Correlation Between Endometriosis and Pelvic Pain

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Abstract

Study Objective. *To evaluate the relationship between prevalence and severity of chronic pelvic pain (CPP) and stage, site, and type of endometriosis.*
Design. *Prospective, observational study (Canadian Task Force classification II-2).*
Setting. *University Hospital.*
Patients. *Of 90 consecutive women with biopsy-proved endometriosis, laparoscopy was performed in 69 for pelvic pain and in 21 for infertility or clinical and ultrasonographic suspicion of ovarian endometriosis.*
Intervention. *Preoperatively, using a 10-point visual analog scale, the severity of dysmenorrhea, CPP, and deep dyspareunia was assessed. During laparoscopy all visible endometriotic lesions were recorded and treated.*
Measurements and Main Results. *Ten women (11.1%) had no pain; 72 had dysmenorrhea (mild in 13, moderate in 37, severe in 22); 55 had CPP (mild in 11, moderate in 25, severe in 19); and 39 deep dyspareunia (mild in 5, moderate in 31, severe in 3). The severity of dysmenorrhea significantly correlated with the presence and extent of pelvic adhesions ($p = 0.004$); the severity of CPP correlated with deep endometriosis on the uterosacral ligaments ($p = 0.0001$) and extent of pelvic adhesions ($p = 0.02$); and deep dyspareunia correlated with deep endometriosis on the uterosacral ligaments ($p = 0.04$). Total pain score significantly correlated with deep endometriosis on the uterosacral ligaments ($p = 0.0001$), peritoneal adhesions ($p = 0.01$), and extent of adnexal adhesions ($p = 0.01$). No significant correlation was found among revised American Fertility Society stage of endometriosis; presence and size of ovarian endometriomas; extent, type, and site of peritoneal lesions; and pain scores. By logistic regression analysis, the presence and intensity of total pain could be predicted simultaneously by the presence of deep endometriosis ($p = 0.0001$) and presence and extent of adnexal adhesions without cystic endometriosis ($p = 0.01$), and by the presence of ovarian endometrioma with periovarian adhesions ($p = 0.03$). Chronic pelvic pain was predicted by both deep endometriosis ($p = 0.0001$) and ovarian endometriomas with adnexal adhesions ($p = 0.03$). Deep dyspareunia was predicted simultaneously by deep endometriosis ($p = 0.01$) and an ovarian endometrioma with periovarian adhesions ($p = 0.008$).*
Conclusion. *Deep endometriosis, pelvic adhesions, and ovarian cystic endometriosis were independent predictors of pelvic pain. These data strongly suggest that it is not the size of ovarian cystic endometriosis but the association with adhesions that causes pelvic pain.*

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Endometriosis can be peritoneal (typical and subtle) implants; cystic ovarian endometriomas, which are frequently associated with adhesions; and deep endometriosis or adenomyosis-like lesions infiltrating the rectovaginal septum and posterior vaginal wall. Endometriosis is frequently associated with pelvic

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pain such as dysmenorrhea, chronic pelvic pain (CPP), deep dyspareunia, and, occasionally, painful defecation. Endometriosis was found in 37% to 74% of women undergoing laparoscopy for CPP.[1,2] Numerous reports failed to correlate the severity of pain symptoms with type and extent of disease. Not all women with endometriosis have pain. It was suggested that fresh atypical (subtle) lesions may cause a functional type of pain such as dysmenorrhea, whereas blue, older, typical lesions may cause an organic type of pain such as deep dyspareunia or CPP.[3] A positive correlation was reported between deep endometriosis, particularly of the rectovaginal septum, and severe pain.[2,4]

Authors do not agree regarding stage of disease, presence of ovarian endometriomas, and intensity of pain.[5–7] This is probably due to the presence of deep endometriosis, stages I and II, as indicated by lack of correlation between pain and stage according to the revised American Fertility Society (rAFS) classification, whereas pain correlated strongly when deep lesions were grouped separately.[8]

Several mechanisms have been proposed to explain the relationship between endometriosis and pain, including peritoneal inflammation, release of chemical mediators of pain, infiltration and tissue damage, and adhesion and scar formation. Red petechial implants of disease produce greater amounts of prostaglandin F than typical powder-burn implants.[9] Endometrioma rupture may cause chemical peritonitis responsible for acute pain. The relationship is still unclear, however. Therefore a prospective study was undertaken to evaluate pain symptoms in women with endometriosis.

Materials and Methods

This prospective, observational study assessed 90 consecutive women (mean age 29 ± 6 yrs, range 14–47 yrs) undergoing laparoscopy between January 1995 and January 1998 because of pelvic pain. Indications for surgery were pain symptoms for more than 6 months in 69 patients, and infertility or clinical and ultrasonographic suspicion of ovarian cystic endometriosis in 21. Pelvic pain was assessed by a questionnaire regarding the presence, characteristics, and localization of pain, and use of analgesics. The severity of dysmenorrhea, CPP, and deep dyspareunia was graded preoperatively by visual analog scale (VAS; zero = no pain–10 = unbearable pain).

During laparoscopy the presence, location, and extent of typical powder-burn lesions, subtle lesions (red flamelike, polypoid, red vesicle, brown lesion, clear vesicle), adhesions, and deep implants (>5 mm), particularly on uterosacral ligaments, were recorded. For all lesions diameter and depth were measured. Endometriosis was staged according to the rAFS.[10] In addition, deep lesions were grouped separately as classes 5 and 6, without and with cystic ovarian endometriosis, as suggested by the Leuven (L)-AFS classification.[8] Complete adhesiolysis was performed, small endometriotic lesions were coagulated with bipolar forceps after biopsy, ovarian endometriomas were completely removed, and lesions on the uterosacral ligaments were excised. Specimens were sent for histologic examination.

Statistical Analysis

Pain scores of 1 to 5 on theVAS were grouped as mild (score 1), 6 to 7 moderate (score 2), and 8 to 10 severe (score 3). Pain was defined as the highest score recorded for CPP, deep dyspareunia, or dysmenorrhea; total pain was defined as the sum of these scores (range 0–9).

Data Analysis

Data analysis was performed using the SAS system (SAS Institute Inc., Cary, NC). Since data were not normally distributed, the Wilcoxon (proc Npar/1/way) and general linear models (proc GLM) were used for single and multiple comparisons and Spearman's rank test for correlations. To analyze the relation between pain scores and laparoscopic observation, logistic regression for ordered data (Proc Logistic) was used.

Results

In the 90 women with endometriosis, dysmenorrhea, CPP, or deep dyspareunia was absent in 11.1%, mild in 8.8%, moderate in 44.4%, and severe in 35.5%. For dysmenorrhea, figures were 20%, 14.4%, 41.1%, and 24.4%; for CPP 38.9%, 12.2%, 27.8%, and 21.1%; and for deep dyspareunia 56.7%, 5.6%, 34.4%, and 3.3%, respectively. The total pain score was zero in 10 women, 1 in 5, 2 in 10, 3 in 13, 4 in 15, 5 in 9, 6 in 20, 7 in 6, and 8 in 2 (Table 1). All 69 patients operated for pain had at least one symptom with a score above 5 by VAS (moderate or severe). Chronic pelvic pain correlated (Spearman) with both deep dyspareunia ($p = 0.02$) and dysmenorrhea ($p = 0.002$), but deep dyspareunia did not correlate with dysmenorrhea.

TABLE 1. Pain in 90 Women with Endometriosis

	Pain			
	None No. (%)	Mild No. (%)	Moderate No. (%)	Severe No. (%)
Dysmenorrhea	18 (20.0)	13 (14.4)	37 (41.1)	22 (24.4)
CPP	35 (38.9)	11 (12.2)	25 (27.8)	19 (21.1)
Deep dyspareunia	51 (56.7)	5 (5.6)	31 (34.4)	3 (3.3)
Any pain	10 (11.4)	8 (8.8)	40 (44.4)	32 (35.6)

Peritoneal implants were found in 65 women and other lesions were found in 8. Endometrial lesions were typical in 33 women, subtle in 5, and both in 27. Red lesions only were found in 14 women and red and white lesions in 18. In 32 women superficial peritoneal lesions were found on peritoneum of the posterior side of broad ligaments and in the pouch of Douglas only; in 3 they were present in the vesicouterine fold only, and in 30 patients in both locations. These lesions covered an area of less than 1 cm in 15 women, between 1 and 3 cm in 27, and more than 3 cm in 23. Deep lesions (>5 mm) were present in 36 women; in 28 they were associated with peritoneal implants (27 typical, 14 subtle) and in 34 with cystic ovarian endometriosis.

Cystic ovarian endometriosis was found in 82 women; it was associated with typical lesions in 54 and with subtle lesions in 26 patients. Cysts were located in one ovary in 65 patients and in both ovaries in 17. Their size ranged between 1.0 to 15 cm (mean 4.6 ± 2.4 cm). Their presence, but not their size (NS), strongly correlated with the presence of periovarian adhesions ($p = 0.004$) and adhesions in the pouch of Douglas ($p = 0.04$). Pelvic adhesions were present in 77 women. In 47 they were limited to the ovary(ies) and posterior leaf of broad ligaments; in 30 patients the pouch of Douglas was involved, with complete obliteration of the cul-de-sac in 10. Enclosure of the adnexa was less than one-third in 27 women, between one-third and two-thirds in 37, and more than two-thirds in 13. In 18 women adhesions involved both ovaries. According to the rAFS, endometriotic lesions were scored, as stage I in 9, stage II in 6, stage III in 47, and stage IV in 28 patients (Table 2).

Chronic pelvic pain significantly correlated with the presence of deep endometriosis on uterosacral ligaments ($p = 0.0001$), the presence of pelvic adhesions ($p = 0.02$), and extent of adnexal adhesions ($p = 0.02$; Table 3). In women with partial pouch of Douglas obliteration only, CPP was absent in 15%, mild in 20%, moderate in 35%, and severe in 30%; figures in patients with complete obliteration were 30%, 20%, 20%, and 30%, respectively (NS). The intensity of dysmenorrhea correlated only with the presence and extent of pelvic adhesions ($p = 0.004$; Figure 1). Deep dyspareunia correlated only with the presence of deep endometriosis on the uterosacral ligaments ($p = 0.04$; Figure 2). The total pain score correlated with deep endometriosis on the uterosacral ligaments ($p = 0.0001$), peritoneal adhesions ($p = 0.01$), and extent of adnexal adhesions ($p = 0.01$).

With the rAFS classification, no correlation was found between stage and intensity of pain symptoms. However with the L-AFS classification, in which

TABLE 2. Laparoscopic Findings

Finding	No., %	Mean (range) Size (cm)	Bilateral No., %	
Ovarian endometrioma	82, 91.1	4.6 (1–15)	17, 20.7	
Peritoneal implants, no., %	65, 72.2	Typical, 33, 50.8	Subtle, 5, 7.7	Both, 27, 41.5
		<1 cm, 15, 23	>1 to <3 cm, 27, 41.5	>3 cm, 23, 35.4
Adnexal adhesions, no., %	<1/3, 27, 35	>1/3 to 2/3, 37, 48	>2/3, 13, 16.9	
Adhesions in pouch of Douglas no., %	Partial obliteration, 20, 26	Complete obliteration, 10, 13		
Deep endometriosis, no., %	36, 40			
Stage, no., %				
I	9, 10			
II	6, 6.6			
III	47, 52.2			
IV	28, 31.1			

TABLE 3. Severity of CPP

	Deep	No deep	Adhesions <1/3	1/31/3 to 2/33	>2–3	Unilateral	Bilateral
No CPP	5	30	12	10	5	19	7
Mild CPP	3	8	4	1	4	8	1
Moderate CPP	17	8	6	13	3	12	10
Severe CPP	11	8	5	10	4	12	8
Totals	36	54	27	34	16	51	26

Severity of CPP correlated with deep endometriosis ($p = 0.0001$) and severity of pelvic adhesions ($p = 0.02$). The women are grouped according to the presence of adhesions and deep endometriosis.

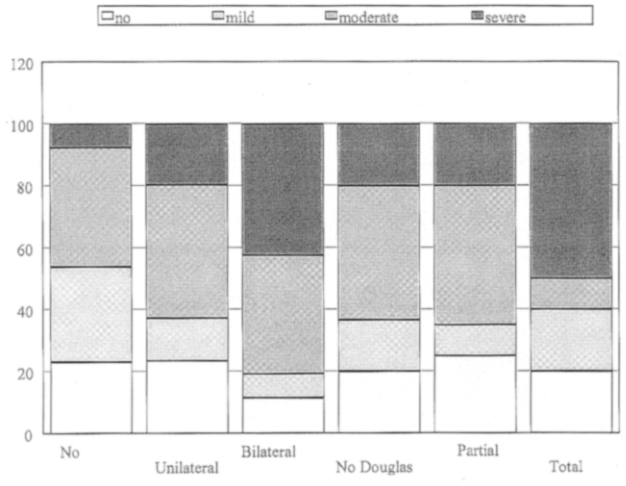

FIGURE 1. Severity of dysmenorrhea increases with severity of pelvic adhesions ($p = 0.004$). The severity of dysmenorrhea in women with no, unilateral, or bilateral ovarian adhesions and in women with a partial or total Douglas obliteration is shown.

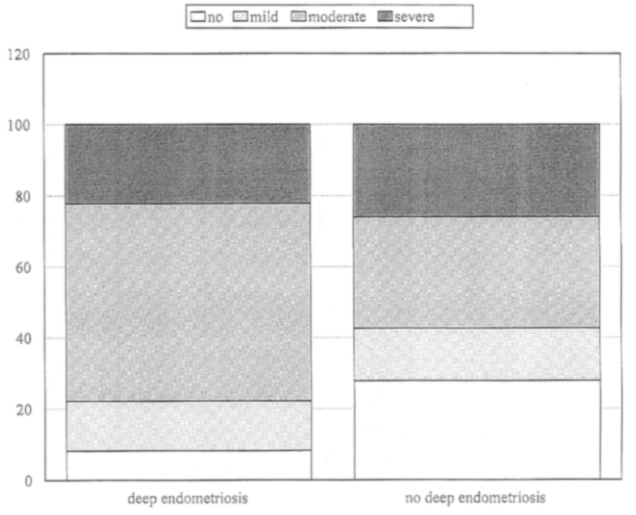

FIGURE 2. Severity of deep dyspareunia in women with and without deep endometriosis on uterosacral ligaments ($p = 0.04$).

patients with deep endometriosis are grouped separately, a strong correlation was found with CPP ($p = 0.0002$) and total pain ($p = 0.0005$). No significant correlation was found between the intensity of pain symptoms and presence and size of ovarian endometriomas, or extent, type, and location of peritoneal lesions.

Using logistic regression, the presence and intensity of total pain correlated simultaneously only with deep endometriosis and either adnexal adhesions or ovarian endometrioma. Since adhesions and cystic ovarian endometriosis were so strongly correlated, women with periovarian adhesions without ovarian cysts were grouped separately. Subsequently, total pain could be predicted by the presence of deep endometriosis ($p = 0.0001$), adnexal adhesions without cystic endometriosis ($p = 0.01$), and ovarian endometrioma with periovarian adhesions ($p = 0.03$). Deep dyspareunia could be predicted simultaneously by deep endometriosis ($p = 0.01$) and ovarian endometrioma with adnexal adhesions ($p = 0.008$). Chronic pelvic pain was predicted by the presence of deep endometriosis ($p = 0.0001$) and ovarian endometrioma with adnexal adhesions ($p = 0.03$).

Discussion

Although pain is a frequent symptom in women with endometriosis, its exact prevalence and type are not well understood. In this study only 11% of women did not complain of pain, whereas mild complaints were voiced by 14.4% of those with dysmenorrhea,

12.2% with CPP, and 5.6% of women with deep dyspareunia. This is surprising since the indication for surgery 69 women was pelvic pain. For the same reason, the overall prevalence of pain symptoms—dysmenorrhea in 80% of patients, CPP in 61.1%, and deep dyspareunia in 43.3%—is probably an overestimation, suggesting that absence of pain must be common in endometriosis.

It was surprising that CPP correlated with both deep dyspareunia and dysmenorrhea, whereas deep dyspareunia did not correlate with dysmenorrhea. To explain it, we suggest that mechanisms causing deep dyspareunia and dysmenorrhea are different, whereas women with long-standing pain from either symptom become more sensitive to pain perception in general and to endometriosis pain in particular.

The role of peritoneal lesions in causing pelvic pain is still unclear. We did not find a correlation among the presence, type, site, or extent of superficial lesions and any pain symptom, in addition to cystic ovarian lesions and deep endometriosis, suggesting that these lesions are relatively less important for pain. Others also found that the severity of dysmenorrhea was not related to the total number of endometriotic implants, or number of typical or atypical implants.[7] On the contrary, significant correlation was seen between the intensity of dysmenorrhea and number of endometrial implants.[11] These data are not necessarily conflicting, if many women with only peritoneal lesions are pain free. According to the population investigated, the prevalence of pain could thus be high or much lower and affect statistical significances. The suggestion that typical and subtle implants can induce different pain symptoms cannot be disregarded: fresh, atypical lesions may cause a functional type of pain such as dysmenorrhea, whereas old, typical, pigmented lesions may cause an organic type of pain such as deep dyspareunia or CPP.[3] Differences in inclusion criteria also could explain reported discrepancies.

Laparoscopic evaluation of endometriosis could fail to reveal the real extent of the disease such as deep lesions. Computer reconstruction of gland histology emphasised how extensive ramifications can be of what appear to be small lesions on the peritoneal surface.[12] Several factors affect nociceptor sensitivity in these women, and assessment of pelvic pain may be influenced by psychologic factors.[13]

To the best of our knowledge this is the first report suggesting that association of pain and cystic ovarian endometriosis is related to adhesions rather than to the cyst itself. Indeed, we did not find a correlation between the presence and size of cystic ovarian endometriosis and pain, and 11 patients with a cyst larger than 7 cm did not have pain. The presence of ovarian endometriotic cysts correlated with the presence of periovarian lesions, which are strongly associated with dysmenorrhea, CPP, and deep dyspareunia, in addition to pain caused by deep lesions. These data extend and confirm the known association between pain and cystic ovarian endometriosis. They also suggest that adhesion formation seems to be independent from the size of ovarian cysts.

Data on the correlation between cystic ovarian endometriosis and pain are conflicting. In one study the frequencies and severity of dysmenorrhea and dyspareunia were less in patients with endometriosis located only on the ovaries than in those with lesions at other sites.[6] Others reported significant association between ovarian endometriomas and dysmenorrhea and severe pelvic pain,[5] and a correlation between severity of dysmenorrhea and ovarian endometriomas.[7] Cystic ovarian endometriosis was an independent predictor of pain other than that associated with deep lesions.[2]

Deep endometriosis is frequently diagnosed in women with CPP,[14] and depth of penetration correlates with the percentage of these patients.[2,7] These data are confirmed and extended by showing that deep endometriosis on the uterosacral ligaments is the strongest predictor of total pain, CPP, and deep dyspareunia.

Adhesions are widely believed to cause pain, but hard data are scanty. Therefore the observation that adhesions have a significant role in pain in women with endometriosis, and that the presence and the extent of adhesions are independent predictors of the total pain score, dysmenorrhea, and CPP, particularly when these adhesions enclosed more than two-thirds of the ovary, is very important.

Data are inconsistent regarding the relationship between rAFS classification and pain. For example, rAFS stage per se did not correlate with the frequency and severity of dysmenorrhea and noncyclic pain in 244 women with pain symptoms.[6] A surprise, the severity of deep dyspareunia was inversely correlated with stage of endometriosis. Moreover, most adolescent patients with severe dysmenorrhea unresponsive to medical therapy had stage I disease.[15] On the other hand, a correlation was seen between severity of dysmenorrhea and endometriosis stage.[7] Also in our study,

rAFS stage did not correlate with the frequency and severity of any pain symptom. This can be explained by the fact that the classification does not take into account deep lesions, which are classified mainly as stage II. This is circumvented by the L-AFS classification, in which women with deep endometriosis, defined as disease infiltrating deeper than 5 mm, are classified separately, as stages 5 and 6. Knowing that deep and cystic endometriosis causes pain and that depth is the strongest predictor, it is not surprising to find a strong correlation between pain and L-AFS since L-AFS classes 3 and 4 contain cystic endometriosis (with more adhesions in class 4), class 5 deep endometriosis, and class 6 deep and cystic endometriosis.

Conclusion

Deep endometriosis, pelvic adhesions, and ovarian cystic endometriosis were independent predictors of pelvic pain. This strongly suggests that the cause of pelvic pain is not the size of ovarian cystic endometriosis but the association with adhesions.

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