Effect of hysterectomy on pain in women with endometriosis: a population-based registry study

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Objective To assess pain symptoms before and after hysterectomy in women with endometriosis.

Design A population-based registry study.

Setting Sweden.

Population Women aged 18–45 years who underwent hysterectomy for endometriosis between 2010 and 2015.

Methods Pain symptoms before hysterectomy and 12 months after surgery were collected from the Swedish National Quality Register for Gynaecological Surgery (GynOp). Pain symptoms were also assessed by follow-up surveys after a median follow-up period of 63 months.

Main outcome measures Pelvic or lower abdominal pain after hysterectomy.

Results The study included 137 women. The proportion of women experiencing pain of any severity decreased by 28% after hysterectomy ($P < 0.001$). The proportion of women with severe pain symptoms decreased by 76% after hysterectomy ($P < 0.001$). The majority of women (84%) were satisfied with the surgical result. Presence of severe pain symptoms after the hysterectomy was associated with less satisfaction ($P < 0.001$). Pain symptoms after surgery, patient satisfaction and the patient’s perceived improvement were not significantly different between women whose ovarian tissue was preserved and women who underwent bilateral oophorectomy.

Conclusions We observed a significant, long-lasting reduction in pain symptoms after hysterectomy among women with endometriosis. Hysterectomy, with the possibility of ovarian preservation, may be a valuable option for women with endometriosis who suffer from severe pain symptoms.

Keywords Endometriosis, hysterectomy, oophorectomy, pain, quality of life.

Tweetable abstract Hysterectomy is a valuable option for women with endometriosis and severe pain symptoms.

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Introduction

Endometriosis is a benign estrogen-dependent inflammatory disease, defined by endometrium-like tissue outside the uterus. The condition is estimated to affect 6–10% of all women of fertile age.\(^1\) Endometriosis is associated with dysmenorrhea, cyclic or acyclic pelvic and lower abdominal pain, dyspareunia, fatigue, reduced fertility and an increased risk of certain ovarian cancers. The disease causes extensive suffering and a significant reduction in the quality of life, primarily due to chronic pain.\(^2\) Although medical therapy is usually considered first, surgical ablation or excision of endometriotic lesions is often performed if medical therapy has failed.\(^3\) Although surgery is effective in many women, symptoms recur in up to 35% of women who undergo surgical excision of their lesions.\(^4\) When other treatments have failed and family planning is completed, hysterectomy, either by laparotomy or a minimally invasive technique with or without oophorectomy, is sometimes offered to the woman with the intention of relieving or alleviating her pain.\(^5,6\) Hysterectomy is associated with risks, and in women with endometriosis, there is a greater risk of complications. It has been suggested that the risk of serious complications during hysterectomy may increase by up to four times in women suffering from endometriosis.\(^7,8\) Although some studies have shown promising results in terms of pain reduction and improved quality of life in the short term, few studies have followed women for over...
endometriosis increases with time, which suggests increased rate in women who underwent surgical treatment for their endometriosis. It is also controversial whether the ovaries should be removed at the time of hysterectomy. Better understanding of the long-term effects of hysterectomy on pain in women with endometriosis is required to improve the medical counselling offered to these women.

The primary objective of this study was to compare the proportion of women with pelvic or lower abdominal pain before hysterectomy to the proportion of women with pelvic or lower abdominal pain after hysterectomy in women with endometriosis. The secondary objectives were to identify the factors that are associated with presence of pain after hysterectomy and to assess the health-related quality of life (HRQoL) in these women.

Methods

The study was designed as a population-based registry study. Data on all registered hysterectomies for the main indication endometriosis, performed in Sweden in 2010–15 were retrieved from the Swedish National Quality Register of Gynaecological Surgery (GynOp). Women aged 18–45 years who underwent hysterectomy for endometriosis were eligible for this study. Women were excluded if they had not ranked pain as the main reason for hysterectomy; if the surgeon had not observed and confirmed the presence of endometriosis during surgery; and if they were aged >50 years at the follow-up survey. A core outcome set was not used, because the core outcome set for endometriosis had not been established when the study was initiated. Women were not involved in the development of the study, as it was based on an established quality register. The authors received no specific funding for this work.

The Swedish National Quality Register of Gynaecological Surgery (GynOp)

GynOp is the national quality register for gynaecological surgery in Sweden. It recorded around 80% of all benign hysterectomies performed in Sweden in 2010–15. The register includes information submitted by the woman before and 12 months after surgery using validated questionnaires, including patient-reported outcome measures as well as information submitted by the surgeon at the time of surgery.

Data processing

The data retrieved from GynOp were organised into three domains. The first domain consisted of data collected in preoperative surveys, including general health, demographics and symptoms (pain, the severity of pain on a rating scale and the symptom that was the main reason for seeking medical care). The second domain consisted of data submitted by the surgeon at the time of surgery, and included the type and extent of surgery performed, perioperative findings and complications (if any). The third domain consisted of information collected with a questionnaire sent to the women 12 months after surgery. The questionnaire with answers was later available to the surgeon who performed the hysterectomy. The questionnaire included questions about pain symptoms and the grading of pain severity. The questions were identical to those included in the preoperative questionnaire. The first question was: Do you have pain in the pelvic area/lower abdomen? The possible responses were ‘yes’ or ‘no’. The severity of pelvic or lower abdominal pain was graded separately as follows: no pain, mild pain, moderate pain, severe pain or unbearable pain. The women also assessed their overall satisfaction with the surgical result as follows: very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied or very dissatisfied. They also graded the improvement in their clinical condition after surgery as follows: greatly improved, improved, unchanged, worse or much worse.

Follow-up questionnaire at 37–107 months

After the data were retrieved from GynOp, a follow-up questionnaire was sent to assess the woman’s health after a much longer follow-up period of 37–107 months, with a median of 63 months. This questionnaire included the same questions as the preoperative and 12-month postoperative questionnaires and was blinded to the surgeon who performed the hysterectomy. The 37- to 107-month follow-up survey also included an endometriosis health profile questionnaire (Endometriosis Health Profile-30, EHP-30).

Because the EHP-30 was only included in the final follow-up survey, the results are solely descriptive and could not be used for statistical comparisons.

Endometriosis health profile questionnaire (EHP-30)

Jones et al. first developed EHP-30, a disease-specific questionnaire, to measure the health status of women with endometriosis. This instrument contains a core questionnaire that focuses on endometriosis-related complaints, with 30 items and five scales covering the domains: pain, control and powerlessness, emotional wellbeing, social support and self-image. Each scale is scored from 0–100, with higher scores indicating worse HRQoL.

Statistical analysis

All statistical analyses were performed with SPSS version 24 (SPSS; IBM Corp., Armonk, NY, USA). Descriptive statistics were used to present the data, which were divided into categorical and continuous variables. Continuous variables are presented as medians (interquartile range). Categorical
variables are presented as frequency counts and percentages.

The main outcome measures were the proportion of women with pelvic or lower abdominal pain, of any severity and the proportion of women with severe or unbearable pain specifically.

Four different dichotomous (yes/no) outcome variables were used; presence of pelvic or lower abdominal pain of any severity, presence of severe or unbearable pelvic or lower abdominal pain, patient satisfied with the surgical result and patient reported improvement after surgery.

Dichotomous explanatory variables were used: age at surgery (<40/≥40 years), symptom duration before surgery (<10/≥10 years), endometriosis stage (<III/≥III), bilateral oophorectomy (yes/no) and surgical approach (laparotomy/minimally invasive).

In addition to comparison of outcomes between women aged <40 and ≥40 years, outcomes for the youngest women (<35 years) were analysed specifically.

McNemar test was used to compare outcome variables between three measurements (before surgery, 12 months after surgery and 37± months after surgery).

The association between lack of satisfaction with the surgical result and presence of pelvic or lower abdominal pain 37+ months after surgery was analysed using Pearson chi-square test.

Logistic regression was used to investigate the association between explanatory variables and outcome variables 37+ months after the surgery. Each explanatory variable was run in a separate model.

The scores from each domain of the EHP-30 survey were compared between two groups according to presence of pain, using Mann–Whitney U test. P < 0.05 was deemed to indicate statistical significance.

The power calculation was based on the following assumptions. In a group of patients with endometriosis, there is a clinically relevant amelioration of pain symptoms with a reduction on a visual analogue scale from 7.47 (SD 2.45) points preoperatively to 3.46 (SD 2.91) points 36 months after hysterectomy.15 If α = 0.05 and power of 80%, then, seven patients were required to show a significant difference in the main outcome.

Results

After the inclusion and exclusion criteria were applied, 137 women were included in the study (Figure 1). The median age was 41 (37.5–43.0) years at the time of surgery. The median duration of symptoms was 10 years. Eighty-seven of the women (63.5%) reported previous or ongoing hormonal treatment. All of the women underwent hysterectomy between 2010 and 2015. Both ovaries were removed in 40.9% of women. Endometriosis was confirmed by the surgeon in all women and was staged in 59.9% of women. Surgery was limited to the uterus and adnexa in 62.8% (n = 86) of women. Other interventions performed during the surgery were removal of adhesions (n = 28), destruction or removal of peritoneum (n = 18) and procedures engaging the colon or rectum (n = 6). Surgical complications occurred in 3.6% of women and included intestinal injury (n = 3), perioperative blood loss >1000 ml (n = 1), and intestinal and urinary bladder injury (n = 1) (Table 1).

In total, 72.3% (n = 99) of the 137 women included completed the follow-up questionnaire at 12 months after hysterectomy, and 68.6% (n = 94) of them completed the follow-up questionnaire at 37–107 months after hysterectomy. The remaining women (n = 38 and n = 43, respectively) were lost to follow up. There were no significant differences between the women who answered the follow-up
There was a significant decrease in the proportion of women with pelvic or lower abdominal pain, both pain of any severity and severe or unbearable pain. The decrease was seen both 12 and 37+ months after surgery and was seen independently of whether bilateral oophorectomy was performed or not. No significant change in the proportion of women suffering from severe or unbearable pain, both 12 months (P = 0.008) and 37+ months after the surgery (P = 0.004) compared with before surgery. Ten of the 11 women (90.9%) younger than 35 years at time of hysterectomy reported improved symptoms and were satisfied with the surgery 37+ months after the hysterectomy.

HRQoL was assessed using the EHP-30 37+ months after surgery. The scores for the five domains were: pain, 6.82 (0.00–38.64); control and powerlessness, 16.67 (0.00–58.33); emotional wellbeing, 25.00 (0.00–41.67); social support, 25.00 (0.00–56.25) and self-image, 16.67 (0.00–58.33). Women with presence of pain, both of any severity and severe or unbearable, 37+ months after surgery had significantly higher (worse) scores in all domains regarding HRQoL compared with women negating any pain (P < 0.001) and severe or unbearable pain (P < 0.001), respectively.

**Discussion**

**Main findings**

There was a long-lasting reduction in pain symptoms after hysterectomy among women with endometriosis. Three out of four women reporting severe or unbearable pain before the hysterectomy negated these symptoms after surgery. Mild or moderate pain was commonly reported after hysterectomy, but pain symptoms were improved in the majority of women and more than 80% were still satisfied with the surgical result several years after surgery. Lack of satisfaction was associated with presence of severe or unbearable pain 37+ months after the hysterectomy, but not with pain of any severity. There were no significant differences in pain symptoms, patient satisfaction or patient improvement between women who underwent bilateral oophorectomy and those whose ovaries were preserved.

**Strengths and limitations**

This study was based on prospectively collected national data, had a relatively long follow-up period, and used patient-reported outcome measures. As endometriosis is commonly found accidentally during surgical procedures and many of these patients have no symptoms related to endometriosis, we included only women where the actual indication for surgery was endometriosis, and whose main complaint before surgery was pain and only for whom the diagnosis was confirmed by the surgeon. Although women

| Table 1. Baseline demographic and perioperative characteristics (n = 137) |
|-----------------------------|------------------|
| **Variable**                | **Value**        |
| Age at time of surgery (years), median (IQR) | 41 (37.5–43)    |
| Duration of symptoms (years), median (IQR) | 10 (2–20)        |
| Number of deliveries, median (IQR) | 1 (0–2)          |
| Employment before surgery, n (%) | 115 (84.6)     |
| Smoker, n (%) | 17 (12.4)       |
| Surgical approach, n (%) | 72 (52.6)       |
| Minimally invasive | 65 (47.4)       |
| Extent of hysterectomy, n (%) | 6 (4.4)         |
| Total hysterectomy | 131 (95.6)      |
| Bilateral oophorectomy, n (%) | 56 (40.9)     |
| Yes | 81 (59.1)       |
| No | 55 (40.1)       |
| Endometriosis in the surgical field, n (%) | 12 (8.8)        |
| Yes, not staged | 10 (7.3)        |
| Yes, minimal (stage I) | 33 (24.1)      |
| Yes, mild (stage II) | 27 (19.7)       |
| Yes, moderate (stage III) | 115 (84.6)     |
| Yes, severe (stage IV) | 131 (95.6)      |
| Perioperative blood loss (ml), median (IQR) | 150 (50–300)    |
who did not rank pain as the main complaint before hysterectomy were excluded, still, for unknown reasons, eight women that met the criteria negated the presence of any pelvic or lower abdominal pain later (see Table 2). The lack of certain information in the register such as the women’s hormonal treatment status after the hysterectomy and histopathological analysis of the uterus (for signs of adenomyosis), was a limitation. Another limitation of the study was the somewhat large proportion of women lost to follow up. However, no significant differences were detected at baseline between the responding group and the group that was lost to follow up.

Table 2. Pain symptoms, patient satisfaction and improvement in women with endometriosis (in three groups; all women and according to bilateral oophorectomy or not) compared among three measurements (McNemar’s test)

| A. Preop. | B. 12 months postop. | C. ≥37 months postop. | Change* A. to B. | Change* A. to C. | Change* B. to C. |
|-----------|----------------------|-----------------------|-----------------|-----------------|-----------------|
| **Pain, any severity** | | | | | |
| Overall | 94.2% (of 137) | 51.5% (of 99) | 68.1% (of 91) | −45.3% * | −27.9% * | +27.6% |
| Oophor-ectomy | 94.6% (of 56) | 50.0% (of 42) | 75.7% (of 37) | −46.2% * | −22.2% * | −26.4% |
| Ovary preserved | 93.8% (of 81) | 52.6% (of 57) | 63.0% (of 54) | −44.5% * | −32.0% * | −28.7% |
| **Pain, severe or unbearable** | | | | | |
| Overall | 85.8% (of 127) | 20.9% (of 86) | 21.6% (of 88) | −75.0% * | −76.0% * | −17.8% |
| Oophor-ectomy | 88.5% (of 52) | 21.1% (of 38) | 20.0% (of 35) | −74.2% * | −78.1% * | −25.0% |
| Ovary preserved | 84.0% (of 75) | 20.8% (of 48) | 22.6% (of 53) | −75.7% * | −74.4% * | −11.3% |
| **Satisfied with surgery** | | | | | |
| Overall | 76.5% (of 98) | 84.3% (of 89) | | +6.2% * | | |
| Oophor-ectomy | 71.4% (of 42) | 86.8% (of 38) | | +20.9% * | | |
| Ovary preserved | 80.4% (of 56) | 82.4% (of 51) | | −2.7% * | | |
| **Improved after surgery** | | | | | |
| Overall | 85.7% (of 98) | 90.3% (of 93) | | +4.5% * | | |
| Oophor-ectomy | 85.4% (of 41) | 89.5% (of 38) | | +7.3% * | | |
| Ovary preserved | 86.0% (of 57) | 90.9% (of 55) | | +2.5% * | | |

n, number of patients in analysis. Significant changes are showed in bold.
*Analysis based only on patient’s data present in both measurements.
Hysterectomy in women with endometriosis

Interpretation

Persistent or recurrent pain after the surgical treatment of endometriosis is a difficult clinical condition. The reported recurrence rate varies (6–67%).\textsuperscript{11,16,17} The retrospective design of many studies regarding hysterectomy for endometriosis may cause many uncertainties, as the pain described by the patient is rarely described in detail, the extent of the surgery is often uncertain and the diagnostic criteria used vary.\textsuperscript{18} Namnoum et al.\textsuperscript{19} reported that symptoms recurred in up to 62% of women after hysterectomy for endometriosis, but they did not specify the symptom severity, which could partly explain the high rate because even mild pain could be counted as symptom recurrence. Notably, although many women in our study reported some pain after hysterectomy, this was not associated with a lack of satisfaction with the surgical result. More importantly, the vast majority of women who reported severe or unbearable pain before the hysterectomy improved after hysterectomy and negated these symptoms both 12 and 37+ months after surgery. This could explain the large proportion of women being satisfied with the surgery even though many still had pain to some degree.

Whether to perform a bilateral oophorectomy at the time of hysterectomy for endometriosis has been a matter of discussion for decades, with no clear consensus.\textsuperscript{20,21} Bilateral oophorectomy and the induction of early menopause may increase all-cause mortality.\textsuperscript{22} However, a review article published in 2014, which evaluated the current evidence, suggested that pain relief is better achieved if the surgery involves the removal of the ovaries. The authors suggested that ovarian preservation carries a six-fold greater risk of recurrent pain than oophorectomy.\textsuperscript{11} The authors referred to the study by Namnoum et al.\textsuperscript{16} mentioned above, in which the ovaries were preserved in 29 patients. To our surprise, we found no significant difference in pain recurrence between women whose ovaries were preserved and those who underwent bilateral oophorectomy. To determine whether this discrepancy resulted from a lack of power in our study, we calculated the sample size and power required to show a significant difference, based on the results of Namnoum et al.\textsuperscript{19} (α = 0.05, power 80% and 12 patients in each group). Our results were based on 54 women with preserved ovarian tissue and 37 women who underwent bilateral oophorectomy. Therefore, our data do not support the notion that ovarian preservation is associated with a greater risk of persistent pain than bilateral oophorectomy. Two additional studies that addressed this question have reported similar conclusions.\textsuperscript{23,24}

In recent years, abdominal hysterectomies have declined in favour of laparoscopic hysterectomies.\textsuperscript{25} Based on the work of Chalermchokchareonkit et al.\textsuperscript{6} a minimally invasive technique is probably advisable for women with endometriosis because the rates of complications and blood loss are lower and hospitalisation is shorter. Nevertheless, we found no difference in long-term pain relief between women who underwent hysterectomy via laparotomy or a minimally invasive technique.

Prolonged exposure to pain could trigger a state of central sensitisation, with an altered perception of pain.\textsuperscript{26} It was recently shown that women with chronic pelvic pain had a lower pain threshold than healthy controls and that pain threshold decreases with increasing symptom duration.\textsuperscript{27,28} This supports the idea that prolonged exposure to pain increases the risk of developing an altered perception to pain, which could be harder to treat with hormonal and surgical means. Although we did not find an association of such, this may help explain why some women with endometriosis seem resistant to medical and surgical treatment of their pain, and we encourage further research in the

Table 3. Logistic regression analysis between explanatory variables and poor surgical outcomes at ≥37 months after surgery

|                                  | Any pain at follow up OR (95% CI) | Severe pain at follow up OR (95% CI) | Lack of satisfaction at follow up OR (95% CI) | Lack of improvement at follow up OR (95% CI) |
|----------------------------------|----------------------------------|-------------------------------------|---------------------------------------------|---------------------------------------------|
| **Patient age <40 years**        |                                  |                                     |                                             |                                             |
|                                  | 1.78 (0.72–4.44) P = 0.22         | 1.32 (0.48–3.66) P = 0.60            | 1.13 (0.35–3.57) P = 0.84                   | 1.75 (0.44–6.98) P = 0.43                   |
| **Symptoms for ≥10 years**       |                                  |                                     |                                             |                                             |
|                                  | 1.01 (0.41–2.50) P = 0.99         | 1.13 (0.40–3.20) P = 0.82            | 0.78 (0.23–2.67) P = 0.69                   | 2.44 (0.57–10.47) P = 0.23                   |
| **Endometriosis stage ≥III**     |                                  |                                     |                                             |                                             |
|                                  | 0.83 (0.22–3.10) P = 0.79         | 5.38 (0.63–45.83) P = 0.12           | 0.71 (0.22–2.31) n/a*                       | 1.18 (0.29–4.70) n/a*                       |
| **Ovarian tissue preserved**     |                                  |                                     |                                             |                                             |
|                                  | 1.83 (0.72–4.65) P = 0.20         | 0.85 (0.30–2.44) P = 0.82            | 0.65 (0.24–1.81) P = 0.41                   | 1.11 (0.35–3.50) P = 0.86                   |
| **Surgery by laparotomy**        |                                  |                                     |                                             |                                             |
|                                  | 0.65 (0.27–1.60) P = 0.35         | 0.65 (0.24–1.81) P = 0.35            | 1.11 (0.35–3.50) P = 0.86                   | 1.73 (0.41–7.40) P = 0.46                   |

CI, confidence intervals; OR, odds ratio.
*Analysis not possible because no women with endometriosis stage 1 or 2 reported lack of satisfaction or lack of improvement at follow up.
field. The multifactorial nature of chronic pelvic pain should also be kept in mind. History of sexual assault and pain catastrophising, for example, has been shown to independently be associated with more severe pain symptoms in women with chronic pelvic pain.39

The women’s age at time of hysterectomy could possibly affect the outcomes.30 In our study, the majority of study participants were closer to 40 and only 16 women were younger than 35 years old. Although, we found no association between the woman’s age and a poor surgical outcome, conclusions regarding outcomes in younger women should be drawn with caution.

EHP-30 is the validated questionnaire used to measure HRQoL in women with endometriosis. In our study, the scores for all five EHP-30 domains were low several years after surgery. Pain can have a severe negative impact on HRQoL. By relieving pain, the woman’s HRQoL may improve. This is supported by our results insofar as the hysterectomy has a positive long-term impact on HRQoL among women with endometriosis. This was further supported by another study that showed improved HRQoL among women with endometriosis 3 months after hysterectomy.9

Conclusion
Hysterectomy, with the possibility of ovarian preservation, may be a valuable treatment option for women who suffer from endometriosis and severe pelvic or lower abdominal pain and who have completed their families. More studies are required to identify the factors affecting the persistence and/or recurrence of pain after surgery for endometriosis.

Disclosure of interests
The authors have no conflicts of interests to declare in relation to this article. Completed disclosure of interests forms are available to view online as supporting information.

Contribution to authorship
All five authors contributed substantially to the conception and planning of the study. AS collected the data. The data analysis was performed by AS and ST. All authors contributed to the interpretation of the data. AS wrote the first draft of the manuscript. The manuscript was revised by MB, MJ, TB and ST together with AS. All five authors approved the final submitted version of the manuscript.

Details of ethics approval
This study was approved on 21 November 2017 by the Regional Ethical Review Board in Umeå, Sweden (dnr. 2017-407-32M).

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