Deep dyspareunia in endometriosis: Role of the bladder and pelvic floor

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Abstract

Background. The etiology of endometriosis-associated deep dyspareunia may include direct endometriosis-specific factors (e.g., Stage or invasiveness of disease) and/or indirect contributors such as bladder/pelvic floor dysfunction (e.g., 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 – December 2016) at a tertiary centre for endometriosis. Included were women aged 18-49 years who had surgical removal and histopathological 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 (e.g., deep infiltrating endometriosis) and demographic factors (e.g., 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 pre-operative 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=1.99, 95% CI: 1.15-3.44, p=0.013 and AOR=1.94, 95% CI: 1.11–3.38, p=0.019, 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=1.90, 95% CI: 1.01 – 3.57, p=0.048, painful bladder syndrome: AOR=2.51, 95% CI: 1.25 – 5.02, p=0.01).

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 deep dyspareunia.

Key Words. Endometriosis; Deep dyspareunia; Central sensitization; Bladder/pelvic floor tenderness; Painful bladder syndrome.

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 which become attached to the pelvic peritoneum, reproductive organs (e.g.., ovaries, fallopian tubes), or other visceral organs in the abdominopelvic cavity [4, 5]. The three anatomic subtypes of endometriosis are: superficial peritoneal endometriosis, ovarian endometrioma cysts, and deep infiltrating endometriosis (lesions infiltrating >=5mm) [6-8]. The American Society for Reproductive Medicine (ASRM) classification system for endometriosis (Stage I-IV) is based on anatomical severity, including amount of each anatomic subtype of endometriosis [9]. In terms of symptoms, 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 decreased sexual quality of life and negative impacts on relationships [11]. Since traditional hormonal and surgical therapy does not always lead to successful treatment of deep dyspareunia in women with endometriosis [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 (e.g., stage, location, depth of invasion), it is important to consider other comorbid conditions (e.g., painful bladder syndrome), myofascial contributors, and central sensitization of the nervous system 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 of these studies involved a mixed sample of women with and without endometriosis; and in the women with endometriosis, endometriosis-specific features could not be assessed as detailed surgical data was 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 (i.e., 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 to examine associations between multifactorial characteristics and different types of pelvic pain [16].

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, post-menopausal status (spontaneous or surgical), missing dyspareunia severity scores, and absence of pre-operative pelvic exam (e.g., due to severe vaginismus) (Figure 1).

The registry dataset includes the following sources of data [16]. Prior to the gynecologist assessment, patients complete an online questionnaire including information on severity of deep dyspareunia and past medical history. During the assessment, physical exam data are prospectively entered online by the gynecologist. In patients who proceed with surgery at the centre, surgical data are prospectively entered online by the gynecologist as per the recommendations of the Endometriosis Phenome and Biobanking Harmonisation Project (EPHect) [17].

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 histological confirmation of endometriosis.

The primary outcome was the pre-operative severity of deep dyspareunia on an 11-point numeric rating scale (0 being no pain and 10 being worst pain imaginable) [16], categorized into none-mild (0-3), moderate (4-6), and severe (7-10) pain.

The main variables of interest from the registry were as we have previously reported [15]: 1) tenderness of the bladder or pelvic floor (levator ani) during the pelvic exam at the gynecologist assessment, grouped as a single variable due to common risk factors [15]; and 2) painful bladder syndrome (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: 1) abdominal wall pain (diagnosed by the Carnett test) [18]; 2) irritable bowel syndrome (Rome III diagnostic criteria); 3) demographic factors (e.g., age, parity, body mass index [BMI]); and 4) 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, 19]. 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 pre-operative 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 pre-operative exam but without any surgically confirmed endometriosis of the cul-de-sac (which could represent referred pain); and a tender uterus/cervix on pre-operative 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 the associations with bladder/pelvic floor tenderness (present/absent) and 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 ($p < 0.05$) were then entered into ordinal logistic regression models with deep dyspareunia as the primary outcome categorized into the three groups (0-3, 4-6, 7-10). Two 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 = 0.05. Ordinal regression was utilized 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. 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 ($X^2=6.58$, $p=0.037$). Therefore, with power = 0.80 and $\alpha = 0.05$ 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

Four hundred and twenty-four 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=0.003) and painful bladder syndrome (X^2=12.18, p=0.002), as well as cul-de-sac nodule (X^2=6.99, p=0.03) and uterus and/or cervix tenderness (X^2=6.54, p=0.038) (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=0.007) and painful bladder syndrome (X^2=7.24, p=0.027), as well as positive Carnett test (X^2=6.17, p=0.046) and younger age (r=-0.18, p=0.03) (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=0.019) and painful bladder syndrome (AOR=1.99, 95% CI 1.15-3.44, p=0.013). In addition, it was associated with the presence of a cul-de-sac nodule (AOR=0.41, 95% CI 0.19-0.87, p=0.021) (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=0.01), and painful bladder syndrome (AOR=1.90, 95% CI 1.01-3.57, p=0.048) (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, demonstrating the importance of 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 [20, 21] due to hyperactive nerve firing within the skeletal muscle reflex arc due to muscle fibre trauma [20] [23]. Sensitization could manifest as hyperalgesia and allodynia [24, 25] in normally non-tender structures (e.g., 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 (e.g. bladder) or somatic (e.g. pelvic floor) structures [26].

Strengths of the study include its prospective nature and appropriately powered sample size, as well as stringent surgical phenotyping combined with detailed patient-reported and physical examination data in the registry. Limitations 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 predicted whether deep dyspareunia severity improves after surgical removal of endometriosis. Generalizability is affected by the tertiary referral setting of the study.

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 (e.g. location or invasiveness of disease). This raises the possibility of nervous system or myofascial

mechanisms in deep dyspareunia, even in women 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 as it may guide management [12]. For example, even in the patient with advanced Stage endometriosis that requires surgery, there may still be a peri-operative 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 health care 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, in order 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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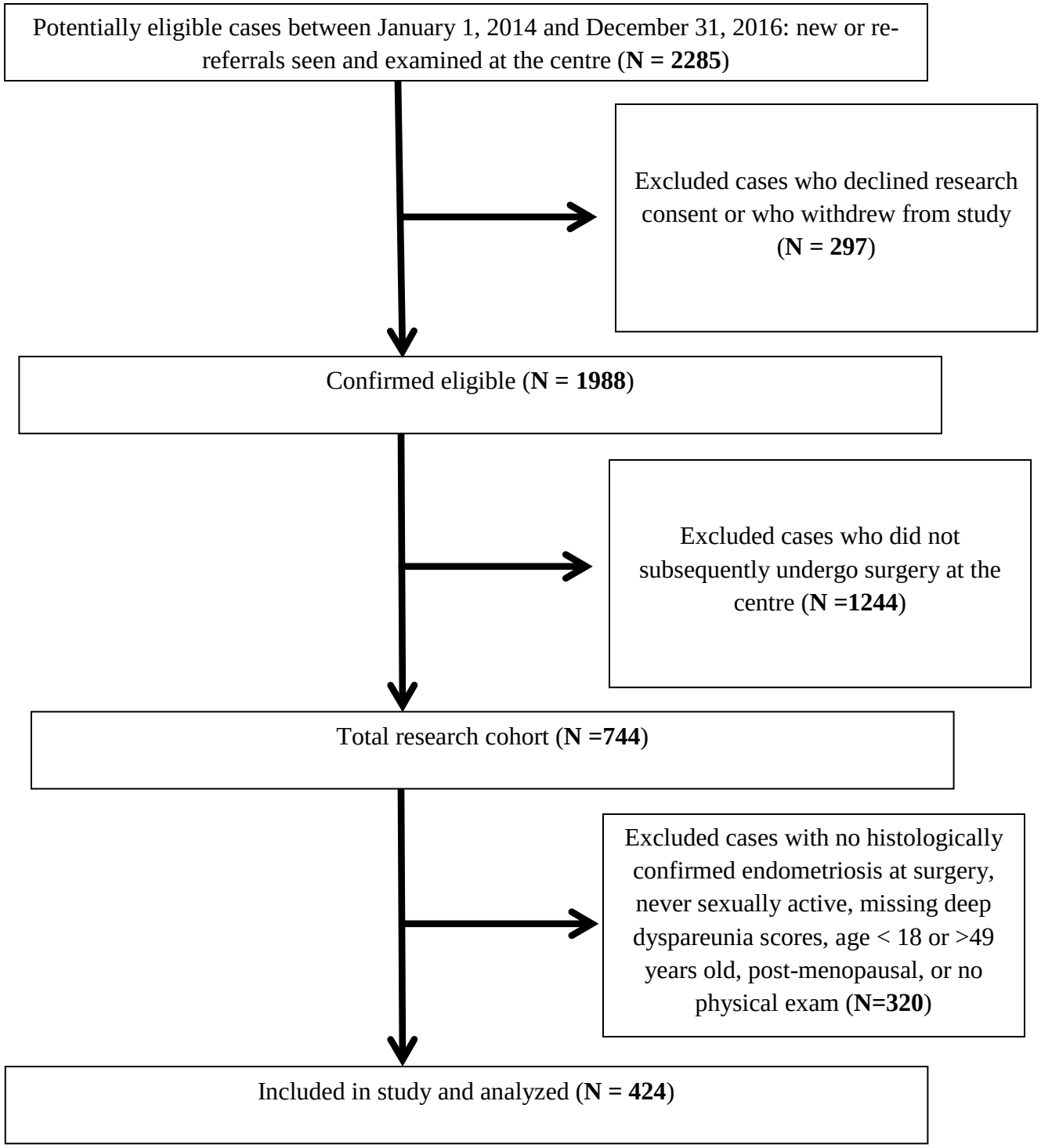

Figure 1. Study population flowchart.

392 **Table 1**. Demographic and clinical characteristics of women with endometriosis.

	Stage I/II (n=263)	**Stage III/IV (n=148)**
Characteristic	**Mean ± SD or Percentage (frequency)**	**Mean ± SD or Percentage (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 No	49.8% (131) 50.2% (132)	49.3% (73) 50.7% (75)
Abdominal wall pain Carnett test positive Carnett test negative	 35.7% (94) 64.3% (169)	 18.2% (27) 81.8% (121)
Cul-de-sac nodule at surgery Yes No	 11% (29) 89% (234)	 25% (37) 75% (111)
Cul-de-sac obliteration at surgery (partial or complete) Yes No	 3% (8) 97% (255)	 53.4% (79) 46.6% (69)
Cul-de-sac tenderness on exam, and cul-de-sac endometriosis at surgery Yes No	 62.4% (164) 37.6% (99)	 38.5% (57) 61.5% (91)
Cul-de-sac tenderness on exam, and no cul-de-sac endometriosis at surgery Yes No	 9.9% (26) 90.1% (237)	 13.5% (20) 86.5% (128)
Deep Dyspareunia Mild (0-3) Moderate (4-6) Severe (7-10)	 12.2% (32) 18.3% (48) 69.6% (183)	 27.7% (41) 23% (34) 49.3% (73)

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

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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	**0.003**
Yes		5%[1] (6)	18% (21)	77% (93)		
No		18%[1] (26)	19% (27)	63% (90)		
Painful bladder syndrome	263				12.18	**0.002**
Yes		5% (7)	18% (23)	77% (101)		
No		19% (25)	19% (25)	62% (82)		
Cul-de-sac tenderness	263				4.87	0.088
Yes		10% (17)	16% (28)	74% (128)		
No		17% (15)	22% (20)	61% (55)		
Cul-de-sac nodule	263				7.00	**0.03**
Yes		21% (6)	31% (9)	48% (14)		
No		11% (26)	17% (39)	72% (169)		
Cul-de-sac obliteration (partial)	263				2.66	0.27
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	0.93
Yes		12% (19)	18% (30)	70% (115)		
No		13% (13)	18% (18)	69% (68)		
Cul-de-sac	263				3.29	0.19

tenderness and no cul-de-sac endometriosis						
Yes		4% (1)	11% (3)	85% (22)		
No		13% (31)	19% (45)	68% (161)		
Uterus/cervix tenderness	263				6.54	**0.038**
Yes		7% (6)	14% (12)	79% (70)		
No		15% (26)	21% (36)	64% (113)		
Irritable bowel syndrome	263				1.78	0.41
Yes		10% (15)	17% (26)	73% (108)		
No		15% (17)	19% (22)	66% (75)		
Abdominal wall pain	263				3.05	0.22
Carnett pos		8% (7)	19% (18)	73% (69)		
Carnett neg		15% (25)	18% (30)	67% (114)		
Parity	261				2.79	0.25
Yes		9% (9)	16% (17)	75% (78)		
No		15% (23)	19% (30)	66% (104)		
Current hormonal suppression	263				2.21	0.33
Yes		9% (7)	22% (18)	69% (56)		
No		14% (25)	16% (30)	70% (127)		
Continuous Variables					*Spearman Correlation Coefficient (r)*	
Age	263	--	--	--	-0.038	0.54
BMI group	259	--	--	--	0.093	0.13

[1]Percentages are for each row (e.g. % based on the sum for the "yes" row, and % based on the sum for the "no" row)

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

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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	**0.007**
Yes		12%[1] (6)	24% (12)	64% (32)		
No		36%[1] (35)	22% (22)	42% (41)		
Painful bladder syndrome	148				7.24	**0.027**
Yes		18% (13)	25% (18)	57% (42)		
No		37% (28)	21% (16)	42% (31)		
Cul-de-sac tenderness	148				4.12	0.13
Yes		21% (15)	27% (20)	52% (38)		
No		35% (26)	19% (14)	46% (35)		
Cul-de-sac nodule	148				0.23	0.89
Yes		30% (11)	24% (9)	46% (17)		
No		27% (30)	23% (25)	50% (56)		
Cul-de-sac obliteration (partial or complete)	148				0.53	0.77
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	0.083
Yes		18% (10)	28% (16)	54% (31)		
No		34% (31)	20% (18)	46% (42)		

Cul-de-sac tenderness and no cul-de-sac endometriosis Yes No	148	 25% (5) 28% (36)	 35% (7) 21% (27)	 40% (8) 51% (65)	1.93	0.38
Uterus/cervix tenderness Yes No	146	 19% (7) 30% (33)	 32% (12) 20% (22)	 49% (18) 50% (54)	3.08	0.21
Irritable bowel syndrome Yes No	148	 25% (20) 31% (21)	 26% (21) 20% (13)	 49% (40) 49% (33)	1.27	0.53
Abdominal wall pain Carnett pos Carnett neg	148	 11% (3) 31% (38)	 37% (10) 20% (24)	 52% (14) 49% (59)	6.17	**0.046**
Parity Yes No	147	 30% (15) 27% (26)	 20% (10) 25% (24)	 50% (25) 48% (47)	0.46	0.80
Current hormonal suppression Yes No	148	 20% (8) 31% (33)	 18% (7) 25% (27)	 62%(25) 44% (48)	3.82	0.15
Continuous Variables					*Spearman correlation coefficient (r)*	
Age	148	--	--	--	-0.18	**0.03**
BMI group	148	--	--	--	0.033	0.69

[1]Percentages are for each row (e.g. % based on the sum for the "yes" row, and % based on the sum for the "no" row)

Table 4. Multivariable ordinal regression models

Factor	Stage I/II (N=263)			Stage III/IV (N=148)		
	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)	0.01
Painful Bladder Syndrome	0.69	1.99 (1.15 – 3.44)	0.013	0.64	1.90 (1.01 - 3.57)	0.048
Cul-de-sac nodule	-0.89	0.41 (0.19 – 0.87)	0.021	--	--	--

B denotes the Beta coefficient, AOR denotes adjusted odds ratio.

433 **Appendix: Other clinical characteristics of the study sample.**

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	Stage I/II (n=263)	**Stage III/IV (n=148)**
Clinical characteristic	**Percentage (frequency)**	**Percentage (frequency)**
Superficial Dyspareunia		
Mild (0-3)	49.8% (131)	55.4% (82)
Moderate (4-6)	22.1% (58)	20.9% (31)
Severe (7-10)	28.1% (74)	23.6% (35)
Dysmenorrhea		
Mild (0-3)	4.6% (12)	5.4% (8)
Moderate (4-6)	8.7% (23)	7.4% (11)
Severe (7-10)	86.7% (228)	87.2% (129)
Dyschezia		
Mild (0-3)	41.8% (110)	44.6% (66)
Moderate (4-6)	27% (71)	21.6% (32)
Severe (7-10)	31.2% (82)	33.8% (50)
Chronic Pelvic Pain		
Mild (0-3)	17.1% (45)	23% (34)
Moderate (4-6)	22.1% (58)	27.7% (41)
Severe (7-10)	60.8% (160)	49.3% (73)
Back Pain		
Mild (0-3)	21.7% (57)	25% (37)
Moderate (4-6)	34.2% (90)	33.1% (49)
Severe (7-10)	44.1% (116)	41.9% (62)
Marital status		
Married	48.7% (128)	58.8% (87)
Other	50.6% (133)	40.5% (60)
Missing	0.8% (2)	0.7% (1)
Highest level of education		
Some high school	3.4% (9)	3.4% (5)
Graduated high school or earned GED	11.4% (30)	4.7% (7)
Some college	27.4% (72)	20.3% (30)
Graduated 2 years college	13.7% (36)	12.8% (19)
Graduated 4 years college	24% (63)	30.4% (45)

Post-grad degree	17.5% (46)	21.6% (32)
Other	1.9% (5)	6.1% (9)
Missing	0.8% (2)	0.7% (1)
Sexual Orientation		
Heterosexual	95.4% (251)	89.2% (132)
Other	4.2% (11)	10.8% (16)
Missing	0.4% (1)	0% (0)
Annual socio-economic status		
Less than $20,000	11.8% (31)	11.5% (17)
$20,000 to $39,999	13.3% (35)	18.2% (27)
$40,000 to $59,999	14.4% (38)	10.8% (16)
$60,000 to $79,999	17.5% (46)	22.3% (33)
$80,000 to $99,999	14.4% (38)	13.5% (20)
$100,000 or more	27.8% (73)	23% (34)
Missing	0.8% (2)	0.7% (1)
Smoking		
Yes	13.7% (36)	12.8% (19)
No	85.6% (225)	86.5% (128)
Missing	0.8% (2)	0.7% (1)
Alcohol		
Yes	66.2% (174)	57.4% (85)
No	33.1% (87)	41.9% (62)
Missing	0.8% (2)	0.7% (1)
Ethnicity		
Caucasian	81.7% (215)	49.3% (73)
Non-Caucasian	17.9% (47)	50.7% (75)
Missing	0.4% (1)	0% (0)

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