generator, the pelvic floor spasm could transmit sensory information via peripheral nerves and then to central neurons, leading to amplification of signaling and establishing hyperalgesic priming after the initial peripheral pathology has been resolved (Dodds et al., 2019;Eller-Smith et al., 2018). In our previously reported case series of women this cohort who received open-label onabotulinumtoxinA to treat pelvic floor muscle spasm, we observed a reduction in pelvic floor muscle spasm that was associated with a decrease in patient-reported pain and disability(Tandon et al., 2019). Whether this clinical improvement was associated with reduction in myofascial dysfunction or sensitization awaits further study.

One main strength of this study is the application of a standardized, thorough clinical phenotyping evaluation that integrates the gynecologic and physiatry examinations by expert clinicians in these fields. Limiting participants to women with surgically diagnosed endometriosis who had optimized conventional and pain management treatment to the extent possible prior to enrollment aids in establishing the phenotype. Additionally, our cohort is representative of the broader population of women living with endometriosis-associated pelvic pain, given their high rates of non-menstrual pelvic pain, dysmenorrhea, and dyspareunia. The study is similarly generalizable in that we include participants on hormone therapy to suppress menses, reflecting standard medical management of patients with endometriosis.

This study has some limitations. A single physiatrist performed the neuro-musculoskeletal exam and a single gynecologist performed the abdominopelvic exam, so interrater reliability

could not be assessed. While we standardized our approach to evaluate pelvic myofascial pain in this cohort, there is no standardized examination that is universally accepted. Clinical techniques to evaluate pelvic myofascial pain vary significantly, suggesting a need to standardize this assessment to aid characterization and management of each patient's pain (Meister et al., 2018). Another limitation is our small sample size, as reflected in odds ratios with wide confidence intervals. As our study focused only on women with chronic pelvic pain associated with endometriosis, it is not known whether these findings are more generally representative of women with chronic pelvic pain initiated by other conditions.

Pain and sensitization beyond the pelvis have rarely been studied in women with endometriosis-associated chronic pelvic pain. The clinical importance of these findings underscore the complementary nature of a standardized pain-focused gynecologic assessment and a broader neuro-musculoskeletal examination. Together, these provide a more comprehensive picture of the individual patient's chronic pain phenotype that could inform a more holistic approach to treatment. Our observations also suggest the prevalence of widespread myofascial dysfunction in women with endometriosis-associated chronic pelvic pain, supporting the role of central sensitization in the maintenance of pain after surgical resection and with ongoing hormonal management. In turn, those with widespread pain, sensitization, and myofascial dysfunction may have pain generators outside the pelvic floor that will likely not respond to localized pelvic treatment or surgery. These diffuse and focal myofascial and central nervous system manifestations warrant consideration in pain management in this population. increased recognition of myofascial dysfunction and sensitization in the diagnosis and treatment of chronic pain conditions could elucidate more effective and targeted therapeutic approaches and improve patient outcomes.

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Significance:

What's already known:

- Women with endometriosis often have pelvic pain persisting after surgery despite hormonal therapies.
- These women have regional pelvic sensitization and myofascial dysfunction.

What does this study add:

- Pelvic floor muscle spasm is a major pain focus in this population.
- Sensitization and myofascial dysfunction are widespread, beyond the pelvic region.
- On-going pelvic floor spasm may initiate or maintain sensitization.
- Myofascial/sensitization manifestations warrant consideration when managing pain in this population.

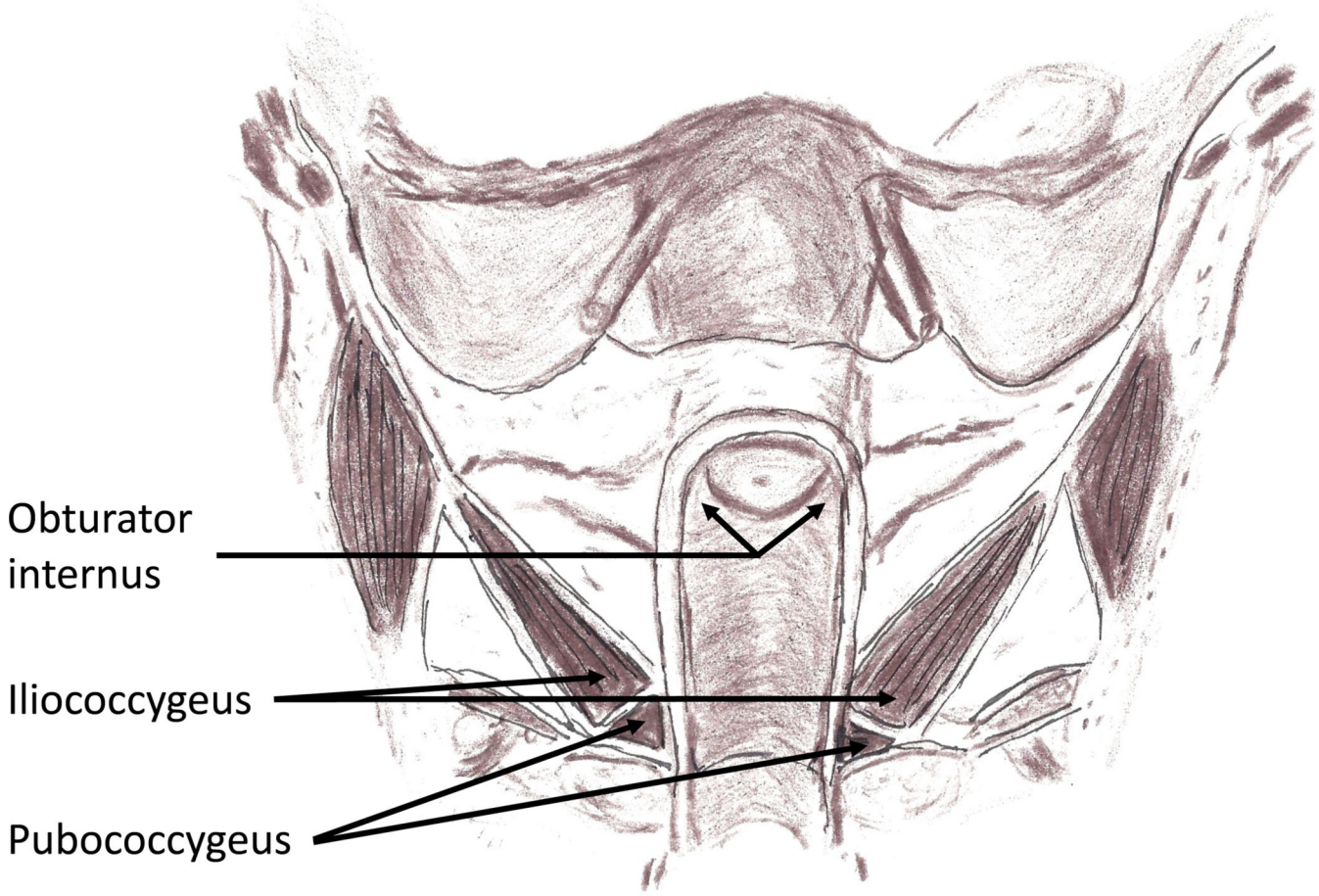

Fig. 1:
Coronal cross-section of pelvic floor muscles examined.

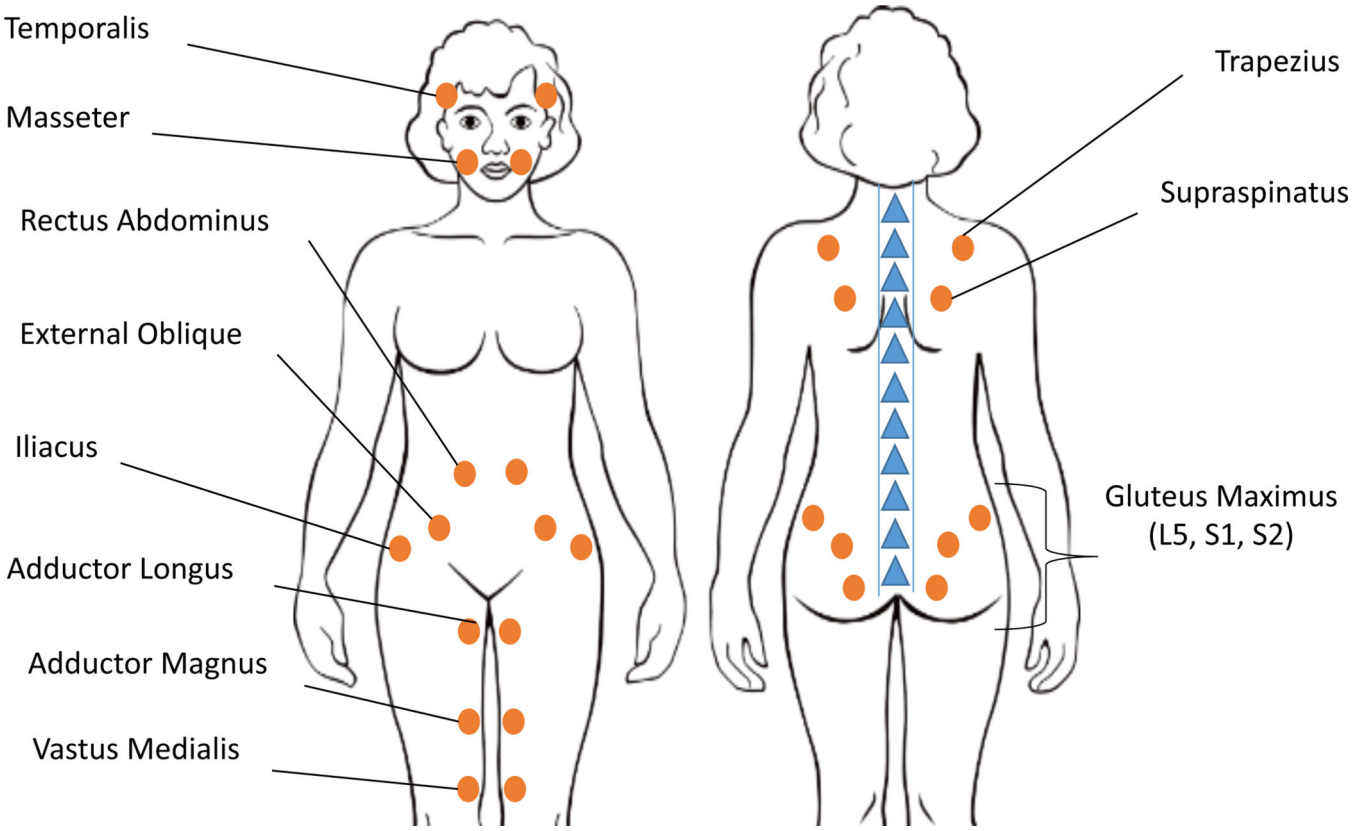

Fig. 2: Muscles, dermatomes, and interspinous ligaments assessed in the neuro-musculoskeletal examination.

Circles: Muscles assessed for myofascial trigger points and pressure-pain thresholds.

Triangles: Interspinous ligament pressure-pain thresholds measured every other segment from cervical-1 to sacral-1.

Lines: Paraspinal allodynia and hyperalgesia from dermatomes cervical-2 to sacral-2.

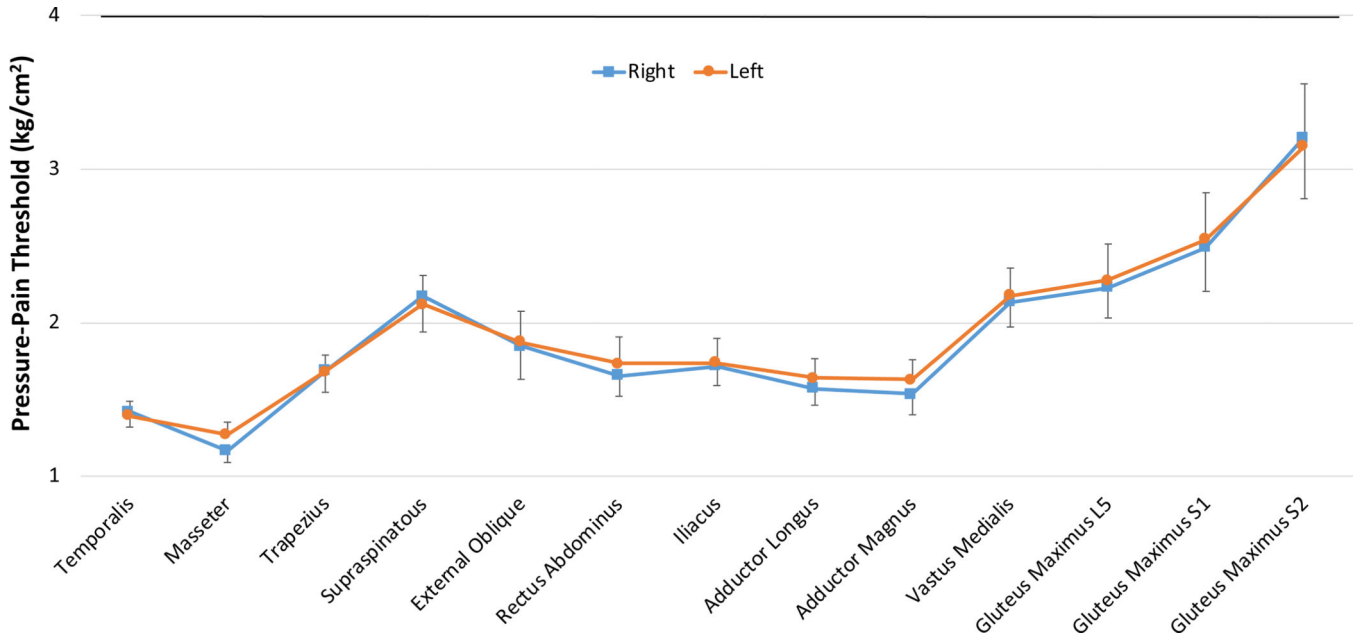

Fig. 3: Pressure-pain thresholds over myofascial trigger points.

All participants had lowered pressure-pain threshold (< 4 kg/cm^2) in more than half of the assessed trigger point regions.

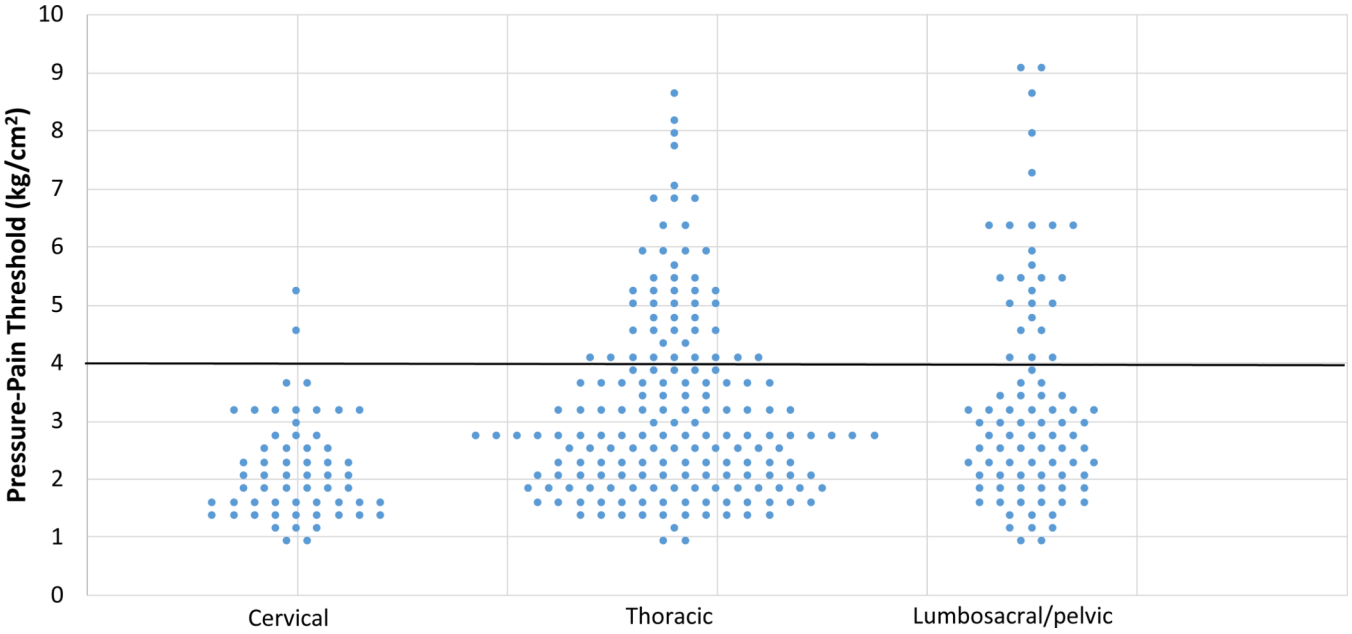

Fig. 4: Pressure-pain thresholds over interspinous ligaments.

Distribution of pressure-pain thresholds by cervical, thoracic, and lumbosacral/pelvic region. The lowered pressure-pain threshold is indicated by the line at 4 kg/cm^2.

Table 1:

Baseline demographics of participants with endometriosis-associated chronic pelvic pain

Characteristic	N=30	%
Age (y)		
Median (IQR; range)	30.0 (26.5–33.9; 18–50)	
Years of Pain[a]		
Mean (SD; range)	11.5 (6.5; 2–25)	
Race		
White	21	70
Black	3	10
Hispanic	4	13
Other	2	7
Education Level		
High school	2	7
Associates[b]	3	10
Bachelors/Graduate[b]	25	83
Employment Status		
Student/employed	28	93
Unemployed	2	7
Hormone Use		
Oral contraceptive pills (OCPs)[c]	6	20
Intrauterine device (IUD)	13	43
Both IUD and OCPs	1	3
IUD, Progestin and Lupron	1	3
Depo Provera	2	7
None	7	23

IQR=inter-quartile range (25th percentile-75th percentile)

SD=standard deviation

[a]At study enrollment

[b]Based on graduation or current enrollment

[c]5 of 6 women took OCPs continuously such that hormonal treatment in 22 of 30 served to suppress menses.

Percentages may not add to 100 due to rounding.