

An eight-year retrospective analysis of laparoscopic surgery for endometriosis, outcomes and complications in a large multicenter unit

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Summary

Background: Endometriosis is a chronic inflammatory condition affecting up to 10% of the female population. Management often involves surgical treatment with excision or ablation of lesions. **Aim:** To evaluate the surgical outcomes and complications rates of endometriosis related laparoscopic surgery. **Materials and Methods:** A retrospective review of all women who underwent endometriosis-related surgery over an eight-year period in a multicenter gynecological unit. **Results:** A total of 972 patients met the inclusion criteria. Six hundred and fifty-eight (67.9%) women had Stage 1 or 2 endometriosis and 314 (32.1%) had stage 3 or 4 endometriosis. The patients with stage 3 or 4 endometriosis were more likely to have longer operative times (105 vs. 65 minutes, $p = 0.001$), more likely to require a conversion to laparotomy (12 vs. 6 $p = .002$) and were more likely to suffer from a complication (16 vs. 9, $p = 0.003$). The stage of endometriosis was found to be the only independent variable related to surgical complications and conversions to laparotomy. **Conclusion:** Surgery is an effective treatment option for all women with endometriosis, however it is significantly more effective in women with moderate to severe endometriosis, although they are at higher risk of complications.

Key words: Complications; Endometriosis; Laparoscopy; Outcomes; Surgery.

Introduction

Endometriosis is a chronic, inflammatory condition caused by deposits of endometrium-like tissue outside the uterus. Estimates of prevalence are between 2-10% of the female population and in up to 50% of women with fertility issues [1]. The most commonly reported symptom of endometriosis is pain, be it dysmenorrhea, pelvic pain unrelated to menstruation or dyspareunia and while deep infiltrating endometriosis can be diagnosed on ultrasound or magnetic resonance imaging, superficial or peritoneal endometriosis cannot [2]. The most recent European Society of Human Reproduction and Embryology (ESHRE) guidelines, published in 2014, outlining the recommended management of endometriosis, advise that when diagnosed on laparoscopy, clinicians should treat endometriosis and that excision of the lesions is preferred [1]. A review published in 2012, suggests that in women with deep infiltrating endometriosis who have undergone rectovaginal surgery, more than 85% of women have complete resolution of their pain symptoms, and the rate of spontaneous conception is up to 60% [3, 4]. Surgery for deep lesions is effective for treatment of pain but has a higher complication rate [1]. A study by Kondo *et al.* [5] reported that the intra-

operative complication rate for excision of deep infiltrating endometriosis was as high as 2.1%, with a 2.3% rate of conversion to laparotomy.

The aim of this study was to evaluate the surgical outcomes and complications rates of endometriosis related laparoscopic surgery in a multicenter tertiary referral health service over a period of eight years. The authors wanted to observe the differences in characteristics, complications, and outcomes for different stages of endometriosis, comparing American Society for Reproductive Medicine (ASRM) stage 1-2 and ASRM stage 3-4.

Materials and Methods

This is a retrospective cohort study performed at a multicenter teaching health service which provides a full gynecological service, as well as other surgical specialties such as general surgery, colorectal surgery, and urology. All women who underwent any laparoscopic surgery for endometriosis at any of the four centers in the network between January 2009 and September 2016 were included.

Patient histories were identified through diagnosis-related group (DRG) coding of 'endometriosis' from their discharge summaries. These were then refined for patients admitted under gynecology, gynecological oncology, general surgery or urology.

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Table 1. — Characteristics of study population overall and by stage of endometriosis.

	Total population (n=972)	Stage 1-2 (n=658)	Stage 3-4 (n=314)	p value
Smoking status (ex/current)	350 (36.0%)	258 (39.5%)	92 (29.6%)	0.003
Chronic pain	92 (9.7%)	68 (10.5%)	24 (7.9%)	0.21
Had a past vaginal birth	278 (29%)	171 (26.4%)	107 (35.0%)	0.006
Had a past cesarean birth	141 (15%)	100 (15.4%)	41 (13.4%)	0.43
Previous laparotomy	76 (7.8%)	45 (6.8%)	31 (9.9%)	0.10
Previous laparoscopy	372 (38.6%)	245 (37.5%)	127 (40.7%)	0.34
Level of surgeon				
General gynecologist	176 (18.1%)	124 (18.8%)	52 (16.6%)	<0.001
Specialist endoscopic gynecological surgeon	193 (19.9%)	87 (13.2%)	106 (33.8%)	
Trainee	428 (44%)	332 (50.5%)	96 (30.6%)	
Fellow	166 (17.1%)	107 (16.3%)	59 (18.8%)	
Other	9 (0.9%)	8 (1.22%)	1 (0.32%)	
BMI (kg/m ²) †	25.8 (6.2)	25.6 (6.1)	26.1 (6.4)	0.32
Age at operation (years) †	33.9 (8.7)	32.4 (8.5)	37.2 (8.3)	<0.001
Ethnicity – Caucasian	672 (69.1%)	493 (74.9%)	179 (57.0%)	<0.001

N (%) unless otherwise stated. † Mean (SD).

Table 2. — Factors associated with operative time.

	Crude regression co-efficient (95%CI)	p value	Adjusted regression co-efficient (95%CI)	p value
Chronic pain	-8.2 (-18.5 to 2.13)	0.12	-3.46 (-13.0 to 6.10)	0.48
Previous laparotomy	9.1 (-2.19 to 20.3)	0.14	3.04 (-7.6 to 13.6)	0.57
Previous laparoscopy	6.29 (0.05 to 12.5)	0.048	3.11 (-2.59 to 8.91)	0.28
Level of surgeon				
General gynecologist	1	-	1	-
Specialist endoscopic gynecological surgeon	42.6 (33.3 to 51.9)	<0.001	30.0 (20.9 to 39.1)	<0.001
Trainee	2.53 (-5.5 to 10.5)	0.53	7.51 (-0.08 to 15.1)	0.053
Fellow	19.4 (9.8 to 28.9)	<0.001	14.4 (5.33 to 23.4)	0.002
Other	-7.71 (-39.4 to 23.9)	0.63	-2.51 (-37.6 to 32.5)	0.89
BMI (kg/m ²)	0.29 (-0.22 to 0.81)	0.26	0.14 (-0.32 to 0.60)	0.56
Age at operation per 5 years	6.1 (4.4 to 7.8)	<0.001	1.55 (-0.20 to 3.31)	0.08
Ethnicity – not Caucasian	6.99 (0.38 to 13.6)	0.04	-2.46 (-9.0 to 4.1)	0.46
Endometriosis stage	20.0 (17.7 to 22.4)	<0.001	18.1 (15.5 to 20.7)	<0.001

Unit increase (minutes) in operative time per respective variable before (crude) and after adjustment for each variable. NB: total population n= 972.

Patients were excluded if they did not have full computerized medical records, were admitted to the emergency department or another unit not in the inclusion criteria, never underwent surgery or had a planned laparotomy. Patients were also excluded if they did not have visually confirmed endometriosis on their laparoscopy or were diagnosed with adenomyosis only.

The authors examined each history individually. Demographics including age, height, weight, BMI, smoking status, parity and mode of delivery, and previous surgeries were extracted and entered into a database. Presenting symptom, initial ultrasound, and type of initial surgery were all recorded. Endometriosis staging was performed according to the revised ASRM classification system and was retrospectively assigned by the authors using operation reports and photos where available. Following this, surgical findings including, complications, length of surgery, surgical operator experience, and length of stay were entered into the database. Finally, if a patient had a six-week post-operative review in the outpatient department, the level of subjective improvement in pain was recorded, based on the descriptions noted, for example no improvement, mild improvement or complete resolution. The number of total laparoscopies for endometriosis for each patient was also recorded.

All data were assessed for normality. Descriptive statistics of the population were tabulated. Demographics, surgical risk fac-

tors, and outcomes were compared by stage of endometriosis group (stage 1 and 2 compared to stages 3 and 4) using standard techniques (Chi² or independent *t*-test). The association between risk factors, operative time and time to discharge was determined using linear regression. All variables were also included and assessed in the multivariate model. Linear assumptions were confirmed by Qnorm plots. The association between risk factors, conversion to laparotomy and surgical complications was determined using logistic regression. All risk factors were also included and assessed in the multivariate model. A *p* value < 0.05 was considered statistically significant. All analyses were performed using the Stata/IC 12.1.

Results

Three thousand and thirty-four patients presented during the studied period. Of these, 2,150 patients underwent surgical treatment. Nine hundred and seventy-two patients met the inclusion criteria, had sufficient data in their computerized records, and were therefore included in the analysis.

The average age of the patients was 33.9 (range 15-64, SD 8.7) years with a mean BMI of 25.8 (range 15.2-52.1,

Table 3. — Factors associated with time to discharge.

	Crude regression co-efficient (95%CI)	p value	Adjusted regression co-efficient (95%CI)	p value
Chronic pain	0.03 (-0.20 to 0.25)	0.93	0.02 (-0.21 to 0.24)	0.89
Previous laparotomy	0.26 (0.01 to 0.51)	0.04	0.22 (-0.04 to 0.47)	0.10
Previous laparoscopy	0.14 (0.005 to 0.27)	0.04	0.07 (0.06 to 0.21)	0.28
Level of surgeon				
General gynecologist	1	-	1	-
Specialist endoscopic gynecological surgeon	0.30 (0.04 to 0.51)	0.005	0.21 (-0.005 to 0.43)	0.06
Trainee	-0.13 (-0.31 to 0.05)	0.15	-0.02 (-0.20 to 0.16)	0.86
Fellow	0.05 (-0.17 to 0.26)	0.67	0.04 (-0.18 to 0.25)	0.74
BMI (kg/m ²)	0.003 (-0.008 to 0.01)	0.56	-0.003 (-0.014 to 0.008)	0.63
Age at operation	0.14 (0.10 to 0.17)	<0.001	0.08 (0.04 to 0.13)	<0.001
Ethnicity – Caucasian	0.12 (-0.03 to 0.26)	0.11	-0.03 (-0.19 to 0.12)	0.69
Endometriosis Stage	0.27 (0.22 to 0.33)	<0.001	0.21 (0.15 to 0.27)	<0.001

Unit increase (days) for time to discharge per respective variable before (crude) and after adjustment for each variable. NB: total population n= 972.

Table 4. — Outcomes between stages.

	Stage 1-2	Stage 3-4	p value
Pain improvement/resolution			
Not applicable/not available	391 (59.5%)	138 (43.7%)	<0.001
No improvement	99 (15.1%)	29 (9.2%)	
Improvement	106 (16.1%)	82 (26%)	
Resolved	61 (9.3%)	67 (21.3%)	
Pain resolved/improved	167 (62.3%)	149 (83.7%)	<0.001
Those with pain §			

† Median (IQR), ‡ n (%), § N/A removed.

SD 6.2) kg/m². Patients with stage 1-2 endometriosis in this research population had significantly less vaginal deliveries than patients with stage 3-4 endometriosis, they were also significantly younger, and were more likely to be Caucasian and smokers. Other demographic variables of the study population are presented in Table 1. Regarding the surgeries performed, 17.5% were purely diagnostic, 8.7% underwent only ablation of their endometriosis, 60.5% had excisional surgery, and the remainder (13.3%) were classified as other indicating that they underwent hysterectomies or treatment of endometriomas only, all of which were included in the analysis. Patients underwent between one and eight surgeries in the study period. Patients with stage 3-4 endometriosis were more likely to have a specialist endoscopic gynecologic surgeon as the primary operator (*p* < 0.001) (Table 1). Patients who preoperatively were diagnosed with endometriosis involving the bowel, had a combined procedure with a colorectal surgeon.

The most common indication for surgery was pain (56%), while infertility alone (9%) and isolated menstrual disturbances (5%) were less common. Surgery for a combination of two or more factors was indicated in 30% of the population. Six hundred and fifty-eight (67.9%) patients had stage 1 or 2 endometriosis and 314 (32.1%) had stage 3 or 4 endometriosis.

With regards regard to surgical outcomes, the mean operative time was significantly higher in the stage 3-4 endo-

metriosis group in comparison to the stage 1-2 group (105 vs. 65 minutes, *p* = 0.001, range 15-330 minutes vs. 15-245 minutes), as was the conversion to laparotomy (12 vs. 6 *p* = 0.002) and the complication rate (16 vs. 9 *p* = 0.003). Multivariate analysis was performed to exclude other confounders and determine the actual significance of each variable. For each increasing stage of endometriosis there was an associated 18.1-minute increase in surgical time (95% CI 15.5-20). Compared to an operation performed by a general gynecologist, surgery performed by a gynecological endoscopic surgeon was associated with a 30.0-minute increase (95% CI 20.9-39.1) and surgery performed by a fellow with a 14.4 minute (95% CI 5.33-23.4) increase in operative time (Table 2). Based on the multivariate analysis to determine risk factors for conversion to laparotomy, increasing stage of endometriosis emerged as the only statistically significant risk factor (OR 1.87, 95% CI 1.15-3.04).

In the stage 1-2 group there was one major intraoperative complication resulting from a trocar injury to bladder, recognized on cystoscopy, and sutured laparoscopically. In the stage 3-4 group there were six major intraoperative complications including two significant cystotomies requiring conversion to laparotomy, one patient had significant adhesions, and the decision was made to convert to Pfannenstiel laparotomy after entry with the laparoscope, the patient ended up with a full thickness rectal defect requiring a low resection and Hartmann's procedure, one patient had a retained rectal instrument which was removed day three post-procedure and she had an uneventful recovery, two patients had full thickness injuries to the rectosigmoid, were converted to laparotomy, and had a primary repair of the defect. None of these patients had planned combined procedures with a colorectal surgeon. There were four patients in the entire cohort that required blood transfusions. With regards to postoperative complications, the Clavien-Dindo classification system [6] was used with grades I and II classified as minor complications and grades III and IV considered to be major complications. Major complications included returning to operating theatre for the retained in-

strument and the Hartman's procedure both described above, for a bleeding vaginal laceration that required suturing, and for hydronephrosis requiring stenting due to a pelvic collection. The only significant factor that was associated with an increase in both major and minor complication was the stage of endometriosis, with an adjusted odds ratio of 1.58 (95% CI 1.07-2.33, $p = 0.002$). Other factors that on univariate analysis were independently associated with an increase in any complication included previous laparotomy, increasing age, and ethnicity other than Caucasian, although when adjusted for other variables in the multivariate analysis, they were not significant. Factors that did not affect complication rates included BMI, level of surgeon, and previous laparoscopy.

The mean time to discharge was less than two days in both groups, however as the stage of endometriosis increased, there was an associated increase in length of stay ($p < 0.001$). Also, for each additional year of age at operation, there was an associated increase of 1.92 hours (0.08 days) in time to discharge ($p < 0.001$) (Table 3). Although this is statistically significant, these differences may be of little clinical or economic significance.

The data demonstrated that 71% of all patients with endometriosis who had a six-week post-surgical review had symptom improvement or resolution. However, these rates were higher in the patients who had been treated for stage 3 or 4 endometriosis, in comparison with the stage 1 or 2 group (83.2% vs. 62.8%, $p < 0.001$) (Table 4).

Discussion

The primary objective of this study was to identify the outcomes and complications of endometriosis related laparoscopic surgery in one multicenter tertiary referral center. Of note, the management of endometriosis in the present center utilizes a multidisciplinary approach, involving medical therapy and referral to pain specialists, psychologists, and naturopaths. Surgery is another option for treating these patients. Patients with bowel endometriosis, undergo a combined surgical approach, with pre-operative colorectal review, colonoscopy if necessary, and careful planning of their procedure, which is undertaken by an experienced bowel surgeon and a gynecological surgeon with endometriosis expertise. All surgeries in this series occurred in a surgical training center, with surgeons being of varying stages in their careers and in their training. It is important to recognize that despite this, the complication and conversion rates are fairly similar to those reported in the literature.

Although more than half (52.5%) of patients in the stage 3-4 endometriosis group were more likely to be older at their first surgery and treated surgically by a gynecological endosurgeon or a fellow training in the same, the longer operative times, difference in number of complications, and conversion to laparotomy may be

accounted for by the increased complexity of their surgeries in comparison to those in patients with stage 1-2 endometriosis.

In the stage 3-4 endometriosis group, conversion to laparotomy occurred in 3.8% of cases (12 out of 314 procedures) and the rate of major complications was 1.6% for intraoperative complication (5 of 314) and 0.6% for post-operative complications (2 of 314). This is in keeping with rates documented in the literature. In the series reported by Kondo *et al.* [5], there was a conversion rate of 13 out of 560 women (2.3%) and an intraoperative complication rate of 1.05% and 4.3% for postoperative complications. In the study by Darai *et al.* [7], 10% of women who underwent laparoscopic bowel resection due to deep infiltrating endometriosis required conversion to laparotomy (7 out of 71) and had a major complication rate of 12.6%. In an Australian series by Wills *et al.* [8], the complication rate for patients undergoing surgical removal of colorectal endometriosis was 11.4%, with a conversion to laparotomy rate of 7.5%. Magrina *et al.* [9] reported a major complication rate of 1.4% in patients undergoing laparoscopy or robotic surgery for stage 3-4 endometriosis. Additionally, their length of stay was similar (mean of 1.0 days vs. median of 1.0 days). However, they reported a mean operating time of 130.4 minutes was longer (105 minutes in the stage 3-4 endometriosis group), with a lower conversion to laparotomy rate (0.6%) compared with 3.8%.

For the patients with deep infiltrating endometriosis, improvement rates reported in this series were similar to that in the literature, with Bassi *et al.* reporting significant improvement in all pain related symptoms ($p < 0.001$) in their study of 151 women who underwent segmental bowel resection [4]. The discrepancy in improvement rates between the stages of endometriosis may be due to inability to completely excise mild endometriosis, as the lesions may be invisible to the surgeon. Alternatively, it may be that with the advancing skill of the surgeon and with increasing tendencies towards excision, as seen in the stage 3-4 endometriosis group, more lesions may be completely treated. Another explanation might be that the pain in stage 1 or 2 endometriosis was due to another factor and therefore did not improve following excision. A recent systematic review and meta-analysis showed that compared with diagnostic laparoscopy, operative laparoscopy was associated with decreased pain both at six months (OR 6.58, 95% CI 3.31-13.10) and at 12 months (OR 10.00, 95% CI 3.21-31.17) and an improvement in live birth or ongoing pregnancy rate (OR 1.94, 95% CI 1.20-3.16, $p = 0.007$) [2]. There is however difficulty in generalizing outcomes as there are discrepancies in outcome reporting, for example isolating dysmenorrhea from dyspareunia and using pregnancy rates as an outcome between studies as reviewed by Hirsch *et al.* [10].

There are several limitations to this study, including its

retrospective design and the reliance on discharge coding to capture the affected patients. Retrospective endometriosis staging could have over- or under-represented the actual stage of disease. The health network only began the transition to digitalized records in 2010, hence there was limited access to older paper-based files and therefore a large number of patients were excluded. Due to the multi-center nature of the study, surgical approach was not standardized due to differing surgical experience. Additionally, the dataset is incomplete due to many patients undertaking their post-operative reviews with their private gynecologists and therefore the effect of their surgery on their symptoms is unknown. Symptom improvement in patients that were reviewed post-operatively was subjective only and relied on clinical notes. Despite these limitations however, the authors did have a large number of patients and surgeries that did have sufficient data to provide insights into the differences between the stages of endometriosis and that the primary difference between the outcomes was due to the stage of endometriosis

Regarding improvement in pain, the present findings support those of the ESHRE guideline, which states that surgery is an effective treatment for endometriosis. However, the present results indicate that surgical treatment is significantly more effective in subjective symptom resolution for moderate and severe endometriosis, although there is a higher risk of complications with these procedures.

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