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Deep Dyspareunia in Endometriosis: Role of the Bladder and Pelvic Floor

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ABSTRACT

Introduction: The etiology of endometriosis-associated deep dyspareunia may include direct endometriosis-specific factors (eg, stage or invasiveness of disease) and/or indirect contributors such as bladder/pelvic floor dysfunction (eg, related to myofascial mechanisms or nervous system sensitization).

Aim: This study aimed to determine whether bladder/pelvic floor tenderness and painful bladder syndrome were associated with severity of deep dyspareunia in women with endometriosis, regardless of Stage (I/II vs III/IV) or other endometriosis-specific factors.

Methods: Observational study from a prospective patient registry (January 2014 to December 2016) at a tertiary centre for endometriosis. Included were women aged 18 to 49 years who had surgical removal and histopathologic confirmation of endometriosis at the centre. Cases with Stage I/II vs Stage III/IV endometriosis were analyzed separately. Bivariate associations with the primary outcome (severity of deep dyspareunia) were tested for bladder/pelvic floor tenderness, painful bladder syndrome, as well as endometriosis-specific factors identified at the time of laparoscopic surgery (eg, deep infiltrating endometriosis) and demographic factors (eg, age). Multivariable ordinal logistic regression was carried out to adjust for factors associated with the primary outcome.

Main Outcome Measure: Primary outcome was severity of deep dyspareunia on an 11-point numeric rating scale, categorized as none/mild (0−3), moderate (4−6), and severe (7−10), from a preoperative self-reported questionnaire.

Results: Overall, 411 women had surgically confirmed endometriosis: 263 had Stage I/II and 148 had Stage III/IV endometriosis. Among women with Stage I/II endometriosis, severity of deep dyspareunia was associated with both bladder/pelvic floor tenderness and painful bladder syndrome (AOR = 1.94, 95% CI: 1.11−3.38, $P = .019$ and AOR = 1.99, 95% CI: 1.15−3.44, $P = .013$, respectively), independent of endometriosis-specific factors or other factors associated with deep dyspareunia severity. Similar associations were found in women with Stage III/IV endometriosis (bladder/pelvic floor tenderness AOR =2.51, 95% CI: 1.25−5.02, $P = .01$, painful bladder syndrome: AOR = 1.90, 95% CI: 1.01−3.57, $P = .048$).

Clinical Implications: Myofascial or nervous system mechanisms may be important for deep dyspareunia in women with endometriosis, even in those with moderate-to-severe disease (Stage III/IV).

Strengths & Limitations: Strengths include the prospective registry, and histological confirmation of endometriosis and staging by experienced endometriosis surgeons. Limitations include assessment of only one pelvic floor muscle (levator ani).

Conclusion: In women with Stage I/II or Stage III/IV endometriosis, severity of deep dyspareunia was strongly associated with bladder/pelvic floor tenderness and painful bladder syndrome, independent of endometriosis-specific factors, which suggests the role of myofascial or sensitization pain mechanisms in some women with deep dyspareunia.

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Key Words: Endometriosis; Deep Dyspareunia; Central Sensitization; Bladder/Pelvic Floor Tenderness; Painful Bladder Syndrome

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INTRODUCTION

Endometriosis affects approximately 10% of reproductive-aged females and is a common cause of infertility, reduced sexual functioning, and pelvic pain.[1–3] It is the presence of ectopic endometrial cells that have become attached to the pelvic peritoneum, reproductive organs (eg, ovaries, fallopian tubes), or other visceral organs in the abdominopelvic cavity.[4,5] The 3 anatomic subtypes of endometriosis are superficial peritoneal endometriosis, ovarian endometrioma cysts, and deep infiltrating endometriosis (lesions infiltrating ≥5 mm).[6–8] The American Society for Reproductive Medicine (ASRM) classifies endometriosis based on anatomic severity, including amount of each anatomic subtype of endometriosis, from Stage I to IV.[9] Endometriosis is associated with different types of pelvic pain, including dysmenorrhea, chronic pelvic pain, dyschezia, and deep dyspareunia.[10]

Deep dyspareunia affects approximately 50% of women with endometriosis and can result in sexual dysfunction and negative impacts on relationships.[11] Because traditional hormonal and surgical therapy for endometriosis does not always lead to successful treatment of deep dyspareunia,[12] a further understanding of the pathophysiology and associated factors that result in deep dyspareunia is needed.[11,13]

It has recently been proposed that, in addition to endometriosis-specific factors (eg, stage, location, depth of invasion), other comorbid conditions (eg, painful bladder syndrome), myofascial contributors, and central sensitization of the nervous system may be important in the pathophysiology of deep dyspareunia in endometriosis.[12] For example, bladder tenderness was associated with deep dyspareunia in a retrospective study.[14] Also, in a prospective study, tenderness of the bladder or pelvic floor (levator ani), as well as painful bladder syndrome, were observed to be associated with more severe deep dyspareunia, independent of tenderness at other anatomic sites.[15] However, both studies involved a mixed sample of women with and without endometriosis; and in the women with endometriosis, endometriosis-specific features could not be assessed because detailed surgical data were not available.

In this study, we report on women who underwent a detailed preoperative examination, then prospectively underwent surgery at our centre, and were subsequently found to have histologically confirmed endometriosis. Thus, stage and other endometriosis-specific factors (ie, location, depth of disease) were reflective of the state of the disease at the time of the preoperative examination. Using this cohort, we examined whether bladder/pelvic floor tenderness and painful bladder syndrome were associated with severity of deep dyspareunia in women with either minimal/mild disease (Stage I/II) or moderate/severe disease (Stage III/IV).

MATERIALS AND METHODS

Participants

This study involved an analysis of data from a prospective registry for endometriosis and pelvic pain, the Endometriosis Pelvic Pain Interdisciplinary Cohort (EPPIC) (ClinicalTrials.gov #NCT02911090), at the BC Women's Centre for Pelvic Pain and Endometriosis. This cohort of prospectively consented patients has been previously described in detail, and was designed with the objective to examine associations between multifactorial characteristics and different pelvic pain outcomes including deep dyspareunia.[16] For methodology, women who are newly or re-referred to our centre are prospectively consented and recruited to the EPPIC registry, which is housed by the online REDCap database. There is an approximately 85% consent rate for participation in the registry.[16]

The EPPIC registry dataset includes the following sources of data.[16] Prior to the gynecologist assessment, patients complete a standardized online questionnaire including information on severity of deep dyspareunia and other types of pelvic pain, past medical and surgical history, and validated psychological and quality-of-life measures. During a standardized gynecologic assessment, physical exam data are entered by the gynecologist into data collection forms and then prospectively entered online. In patients who proceed with surgery at the centre, surgical data are prospectively entered online by the gynecologist on the day of surgery, including staging of endometriosis, per the recommendations of the Endometriosis Phenome and Biobanking Harmonisation Project (EPHect).[17] Pathologic data (eg, histologic confirmation of endometriosis) are subsequently correlated to the surgical findings and also entered online into the registry.

Inclusion criteria for this study were new or re-referred patients to the centre, and subsequent laparoscopic surgery at the centre with diagnosis and excision of histologically confirmed endometriosis between January 1, 2014 and December 31, 2016. Exclusion criteria were: never sexually active, postmenopausal status (spontaneous or surgical), missing dyspareunia severity scores, and absence of preoperative pelvic exam (eg, due to severe vaginismus) (Figure 1).

Outcome Measures and Covariates

For analysis, patients were divided into those with Stage I/II endometriosis and those with Stage III/IV endometriosis diagnosed (and resected) at the time of surgery at the centre. All excised tissues were sent to Pathology for histologic confirmation of endometriosis.

The primary outcome was the preoperative self-reported severity of deep dyspareunia from the online questionnaire, which we previously validated by showing an association with poorer sexual quality of life independent of superficial dyspareunia and other potential founders.[16,18] The primary outcome involved an 11-point numeric rating scale (0 being no pain and 10 being worst pain imaginable), categorized into none—mild (0—3), moderate (4—6), and severe (7—10) pain. Our question for deep dyspareunia question asks: "If you are currently sexually active or have been sexually active in the past, how painful was deep penetration during sexual activity?" The participants could indicate a score from 0—10 or could check "never sexually active." Women who indicated that they were never sexually

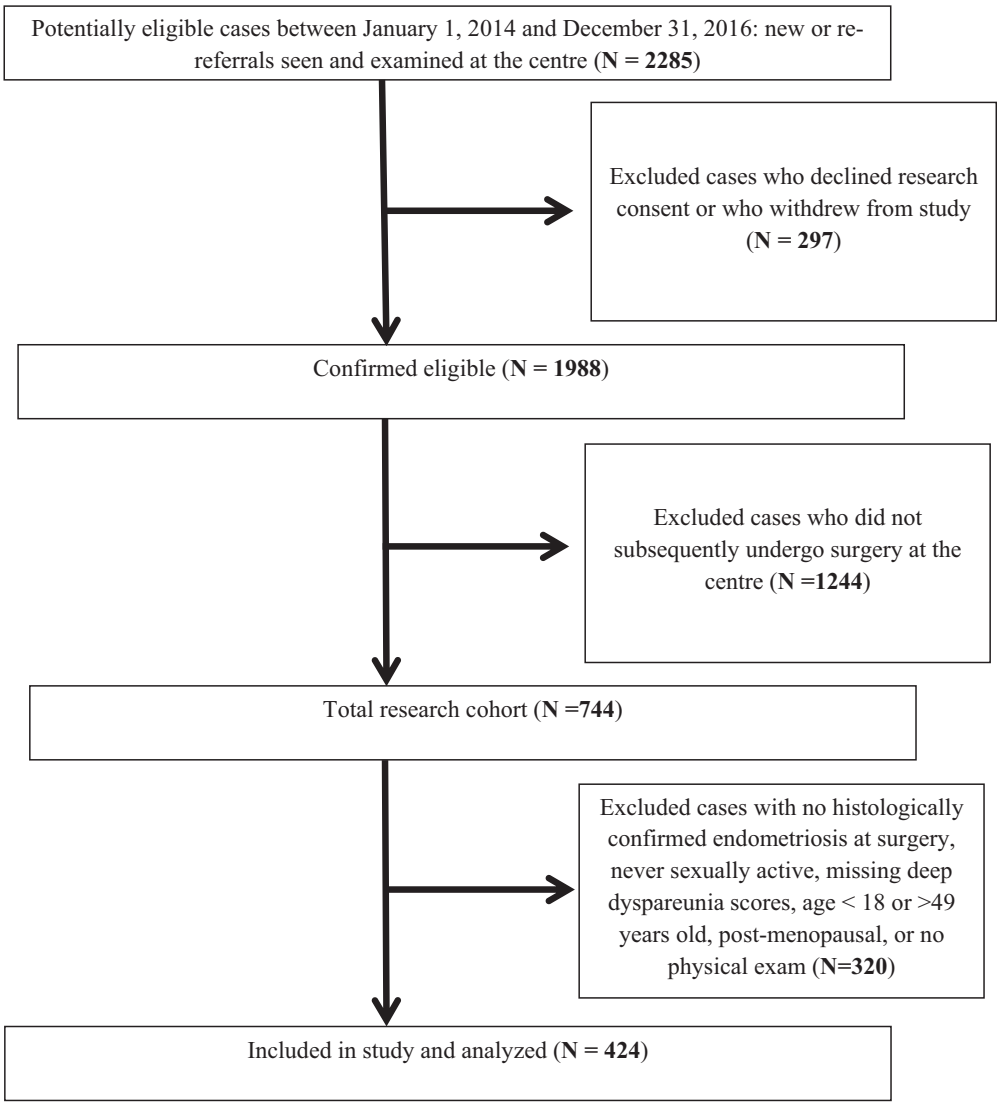

Figure 1. Study population flowchart.

active were excluded from this study. The question was designed to include both penile-vaginal penetration, as well as any type of deep penetration (eg, with sex toy), and to be inclusive of opposite-sex and same-sex sexual interactions.

The main variables of interest from the registry were as we have previously reported.[15] Tenderness (yes/no) of the bladder was assessed by uni-digit palpation at the anterior vaginal wall, while tenderness (yes/no) of the pelvic floor was assessed by uni-digit palpation of the levator ani bilaterally at 3 o'clock and 9 o'clock.[15] Tenderness at each site was separately assessed on pelvic exam at the gynecologist assessment, then grouped as a single variable due to common risk factors: tenderness at either the bladder or pelvic floor vs no tenderness.[15] Painful bladder syndrome was diagnosed using the diagnostic criteria from the American Urological Association or International Continence Society.[15]

Information on other factors potentially associated with deep dyspareunia were also obtained from the registry, and included the following: (i) abdominal wall pain (diagnosed by the Carnett test)[19]; (ii) irritable bowel syndrome (Rome III diagnostic criteria); (iii) demographic factors (eg, age, parity, body mass index [BMI]); and (iv) endometriosis-specific variables. Besides staging (Stage I/II vs Stage III/IV), the endometriosis-specific factors included the status of the cul-de-sac (pouch of Douglas), which has been shown in previous studies to be associated with deep dyspareunia compared to endometriosis of other sites.[15,20] For example, we included surgical diagnosis of an invasive nodule of the cul-de-sac and/or surgical diagnosis of cul-de-sac obliteration (partial or complete), which both constitute evidence of deep infiltrating endometriosis. Another endometriosis-specific factor was tenderness of the cul-de-sac on preoperative exam, in the presence of any surgically confirmed endometriosis of the cul-de-sac ("tender" endometriosis, whether invasive or not). We also included tenderness of the cul-de-sac on preoperative exam but without any surgically confirmed endometriosis of the cul-de-sac (which could represent referred pain);

Table 1. Demographic and clinical characteristics of women with endometriosis

Characteristic	Stage I/II (n = 263) Mean ± SD or % (frequency)	Stage III/IV (n = 148) Mean ± SD or % (frequency)
Age, years	33.2 ± 6.9	36.3 ± 6.3
BMI, kg/m^2		
Underweight, < 18.5	2.3% (6)	4.1% (6)
Normal, 18.5–24.9	58.6% (154)	59.5% (88)
Overweight, 25.0–29.9	22.4% (59)	22.3% (33)
Obese, > 30.0	15.2% (40)	14.2% (21)
Missing	1.5% (4)	0% (0)
Parity		
Previous birth(s)	39.5% (104)	33.8% (50)
No previous births	59.7% (157)	65.5% (97)
Missing	0.8% (2)	0.7% (1)
Hormonal suppression		
Currently taking	30.8% (81)	27% (40)
Not currently taking	69.2% (182)	73% (108)
Bladder or Pelvic floor tenderness		
Yes	45.6% (120)	33.8% (50)
No	54.4% (143)	66.2% (98)
Cul-de-sac tenderness		
Yes	65.8% (173)	49.3% (73)
No	34.2% (90)	50.7% (75)
Uterus or cervix tenderness		
Yes	33.5% (88)	25% (37)
No	66.5% (175)	73.6% (109)
Missing	0% (0)	1.4% (2)
Irritable bowel syndrome		
Yes	56.7% (149)	54.7% (81)
No	43.3% (114)	45.3% (67)
Painful bladder syndrome		
Yes	49.8% (131)	49.3% (73)
No	50.2% (132)	50.7% (75)
Abdominal wall pain		
Carnett test positive	35.7% (94)	18.2% (27)
Carnett test negative	64.3% (169)	81.8% (121)
Cul-de-sac nodule at surgery		
Yes	11% (29)	25% (37)
No	89% (234)	75% (111)
Cul-de-sac obliteration at surgery (partial or complete)		
Yes	3% (8)	53.4% (79)
No	97% (255)	46.6% (69)
Cul-de-sac tenderness on exam, and cul-de-sac endometriosis at surgery		
Yes	62.4% (164)	38.5% (57)
No	37.6% (99)	61.5% (91)
Cul-de-sac tenderness on exam, and no cul-de-sac endometriosis at surgery		
Yes	9.9% (26)	13.5% (20)
No	90.1% (237)	86.5% (128)
Deep dyspareunia		
Mild (0–3)	12.2% (32)	27.7% (41)
Moderate (4–6)	18.3% (48)	23% (34)
Severe (7–10)	69.6% (183)	49.3% (73)

and a tender uterus/cervix on preoperative exam, which we previously showed to also be associated with more severe deep dyspareunia.[15]

Statistical Analysis

The primary outcome (deep dyspareunia severity categorized as none–mild [0–3], moderate [4–6], and severe [7–10]) was examined for associations with bladder/pelvic floor tenderness (present/absent), painful bladder syndrome (present/absent), and other covariates using the chi-square test (categorical variables) or Spearman correlation coefficient (continuous variables). Again, these associations were examined separately in two groups, women with Stage I/II and women with Stage III/IV endometriosis.

Variables with significant bivariate associations ($P < .05$) were then entered into ordinal logistic regression models with deep dyspareunia as the primary outcome categorized into the 3 groups (0–3, 4–6, 7–10). 2 models were fitted, one for the Stage I/II endometriosis group, and another for the Stage III/IV endometriosis group. Backward elimination method was used to derive the final models, with P value criterion = .05. Ordinal regression was used because the assumptions of linear regression were not met when the raw 0–10 values were used for the primary outcome.

Statistical analyses were performed using IBM SPSS Statistics 24 (SPSS Inc, Chicago, IL, USA). Observations with missing data on any of the covariates were excluded from regression analyses.

Sample Size Calculation

A retrospective chart review at the Centre for Pelvic Pain and Endometriosis was initially conducted for the sample size calculation. This review involved data from 48 women who had

surgical removal of deep infiltrating endometriosis between August 2010 and October 2013 and who also completed a questionnaire on deep dyspareunia severity scores. Bivariate analysis indicated that deep dyspareunia severity [categorized into mild (0−3), moderate (4−6), and severe (7−10)] was significantly associated with bladder/pelvic floor tenderness (X^2 = 6.58, P = .037). Therefore, with power = 0.80 and α = 0.05 two-tailed, and prevalence ratio 1.4 or higher, a sample size of 85 was required for the prospective study to find an association between the severity of deep dyspareunia and bladder/pelvic floor tenderness (OpenEpi, Version 3).

RESULTS

Study Sample

424 patients from the registry were selected according to the study criteria (Figure 1, Table 1). In this sample, 263 women had Stage I/II endometriosis and 148 had Stage III/IV endometriosis, while 13 had missing data for stage and were therefore excluded from analyses. In the Stage I/II cohort, 12.2% (32/263) of women reported no/mild deep dyspareunia (0−3 points on the severity scale), 18.3% (48/263) reported moderate/deep dyspareunia (4−6 points), and 69.6% (183/263) reported severe deep dyspareunia (7−10 points). In the Stage III/IV cohort, 27.7% (41/148) of women reported no/mild deep dyspareunia, 23% (34/148) reported moderate deep dyspareunia, and 49.3% (73/148) had severe deep dyspareunia on the pain severity scale (Table 1). Other descriptive variables are shown in the Appendix.

Stage I/II Endometriosis

In women with Stage I/II endometriosis, severity of deep dyspareunia was associated with bladder/pelvic floor tenderness (X^2 = 11.38, P = .003) and painful bladder syndrome (X^2 = 12.18, P = .002), as well as cul-de-sac nodule (X^2 = 6.99, P = .03) and uterus and/or cervix tenderness (X^2 = 6.54, P = .038) (Table 2).

Stage III/IV Endometriosis

In women with Stage III/IV endometriosis, severity of deep dyspareunia was associated with bladder/pelvic floor tenderness (X^2 = 10.05, P = .007) and painful bladder syndrome (X^2 = 7.24, P = .027), as well as positive Carnett test (X^2 = 6.17, P = .046) and younger age (r = -0.18, P = .03) (Table 3).

Multivariable Analyses

In the ordinal logistic regression model for women with Stage I/II endometriosis, severity of deep dyspareunia was independently associated with bladder/pelvic floor tenderness (AOR = 1.94, 95% CI 1.11−3.38, P = .019) and painful bladder syndrome (AOR = 1.99, 95% CI 1.15−3.44, P = .013). In addition, it was associated with the presence of a cul-de-sac nodule (AOR = 0.41, 95% CI 0.19−0.87, P = .021) (Table 4).

Similarly, in women with Stage III/IV endometriosis, severity of deep dyspareunia was independently associated with bladder/pelvic floor tenderness (AOR = 2.51, 95% CI 1.25−5.02, P = .01), and painful bladder syndrome (AOR = 1.90, 95% CI 1.01−3.57, P = .048) (Table 4).

DISCUSSION

In this study of women with surgically and histologically confirmed endometriosis from a tertiary care centre, we found that bladder/pelvic floor tenderness and painful bladder syndrome were associated with severity of deep dyspareunia, regardless of other clinical factors, including endometriosis-specific variables. These findings were observed in women with either minimal-mild (Stage I/II) or moderate-to-severe (Stage III/IV) endometriosis, suggesting a role for bladder/pelvic floor tenderness and painful bladder syndrome regardless of the anatomic load of disease. We hypothesize that one mechanism for deep dyspareunia in endometriosis may involve direct contact with the bladder or levator ani during deep penetration. Alternatively, bladder/pelvic floor tenderness on exam and meeting clinical criteria for painful bladder syndrome could be markers for pelvic floor dysfunction in the sexual context.

The etiology of bladder/pelvic floor tenderness may include intrinsic bladder problems, nervous system sensitization, or myofascial origin.[14] Invasive endometriosis of the bladder or pelvic floor is rare, and would not account for bladder/pelvic floor tenderness in most women with endometriosis. In contrast, painful bladder syndrome is a common comorbid condition in women with endometriosis, and its association with severity of deep dyspareunia suggests that it can account for some cases of deep dyspareunia in women with endometriosis. We also found that bladder/pelvic floor tenderness was associated with deep dyspareunia, independent of painful bladder syndrome, suggesting that myofascial origin or central sensitization may also be important in tenderness of these areas.[15] Myofascial pain could involve tender trigger points in the levator ani or anterior vaginal wall[21,22] due to hyperactive nerve firing within the skeletal muscle reflex arc due to muscle fibre trauma.[21,23] Sensitization could manifest as hyperalgesia and allodynia[24,25] in normally non-tender structures (eg, the bladder and pelvic floor); this could occur by amplification of central nervous system nociceptive pathways, or by viscero-visceral convergence or viscero-somatic convergence at the spinal cord that links gynecologic pain to other visceral (eg, bladder) or somatic (eg, pelvic floor) structures.[26]

Additionally, it was noted that in women with Stage I/II endometriosis, presence of a cul-de-sac nodule was significantly associated with a lower severity of deep dyspareunia. Although this observation seems counterintuitive, the likely reason is that at our centre, many women with this type of presentation are referred primarily for infertility rather than for pain. Thus, this statistical finding may more reflect sample ascertainment, rather than the pathophysiologic role of nodules in deep dyspareunia.

Strengths of the study include its prospective nature and appropriately powered sample size, as well as stringent surgical

Table 2. Bivariate associations with severity of deep dyspareunia (Stage I/II endometriosis)

Factor	N total	None-Mild deep dyspareunia (0–3)	Moderate deep dyspareunia (4–6)	Severe deep dyspareunia (7–10)	Statistics	*P* value
Categorical Variables					*Chi-Squared/Fisher's Exact*	
Bladder/Pelvic floor tenderness	263				11.38	**.003**
Yes		5%* (6)	18% (21)	77% (93)		
No		18%* (26)	19% (27)	63% (90)		
Painful bladder syndrome	263				12.18	**.002**
Yes		5% (7)	18% (23)	77% (101)		
No		19% (25)	19% (25)	62% (82)		
Cul-de-sac tenderness	263				4.87	.088
Yes		10% (17)	16% (28)	74% (128)		
No		17% (15)	22% (20)	61% (55)		
Cul-de-sac nodule	263				7.00	**.03**
Yes		21% (6)	31% (9)	48% (14)		
No		11% (26)	17% (39)	72% (169)		
Cul-de-sac obliteration (partial)	263				2.66	.27
Yes		25% (2)	0% (0)	75% (6)		
No		12% (30)	19% (48)	69% (177)		
Cul-de-sac tenderness and cul-de-sac endometriosis	263				0.14	.93
Yes		12% (19)	18% (30)	70% (115)		
No		13% (13)	18% (18)	69% (68)		
Cul-de-sac tenderness and no cul-de-sac endometriosis	263				3.29	.19
Yes		4% (1)	11% (3)	85% (22)		
No		13% (31)	19% (45)	68% (161)		
Uterus/cervix tenderness	263				6.54	**.038**
Yes		7% (6)	14% (12)	79% (70)		
No		15% (26)	21% (36)	64% (113)		
Irritable bowel syndrome	263				1.78	.41
Yes		10% (15)	17% (26)	73% (108)		
No		15% (17)	19% (22)	66% (75)		
Abdominal wall pain	263				3.05	.22
Carnett pos		8% (7)	19% (18)	73% (69)		
Carnett neg		15% (25)	18% (30)	67% (114)		
Parity	261				2.79	.25
Yes		9% (9)	16% (17)	75% (78)		
No		15% (23)	19% (30)	66% (104)		
Current hormonal suppression	263				2.21	.33
Yes		9% (7)	22% (18)	69% (56)		
No		14% (25)	16% (30)	70% (127)		
Continuous Variables					*Spearman Correlation Coefficient (r)*	
Age	263	—	—	—	-0.038	.54
BMI group	259	—	—	—	0.093	.13

Significant values ($P < .05$) are bolded.
*Percentages are for each row (eg, % based on the sum for the "yes" row, and % based on the sum for the "no" row).

phenotyping combined with detailed preoperative patient-reported and physical examination data in the registry. In particular, all patients had histologically confirmed endometriosis, and stage and endometriosis-specific factors (eg, location or depth of invasion) were reflective of the state of disease at the time of the preoperative examination. Limitations

Table 3. Bivariate associations with severity of deep dyspareunia (Stage III/IV endometriosis)

Factor	N total	None-Mild deep dyspareunia (0–3)	Moderate deep dyspareunia (4–6)	Severe deep dyspareunia (7–10)	Statistics	*P* value
Categorical Variables					Chi-Squared/Fisher's Exact	
Bladder/pelvic floor tenderness	148				10.05	**.007**
Yes		12%* (6)	24% (12)	64% (32)		
No		36%* (35)	22% (22)	42% (41)		
Painful bladder syndrome	148				7.24	**.027**
Yes		18% (13)	25% (18)	57% (42)		
No		37% (28)	21% (16)	42% (31)		
Cul-de-sac tenderness	148				4.12	.13
Yes		21% (15)	27% (20)	52% (38)		
No		35% (26)	19% (14)	46% (35)		
Cul-de-sac nodule	148				0.23	.89
Yes		30% (11)	24% (9)	46% (17)		
No		27% (30)	23% (25)	50% (56)		
Cul-de-sac obliteration (partial or complete)	148				0.53	.77
Yes		27% (21)	25% (20)	48% (38)		
No		29% (20)	20% (14)	51% (35)		
Cul-de-sac tenderness and cul-de-sac endometriosis	148				4.98	.083
Yes		18% (10)	28% (16)	54% (31)		
No		34% (31)	20% (18)	46% (42)		
Cul-de-sac tenderness and no cul-de-sac endometriosis	148				1.93	.38
Yes		25% (5)	35% (7)	40% (8)		
No		28% (36)	21% (27)	51% (65)		
Uterus/cervix tenderness	146				3.08	.21
Yes		19% (7)	32% (12)	49% (18)		
No		30% (33)	20% (22)	50% (54)		
Irritable bowel syndrome	148				1.27	.53
Yes		25% (20)	26% (21)	49% (40)		
No		31% (21)	20% (13)	49% (33)		
Abdominal wall pain	148				6.17	**.046**
Carnett pos		11% (3)	37% (10)	52% (14)		
Carnett neg		31% (38)	20% (24)	49% (59)		
Parity	147				0.46	.80
Yes		30% (15)	20% (10)	50% (25)		
No		27% (26)	25% (24)	48% (47)		
Current hormonal suppression	148				3.82	.15
Yes		20% (8)	18% (7)	62%(25)		
No		31% (33)	25% (27)	44% (48)		
Continuous Variables					*Spearman correlation coefficient (r)*	
Age	148	—	—	—	-0.18	**.03**
BMI group	148	—	—	—	0.033	.69

Significant values ($P < .05$) are bolded.
*Percentages are for each row (eg, % based on the sum for the "yes" row, and % based on the sum for the "no" row).

include the assessment of pelvic floor tenderness of only one muscle (levator ani). Also, in future work, it would be interesting to determine whether bladder/pelvic floor tenderness or painful bladder syndrome predicts change in deep dyspareunia severity after surgical removal of endometriosis. Generalizability is affected by the tertiary referral setting of the study.

Table 4. Multivariable ordinal regression models

	Stage I/II (N = 263)			Stage III/IV (N = 148)		
Factor	B	AOR (95% CI)	*P* value	B	AOR (95% CI)	*P* value
Bladder/Pelvic floor tenderness	0.66	1.94 (1.11–3.38)	0.019	0.92	2.51 (1.25–5.02)	.01
Painful Bladder Syndrome	0.69	1.99 (1.15–3.44)	0.013	0.64	1.90 (1.01–3.57)	.048
Cul-de-sac nodule	-0.89	0.41 (0.19–0.87)	0.021	–	–	–

B = Beta coefficient; AOR = adjusted odds ratio.

In summary, in this study, we found that bladder/pelvic floor tenderness and painful bladder syndrome were associated with more severe deep dyspareunia in women in endometriosis, independent of stage (anatomic load of disease) or other endometriosis-specific variables (eg, location or invasiveness of disease). This raises the possibility of nervous system or myofascial mechanisms in some women with endometriosis-associated deep dyspareunia, even in those with Stage III/IV endometriosis. An association has been found between dyspareunia and decreased pain-pressure thresholds (as a marker of central nervous system sensitization) in the chronic pelvic pain population.[27] A similar quantitative sensory testing study should be done in the endometriosis population to further characterize the relationship between central sensitization, bladder/pelvic floor tenderness and painful bladder syndrome, and severity of deep dyspareunia.

Greater recognition of potential nervous system and myofascial origins of deep dyspareunia in endometriosis, even in women with advanced-stage endometriosis, is important because it may guide management.[12] For example, even in the patient with advanced-stage endometriosis that requires surgery, there may still be a perioperative role for pelvic floor physiotherapy, cognitive therapies, and sexual therapy, to address the nervous system and myofascial components of the deep dyspareunia. In other patients with endometriosis, their deep dyspareunia may be primarily due to the bladder/pelvic floor, rather than the endometriosis lesions, and it may be ideal to avoid surgery in this population and focus on allied healthcare approaches. These latter patients could be classified as having DSM-V genito-pelvic pain penetration disorder, where the deep dyspareunia is not directly due to the underlying disease (endometriosis), but to sensitization/myofascial mechanisms.[12] Further research is needed to accurately phenotype sexual pain in endometriosis, to individualize treatment based on the actual causes of deep dyspareunia in each case, and to avoid unnecessary treatments such as repetitive surgeries.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jsxm.2018.06.007.