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CLINICAL ARTICLE

Biopsychosocial correlates of persistent postsurgical pain in women with endometriosis

Erin T. Carey [a,e,*], Caitlin E. Martin [b], Matthew T. Siedhoff [a], Eric D. Bair [c], Sawsan As-Sanie [d]

[a] Division of Advanced Laparoscopy and Pelvic Pain, University of North Carolina at Chapel Hill, Chapel Hill, USA
[b] School of Medicine, Johns Hopkins University, Baltimore, USA
[c] Endodontics and Biostatistics, University of North Carolina at Chapel Hill, Chapel Hill, USA
[d] Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, USA
[e] Center for Pelvic Pain and Sexual Health University of Kansas, Kansas City, USA

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ABSTRACT

Objective: To examine pain and biopsychosocial correlates over time for women with persistent postsurgical pain after surgery for endometriosis. *Methods:* Cross-sectional study of women who underwent any endometriosis surgery between 2003 and 2006. Following surgery, patients completed validated questionnaires (Short-Form McGill Pain Questionnaire, 12-item Short-Form Health Survey, Beck Depression Inventory, Coping Strategies Questionnaire catastrophizing subscale). The primary outcome was pelvic pain intensity, measured by the McGill total pain score. Bivariate comparisons between each potential predictor and pain intensity were performed using the χ^2 and *t* tests, 1-way analysis of variance, and simple linear regression. *Results:* In total, 79 completed the questionnaires and were included in the present analysis. The McGill affective pain score was negatively correlated with age (β-coefficient –0.12, $P = 0.002$) and positively correlated with catastrophization (β-coefficient 0.66, $P = 0.01$). Women with a history of dyspareunia scored significantly higher on the McGill total pain score ($P < 0.001$); there was no association between pain intensity and endometriosis severity. *Conclusion:* Younger age and catastrophization are correlated with persistent pain following surgery for endometriosis. The severity of endometriosis does not predict persistent pain. Further evaluation of psychosocial factors may identify patients who are least likely to benefit from surgeries for endometriosis-associated pelvic pain.

1. Introduction

Endometriosis is a benign gynecologic disease, affecting 10–15% of reproductive-aged women and being associated with pelvic pain and infertility [1]. Standard treatment of endometriosis includes a combination of medical and surgical management [2]. Although the surgical destruction of endometriosis lesions may result in short-term improvement of most women with pelvic pain, up to 30% of women report no postoperative improvement in pain, and of those that do improve, many have recurrence of symptoms. The degree of short-term pain improvement among the remainder varies [3] and pain frequently recurs without evidence of recurrent disease. Long-term predictors of pain outcomes following endometriosis surgery have not been adequately described; however, postsurgical pain intensity following the excision of endometriosis is associated with the preoperative pain severity [4]. Despite these findings, endometriosis pain severity does not correlate with the stage of disease, indicating a multifactorial etiology of chronic pain in these patients [5].

Depression, somatic awareness, and catastrophization (the emotional distress associated with the feeling that their pain is the worst possible and unlikely to improve) are associated with increased pain intensity in women with pelvic pain prior to gynecologic surgery [6]. In addition to biologic measures, psychosocial dynamics (i.e. depression, anxiety, and coping mechanisms for pain) have been considered additional features affecting the complicated evaluation of chronic pain associated with endometriosis [7–9]. We previously reported that catastrophization and depression have been associated with poor short-term pain outcomes in women with endometriosis [8]; however, absent from the current literature are the association of catastrophization and depression with long-term pain follow-up. This information becomes even more important when weighing the patient risk–benefit ratio prior to performing a surgical intervention for a pain complaint.

The primary aim of the present study was to investigate biopsychosocial factors associated with persistent postsurgical pain (PPSP) in women with endometriosis who have previously undergone surgical intervention for chronic pelvic pain. Psychosocial variables contribute significantly to postoperative outcome measures and are not aptly described in the gynecologic surgery literature.

* Corresponding author at: Department of Obstetrics and Gynecology, University of Kansas, 10777 Nall Avenue Suite 200, Overland Park, KS 66211, USA. Tel.: +1 913 588 6200, +1 816 719 9877; fax: +1 913 945 6036.
E-mail address: erintcarey@gmail.com (E.T. Carey).

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2. Materials and methods

The study included women in the age range 18–50 years who were English-speaking and literate, and who had endometriosis that was laparoscopically treated and pathologically confirmed between April 1, 2003, and September 30, 2006, at a single tertiary referral center—the University of North Carolina. During this time period, 224 women underwent surgery, and of these, 142 eligible women had valid contact information (Fig. 1). In total, 133 women were successfully recruited for study participation and 84 (63.1%) completed the follow-up questionnaires. Five women were excluded from the study as a result of missing the primary pain measurement outcome. The Institutional Review Board of the University of North Carolina, Chapel Hill, NC, USA, approved the study and written informed consent was obtained.

Surgical procedures varied depending on stage of disease and symptoms. Intraoperative findings were taken from the operative reports using a standardized case report form. The stage of disease was documented by the revised American Society for Reproductive Medicine staging system [10].

Eligible women were invited to participate via phone call in October 2008, 2–5 years following the incident surgery for endometriosis. Consenting participants received questionnaires by mail, including a health history form asking for variables such as age, years of education, race, marital status, number of surgeries for pelvic pain, history of hysterectomy, and comorbid pain conditions such as chronic headaches (migraines), irritable bowel syndrome, interstitial cystitis, fibromyalgia, temporomandibular disorder, chronic low back pain, and vulvodynia. Medical records were abstracted using a standardized case report form for additional demographic and clinical variables, such as treatments (e.g. medical and surgical) tried since incident endometriosis surgery.

In addition, the participants completed several validated questionnaires that assessed pain severity and psychologic traits. The primary outcome of persistent pelvic pain was measured by the Short-Form McGill Pain Questionnaire (SF-MPQ) [11]. Because the questionnaires were sent several years after endometriosis surgery, the preoperative values are not known.

The SF-MPQ comprises 2 measurement components: the Pain Rating Index; and the Present Pain Intensity visual analog scale. The Pain Rating Index comprises 15 qualitative reports of pain, specifically 11 sensory and 4 affective components. Participants used a 0–3 pain-intensity scale to document the amount of daily pain experienced in the previous 2 weeks (0 = none, 1 = mild, 2 = moderate, 3 = severe), and the sum of the sensory and affective components produced the McGill total pain score [11]. The test–retest reliability of the SF-MPQ is well established [12], with high intraclass correlations for the subtotal and total pain scores in patients with chronic pain. Given that the 2 components differ in respect to their association with clinical and psychometric variables of interest (sensory and affective components of pain), an exploratory analysis was performed comparing these components separately.

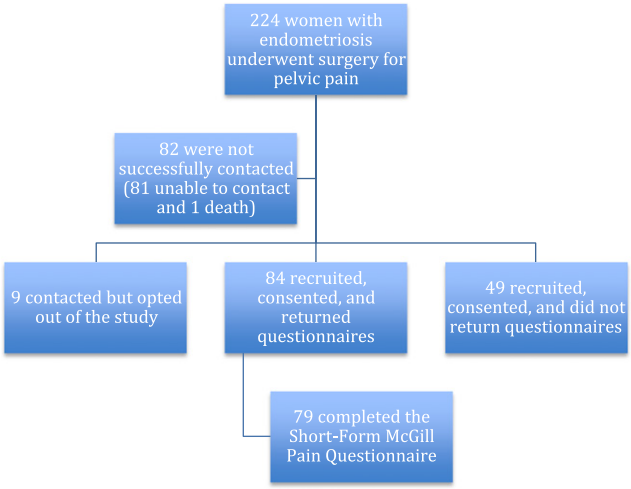

Fig. 1. Flow diagram of study participants.

Participants also completed the Mental Component Summary, a mental health subscale of the 12-item Short-Form Health Survey, with higher numbers associated with improved mental health. The internal consistency using Cronbach α is 0.87 and the test–retest reliability is good (correlation coefficient 0.76) [13].

The Beck Depression Inventory (BDI) was administered to investigate depression symptoms. The BDI consists of 21 items, with higher numbers associated with worse depression. The internal consistency is relatively high, with Cronbach α ranging from 0.79 to 0.90 [14].

Catastrophization was measure by the subscale of the Coping Strategies Questionnaire (CSQ) [15]. The subscale is scored on a scale from 0 to 6, with higher scores indicating worse levels of catastrophizing (none to severe). The internal consistency and reliability are high (Cronbach α, 0.78) [15], and the score is a predictor of health outcomes in chronic pain [16]. In the present study, the CSQ score was evaluated as a continuous scale in the bivariate analysis.

The statistical analysis was performed using Stata version 7.0 (StataCorp; College Station, TX, USA). Five patients did not fully complete the McGill pain scale and were not included in the analysis, but there was otherwise minimal missing data and no imputation was necessary. Bivariate comparisons were performed between each variable and the continuous McGill total pain score as well its affective and sensory components, using χ^2 tests and t tests for binary variables, 1-way analysis of variance for categorical variables with more than 2 categories, and simple linear regression for continuous variables. $P < 0.05$ was considered statistically significant.

3. Results

In total, 79 women completed the follow-up questionnaires. They were aged 24–50 years and primarily non-Hispanic white (65 [82%]), nulliparous (42 [53%]), married (57 [72%]), with at least some college education (70 [89%]). The duration of pelvic pain was 11.9 ± 0.9 years (mean ± standard error), and 36 (46%) women had undergone at least 3 surgeries for the treatment of pelvic pain (Table 1). Fifty-five (70%) women self-reported a diagnosis of at least 1 comorbid pain condition (e.g. fibromyalgia, irritable bowel syndrome, vulvodynia) on the questionnaire, and 19 (24%) women reported 2 or more comorbid pain disorders. Forty-one (52%) women reported a history of depression and/or anxiety.

At the index endometriosis surgery, 28 (35%) women also underwent a hysterectomy (14 [17.7%] with a concurrent bilateral salpingo-oophorectomy) (Table 2). Conventional clinical factors, such as the type of surgery performed or the stage of endometriosis, were not associated with long-term pain outcomes.

The present cohort overall scored slightly above the 25th percentile of the US female population [13] in their physical health and mental health statuses, with Short-form 12 Health Survey scores (mean ± standard error) of 45.59 ± 1.2 and 44.29 ± 1.26, respectively. There was a broad range of reported McGill total pain scores ranging from mild to severe, with a mean of 8.7 ± 1.1 (Table 2). Thirty-nine (49.4%) women reported dyspareunia (Table 3), and of the women with menstrual periods, 13 (27%) reported painful menses. Women with dyspareunia reported a McGill total pain score of 13.2 (95% confidence interval [CI], 10.15–16.25), which was higher ($P < 0.001$) than that in women who did not report dyspareunia (pain score 3.8 [95% CI, 1.53–6.14]). Additionally, women reporting dyspareunia scored 1.7 points higher on the McGill affective pain score than

Table 1
Characteristics of the study population (n = 79).[a]

Characteristic	Data
Age, y	36.4 ± 7.2
Race	
White	65 (82)
Black	11 (14)
Education	
High school	9 (11)
Some college	25 (32)
College	20 (25)
Postgraduate	25 (32)
Parous	
No	42 (53)
Yes	37 (47)
Marital status	
Married	57 (72)
Non-married	22 (28)
Dyspareunia	
No	36 (46)
Yes	39 (54)
Current smoker	
No	59 (75)
Yes	20 (25)
Years of pelvic pain	11.9 ± 7.2
Number of prior abdominal surgeries	
≤2	43 (54)
3–4	24 (30)
≥5	12 (16)

[a] Values are given as mean ± SD or number (percentage).

those without dyspareunia ($P = 0.003$) (Table 3). Dysmenorrhea was not associated with a higher McGill total pain score ($P = 0.973$).

Younger age was associated with higher McGill total pain scores ($P < 0.01$). The McGill affective pain score was negatively correlated with age (β-coefficient –0.12, $P = 0.002$) and positively correlated with catastrophization (β-coefficient 0.66, $P = 0.01$). For each 5-year increase in age, women reported a 2.6-point lower pain score ($P < 0.01$) as well as 0.5 points less on the affective component of the pain score ($P < 0.01$). Nulliparous women also demonstrated higher total ($P = 0.090$) and sensory ($P = 0.084$) pain scores compared with parous women.

Depression, as measured by the BDI, was not associated with differences in pain severity (Table 3). Catastrophization, while not associated with higher McGill total ($P = 0.055$), was associated with higher affective pain scores ($P = 0.010$) (Table 3). For each 1-point increase in the CSQ score, the participants displayed a 0.66 increase in their affective pain scores ($P = 0.010$).

Only 25 (32.1%) participants continued to be pain-free 2–5 years after endometriosis surgery. Of these women, 6 (24%) had an additional surgery following the index operation (2 underwent total hysterectomy with bilateral salpingo-oophorectomy, 2 underwent total hysterectomy without bilateral salpingo-oophorectomy, and 2 underwent excision of endometriosis alone) (Table 4). The majority (21 [84%]) of these pain-free women had 1 or no comorbid pain conditions. Of the 25 pain-free women, 5 (20%) had used antidepressants, 1 (4%) reported use of nonsteroidal anti-inflammatory agents, and 14 (56%) had used a form of hormonal therapy (Table 4); however, only 4 (16%) pain-free women were on hormone therapy at the time of the survey.

The remaining 53 (67%) women reported persistent pelvic pain. The majority (77.4%) of these reported further treatment for their pain (Table 4). Of the 5 (9.4%) women who underwent additional operations, 1 (1.9%) had a total hysterectomy with bilateral salpingo-oophorectomy and 4 (7.5%) had a repeat excision of endometriosis. The 19 (35.8%) women on antidepressants reported a significantly higher pain intensity than those not using antidepressants ($P < 0.01$). In regards to endometriosis-directed treatment, 45 (84.9%) of the 53 women used hormonal therapy (hormone replacement, oral contraceptives, levonorgestrel intrauterine device, gonadotropin-releasing hormone agonist) (Table 4). Twenty-three (43.4%) women with persistent pain were using hormonal therapy at the time of the survey.

4. Discussion

Endometriosis produces pain via nociceptive, inflammatory, and neuropathic mechanisms [17]. The destruction or excision of endometriosis results in greater short-term pain reduction than diagnostic surgery alone [3], and postoperative hormone treatment may reduce the risk of recurrent cyclic, noncyclic, and intercourse-related pain [18]. Clinicians are keenly aware of the difference between superficial implants and deep infiltrating disease, which can cause serious health threats via adjacent tissue destruction. The majority of women in the present cohort, however, reported persistent symptoms following endometriosis surgery directed at pelvic pain, and neither state of disease at the time of incident surgery nor total extirpation (total hysterectomy with bilateral salpingo-oophorectomy) was associated with an improved outcome overall.

Consistent with prior reports [8,19], younger age was associated with higher postoperative pain reports. This finding may be because younger women are at increased risk of disease recurrence [20] or because older women may have decreased nociception [21,22]. Though depressive symptoms were not associated with increased pain severity in the present study, the use of antidepressants was. Interestingly, the affective component of the McGill questionnaire, which measures the emotional constituent of pain, was most affected by catastrophization, reinforcing the psychological aspect of pain modulation.

These varying responses to surgery indicate that endometriosis pain may be mediated by psychological and social factors [9] rather than only pathologic findings. It is known that high psychological distress is associated with postsurgical pain [23] and, specifically, the presence of catastrophization may contribute to the development of PPSP [23,24]. Pinto et al. [22] recently described risk factors for PPSP in women who undergo hysterectomy for benign disease, including younger age,

Table 2
Surgical information from the index surgical procedure and associations with the total and subtotal McGill pain scores (n = 79).[a,b]

Parameter	Frequency	McGill total score	*P* value	McGill affective score	*P* Value	McGill sensory score	*P* value
Entire sample	79 (100.0)	8.7 ± 1.1		1.6 ± 0.3		7.1 ± 0.8	
Disease stage							0.142
1	37 (46.8)	8 ± 7.8	0.178	1.6 ± 2.2	0.435	6.4 ± 5.9	
2	25 (31.6)	10.4 ± 10.8		1.9 ± 2.9		8.6 ± 8.4	
3	12 (15.2)	4.6 ± 7.5		0.75 ± 2.1		3.8 ± 5.8	
4	5 (6.3)	9.4 ± 13.4		1.6 ± 3.0		7.8 ± 10.3	
Type of surgery							0.526
Excision of endometriosis only	51 (64.6)	9.6 ± 9.9	0.483	1.9 ± 2.7	0.459	7.8 ± 7.6	
Hysterectomy without BSO	14 (17.7)	7.9 ± 9.4		1.4 ± 2.2		6.5 ± 7.6	
Hysterectomy with BSO	14 (17.7)	6.4 ± 7.8		1 ± 1.9		5.4 ± 6.1	

Abbreviation: BSO, bilateral salpingo-oophorectomy.
[a] Values are given as number (percentage) or mean ± standard error.
[b] McGill score means and *P* values are based on a 1-way analysis of variance for variables with more than 2 categories.

Table 3
Psychological and pain associations with the total and subtotal McGill pain scores (n = 79).[a]

Parameter	Frequency[b]	McGill total score	*P* value	McGill affective score	*P* value	McGill sensory score	*P* value
≥2 Comorbid pain conditions							
No	60 (75.9)	8.7 ± 1.3	0.983	1.6 ± 0.3	0.736	7.1 ± 1.0	0.930
Yes	19 (24.1)	8.7 ± 1.9		1.8 ± 0.6		6.9 ± 1.4	
Dyspareunia							
No	36 (45.6)	3.8 ± 1.1	<0.001	0.7 ± 0.3	0.003	3.1 ± 0.9	<0.001
Yes	39 (49.4)	13.2 ± 1.5		2.4 ± 0.5		10.8 ± 1.1	
BDI score							
Normal/borderline	63 (79.7)	8.9 ± 1.2	0.742	1.7 ± 0.3	0.744	7.2 (1)	0.754
Mild, moderate, severe depression	16 (20.3)	8 ± 1.9		1.4 ± 0.5		6.6 ± 1.4	
CSQ score	77 (97.5)	1.9 ± 0.9[c]	0.055	0.66 ± 0.3 [c]	0.010	1.2 ± 0.8 [c]	0.108

Abbreviations: BDI, Beck Depression Inventory; CSQ, Coping Strategies Questionnaire.
[a] Values for McGill scores are given as mean ± standard error unless indicated otherwise. Means and *P* values are based on *t* tests for the categorical variables and simple linear regression for the continuous variable.
[b] Values are given as number (percentage). The numbers do not always add up to the total number of participants because of missing data.
[c] Values are given as β-coefficient ± standard error.

those with pre-existing mental illness (including high levels of catastrophizing characteristics) and type of surgery performed (open abdominal procedures are associated with an increased risk of PPSP). Specifically in endometriosis surgery, Eriksen et al. [7] demonstrated that regardless of the presence of anxiety and/or depression preoperatively, women with poor coping skills were more likely to report persistent pain following surgery. As in other reports [8], catastrophization in particular emerged as a predictor of shorter-term PPSP following endometriosis surgery. Although current catastrophizing may not reflect a patient's condition at the time of the incident surgery, this psychological factor may remain unchanged in a person over an extended period of time, affecting trait rather than state aspects of character [25].

The clinical implications of these psychological associations have potential in the pre- and postoperative counseling of patients with pelvic pain. Preoperative identification of patients with high catastrophizing features may allow for a psychological intervention to address surgical expectations in regards to the treatment of pain. In addition, a review of postoperative pain management techniques during the acute and chronic postoperative period may also be warranted in women with high catastrophization scores and, if possible, a minimally invasive surgery approach should be offered.

Table 4
Associations between treatments since index surgery and presence of persistent postsurgical pain.[a]

Treatment	Persistent pain (n = 53)	No pain (n = 25)	*P* value [b]
Any treatment since index surgery	41 (77.4)	13 (52)	0.024
Medical treatment (n = 55)			
Antidepressants	19 (35.8)	5 (20)	0.157
Anti-anxiety	3 (5.7)	1 (4)	0.756
Anticonvulsants	3 (5.7)	1 (4)	0.756
Sleep agents	6 (11.3)	0 (0.0)	0.080
NSAIDs	5 (9.4)	1 (4)	0.401
Opioids	10 (18.9)	2 (8)	0.214
OCPs	29 (54.7)	9 (36)	0.123
HRT	11 (20.8)	4 (16)	0.619
GnRH agonist	2 (3.8)	0 (0.0)	0.325
Levonorgestrel IUD	3 (5.7)	1 (4)	0.756
Additional surgery (n = 11)			
Hysterectomy without BSO	0 (0.0)	2 (8)	0.037
Hysterectomy with BSO	1 (1.9)	2 (8)	0.430
Excision of endometriosis only	4 (7.5)	2 (8)	0.944

Abbreviations: BSO, bilateral salpingo-oophorectomy; GnRH, gonadotropin-releasing hormone; HRT, hormone-replacement therapy; IUD, intrauterine device; NSAIDs, nonsteroidal anti-inflammatory drugs; OCPs, oral contraceptive pills.
[a] Values are given as number (percentage). The total number of participants is 78 because of missing data. Numbers do not sum to total because some women used both medical and surgical treatments.
[b] Pearson χ^2 test.

The present study is limited by its retrospective cross-sectional design and small sample size, which may have affected the ability to detect some associations, such as an association between catastrophization and the McGill total pain score. Given that baseline measures were not available, variables in the present report cannot be viewed as predictors. That certain psychological factors were strongly associated with pain reports emphasizes, however, the complexity of pelvic pain and should encourage clinicians to consider them in preparing a woman for endometriosis surgery. If the measures obtained in the present study are trait characteristics, the associations will be helpful for understanding longer-term effects.

The present study identifies an association between catastrophization and persistent postsurgical pain outcomes in women with endometriosis. Further research in endometriosis-associated outcomes should include evaluation of these psychological factors, particularly pain-coping abilities. Identification of these factors may help identify women who are least likely to benefit from invasive or repetitive surgery, and treatment of these factors or pre-/postsurgical interventions, such as cognitive behavioral therapy, may improve the long-term outcomes for women with chronic pain.

Conflict of interest

The authors have no conflicts of interest.

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