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# The effects and effectiveness of laparoscopic excision of endometriosis: a prospective study with 2–5 year follow-up

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BACKGROUND: This study investigates the outcomes for women up to 5 years after laparoscopic excision of endometriosis. METHODS: In this prospective observational cohort study, 254 women with chronic pelvic pain were referred to two units specializing in minimal access surgical management of endometriosis. Of these, 216 women underwent surgical assessment and 176 were confirmed to have endometriosis. Questionnaires and visual analogue scale (VAS) scores for dysmenorrhoea, non-menstrual pelvic pain, dyspareunia and dyschesia as well as quality of life instruments; the EO-5Dindex and EO-5Dvas, Short-Form 12 (SF-12) and sexual activity questionnaires were completed pre-operatively. Intra-operative details of revised American Fertility Society (rAFS) stage, site of disease, associated tests, duration of surgery and complications were noted. Follow-up was performed by postal questionnaire and chart review. For women who had further surgery, rAFS stage, site of disease, other procedures and histology were all recorded. RESULTS: Pain scores were all significantly reduced at 2-5 years for dysmenorrhoea (median VAS baseline versus follow-up 2–5 years); 9 versus 3.3 (P < 0.0001), non-menstrual pelvic pain 8 versus 3 (P < 0.0001), dyspareunia 7 versus 0 (P < 0.0001) and dyschesia 7 versus 2 (P < 0.0001). Quality of life was improved for the EQ-5D index (P = 0.008 and the EQ-5Q vas (P = 0.03) and for sexual function with pleasure (P = 0.001) and habit (P = 0.012) being improved and discomfort being decreased (P = 0.001). The chance of requiring further surgery as determined by the Kaplan–Meier survival curve was 36%. A rAFS score of >70 was predictive of requiring further surgery (P = 0.03). Of women who had further surgery, endometriosis was found histologically in 68%. CONCLUSIONS: Laparoscopic excision of endometriosis significantly reduces pain and improves quality of life for up to 5 years. The probability of requiring further surgery is 36%. Return of pain following laparoscopic excision is not always associated with clinical evidence of recurrence.

Key words: endometriosis/laparoscopic excision/pelvic pain/quality of life/re-operation for pelvic pain

### Introduction

Endometriosis can have a significant impact on the sufferer, the gynaecologist and the health care system. For the sufferer, quality of life may be significantly decreased (Garry *et al.*, 2000). For the gynaecologist it constitutes a considerable workload, accounting for 10-15% of new referrals (Reiter, 1990). For the surgeon, the diagnosis and treatment of endometriosis accounts for 25-35% of laparoscopies and 10-15% of hysterectomies each year (Lee *et al.*, 1984; Gambone *et al.*, 1990). Finally for the health care system, endometriosis imposes considerable costs; direct costs of surgical therapy are estimated at US\$5805 and for medical treatments US\$2418 (Winkel, 1999). The indirect costs of time away from employment, the burden of pain and its impact on quality of life are also recognized.

Surgical treatment of endometriosis may be effective in relieving dysmenorrhoea, dyspareunia, non-menstrual pelvic pain and dyschesia (Koninckx *et al.*, 1991; Sutton *et al.*, 1994; Garry, 1997; Garry *et al.*, 2000). In a previous report of 57 women followed for 4 months after laparoscopic excision of endometriosis we noted encouraging short-term improvements in these pain syptoms and quality of life. We concluded that longer follow-up was necessary to determine the role of this surgical modality in the treatment of endometriosis (Garry *et al.*, 2000). This paper presents an up to 5 years follow-up for a larger cohort of women.

### Materials and methods

Ethical approval was obtained from the relevant hospital ethics committee. Between March 1996 and September 1998, 254 women

were referred to the minimal access gynaecology units of James Cook University Hospital or St James's University Hospital with symptoms and signs suggestive of endometriosis. Of these, 176 had the diagnosis of endometriosis confirmed histologically and these formed our study group.

Women completed a pre-operative questionnaire that collected demographic data and an assessment of pain using a visual analogue scale (VAS) for four components of endometriosis-related pain; dysmenorrhoea, non-menstrual pelvic pain, dyspareunia and dyschesia. We used an 11-point scale (0–100 mm), with zero representing no pain and 100 representing the worst pain imaginable. Quality of life data were collected using three different and validated instruments. The EQ-5Dindex and EQ-5Dvas are measures of physical functioning and patients' self-rated assessment (Brooks *et al.*, 1997). The Short-Form 12 (SF-12) produces scores of both physical and mental health (Ware *et al.*, 1995). A sexual activity questionnaire was used to collect data pertaining to pleasure, habit and discomfort with intercourse (Thirlaway *et al.*, 1996). Data on the patients' primary presenting problem, full menstrual history and previous medical and surgical therapy for endometriosis were collected.

Following consent for laparoscopic excision of endometriosis, women had surgery performed in a standardized fashion, with no hormonal pre-treatment. All surgery was performed after a pre-operative low residue diet and bowel preparation using 3 l of Klean-prep (Norgine Ltd, UK). Procedures were performed under general anaesthesia as previously described by this group (Garry *et al.*, 2000). Eight surgeons were involved in the procedures, four consultant gynaecologists specializing in minimal access gynaecological surgery and four fellows training in minimal access gynaecological surgery.

Patients were examined under anaesthetic and the findings recorded, including the size and position of the uterus, the presence and position of nodules or plaques, the size and position of the ovaries, the relative mobility of the ovaries and the uterus and fixation to other pelvic or abdominal structures. The stage of disease as defined by the revised American Fertility Society (rAFS) classification system was recorded, as was the use of additional intra-operative tests such as cystoscopy, rectal integrity test or the use of ureteric catheters. Intraoperative complications were noted and additional procedures or surgeries such as ovarian removal or hysterectomy were documented. The diagnosis of endometriosis was confirmed by histological examination of specimens removed at surgery.

Long-term follow-up was performed by postal questionnaire and chart review. A questionnaire was mailed to women at a single time point, regardless of their initial date of surgery. Women were asked to record any additional surgical or medical treatments they required. Details of the findings and procedures undertaken from any repeat surgeries performed were obtained.

Patients who did not respond to the initial postal questionnaire were telephoned and asked to complete the questionnaire. A second questionnaire was sent if the original had been misplaced. A second telephone call was made if no response was achieved within 1 calendar month of the first reminder.

### **Statistics**

Analyses of pain scores and quality of life data were performed using the Wilcoxon rank sum test for paired non-parametric data. Reoperation rate was tabulated using the Kaplan–Meier method survival analysis. Factors contributing to re-operation were assessed by multivariate regression analysis with Weibull distributed error terms. Analysis was undertaken using Statistics Package for the Social Sciences (SPSS for Windows, Microsoft, USA) or Minitab 13 (Minitab Inc., USA). P < 0.05 was considered significant.

### Results

Of 254 women referred with pelvic pain, 216 underwent surgery; of these, 176 patients had histologically confirmed endometriosis following laparoscopic excision of their disease. A total of 135 women had completed data sets for preoperative, intra-operative, and up to 5-year follow-up (representing a 77% follow-up rate, with an average time 3.2 years; range 2–5 years).

### **Demographics**

Average age at the time of surgery was 31 years (range 20–48), 60% of women (80/135) were nulliparous, 17% (24/135) had one child and 23% (31/135) had two or more children. Seventy per cent (93/135) had taken analgesia for pain prior to their surgery. Seventy-three per cent (99/135) of women had taken at least one form of hormonal treatment for symptoms including the oral contraceptive pill, progestagens, danazol and GnRH analogues. Two medical treatments had been tried by 36% (48/135) of the group, three by 15% (20/135) and four by 2% (4/135) of women.

Seventy per cent (95/135) of women had one previous surgery; this was a diagnostic laparoscopy in 54% (73/135) and excision or ablation of endometriosis by laparoscopy or laparotomy in 16% (22/135); 20% (27/135) of women had two previous procedures, two had three previous procedures, two had four previous procedures and one had six procedures prior to being seen at one of our hospitals.

### Presenting symptoms

The primary indication at presentation was non-menstrual pelvic pain in 74% (100/135), dysmenorrhoea in 8% (11/135), dyschesia in 8% (11/135), dyspareunia in 3.5% (5/135) with the remaining 6.5% distributed between menorrhagia, infertility, the finding of a pelvic mass or not specified. Seventy-four per cent (101/135) of women had a second indication for surgery. This was pelvic pain in 20% (27/135), dysmenorrhoea in 13% (18/135), dyspareunia in <1% (1/135) and dyschesia in 25% (34/135). Pelvic mass accounted for 15% (21/135) of the remaining indications. Prior to surgery, 11% (15/135) of women had a barium enema, 5% (7/135) had a sigmoidoscopy, and 3% (4/135) had a magnetic resonance imaging scan.

### **Operative findings**

At the time of surgery, endometriosis was found to be stage I in 14% (19/135, stage II in 28% (39/135), stage III in 17% (23/135) and stage IV in 41% (54/135) of women. Fifty per cent (67/135) of women had no involvement of the cul-de-sac, 18% (24/135) had partial cul-de-sac obliteration and 32% (44/135) had complete cul-de-sac obliteration; 6% (8/135) had a full thickness vaginal lesion. Eight per cent (11/135) of women had a right endometrioma, 18% (24/135) had a left endometrioma, 12% (16/135) had bilateral endometriomas and 62% (84/135) did not have an endometrioma. The uterosacral ligaments were involved by disease in 88% (117/135) of women, both uterosacrals were involved in 57% (76/135), the right only in 18% (24/135) and the left only in 13% (17/135) of

Table I.	Overall	pain	scores:	all	stages	and	indications
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	Median (IQR)	Baseline versus 5 years <sup>a</sup>		
		Z score	P value	
Dysmenorrhoea				
Baseline	9 (7–9)	7.9	< 0.0001	
2–5 years	3.3 (2-7)			
Non-menstrual pelvic pain				
Baseline	8 (6–9)	7.6	< 0.0001	
2–5 years	3 (0–5)			
Dyspareunia				
Baseline	7 (5.5–9)	6.8	< 0.0001	
2–5 years	0 (0-4)			
Dyschesia				
Baseline	7 (4-8)	7.1	< 0.0001	
2–5 years	2 (0-2)			

Values are median visual analogue scale scores.

<sup>a</sup>Wilcoxon rank sum test.

IQR = interquartile range.

women. The average length of surgery was 107 min (range 30-280).

## Other surgical procedures and intra-operative complications

Five women had unilateral oophorectomy, three women had bilateral oophorectomy, and seven women had hysterectomy performed with their index surgery. Six per cent of women (8/135) had ureteric stents placed at the time of surgery, as a precautionary measure. No ureteric complications were noted. Fifty per cent (67/135) of women had a cystoscopy at the end of their surgery with Indigo Carmine (American Regent Laboratory Inc., USA) to test for ureteric patency. Forty-one per cent (55/135) of women had a rectal integrity test with Methylene Blue (0.01% solution diluted to 20 ml with sterile water).

Intra-operative complications included one case of unintentional opening of the rectum. This was diagnosed at the time of surgery, a laparoscopic repair was performed and no postoperative sequelae were noted. In a further three cases, full thickness rectal disease required the rectum to be opened intentionally for disease to be completely excised. In two of these cases, the repairs were performed laparoscopically and in one case a laparotomy and anterior resection with colostomy was required. The colostomy was reversed 6 months later.

Eighteen per cent (24/135) of women had an estimated blood loss of >500 ml. Four per cent of women (5/135) required a blood transfusion; two intra-operatively and three postoperatively. The bladder was opened on two occasions, one due to full thickness disease and the second inadvertently. Both were repaired laparoscopically and no sequelae were noted. One woman suffered a uterine perforation with the Valtchev uterine manipulator and a laparoscopic repair of the defect was performed.

### Results at long-term follow-up

Sixty-seven per cent of women reported that they were improved following surgery, 25% reported that they were worse and 8% reported that their symptoms were unchanged.

For all women in the study, between the index surgery and long-term follow-up, 35% (48/135) required analgesics for pain and 26% (36/135) had received some hormonal therapy. Of these, 48% (23/48) requiring analgesia and 44% (16/36) requiring hormonal treatment had further surgical intervention. For women not requiring surgery, 22% (20/91) required hormonal treatment and 27% (25/91) analgesia. Women who required additional hormonal treatment were more likely to require additional surgery ( $\chi^2 = 4.1$ , P = 0.04), as were women requiring analgesia ( $\chi^2 = 7.2$ , P = 0.007).

### Pregnancy outcomes

Forty per cent of women gave a history of infertility. From the time of index surgery to follow-up, 59% (32/54) of women who had tried to conceive had a pregnancy and 44% (24/54) had a live birth following their surgery.

### Pain scores at 2-5 year follow-up

Table I summarizes pain scores recorded at up to 5 year followup for the group and shows highly significant reductions of all four pain symptoms. Table II presents pain scores by both stage and pain type.

### Further surgical procedures

Time to re-operation is plotted by the Kaplan–Meier method in Figure 1. In the cohort followed, 33% of women required further surgical intervention following their index surgery. The chance of requiring further surgery projected to a time of 60 months is 36%. Multivariate regression analysis was completed to predict whether age, rAFS stage or operative time was predictive for re-operation. None of these factors was predictive for further surgery. However, analysis based on rAFS score, with two groups divided into rAFS scores of >70 and <70, showed a significant difference when they were compared for likelihood of surgical re-intervention. Women who had more severe disease were more likely to require further surgery (Wilcoxon rank sum test,  $\chi^2 = 4.38$ , P < 0.03). The survival curve analysis for these two groups is shown in Figure 2.

Of the 44 women who had further surgery, 32% (14/44) had no visual or histological evidence of residual or recurrent endometriosis. Thirty-eight per cent (17/44) were found to have the same stage of endometriosis as their index surgery, 55% (24/44) had a lesser stage (including no disease) compared with their index surgery and only 7% (3/44) showed progression of disease to a higher stage compared with their index surgery.

Twenty women (15% of the cohort) had a hysterectomy subsequent to their initial surgery. Eleven women in this group had histological evidence of endometriosis removed at the time of their surgery. Two of these eleven had adenomyosis as well as endometriosis. Four women had adenomyosis only with no evidence of endometriosis. One woman who did not suffer with pelvic pain had a hysterectomy for menorrhagia and was noted to have fibroids. Four women had hysterectomy with no demonstrable pathology; in three of these, dysmenorrhoea only was the symptom, and dysmenorrhoea and menorrhagia in the other. One woman with disturbingly rapid progression despite extensive primary surgery required at re-operation abdominal

Table II. Stage versus pain symptom: long-term outcome

Parameter	Baseline versus up to 5 years							
	Stage I $(n = 19)$		Stage II $(n = 39)$		Stage III $(n = 23)$		Stage IV $(n = 54)$	
	Med (IQR)	<i>Z</i> , <i>P</i>	Med (IQR)	<i>Z</i> , <i>P</i>	Med (IQR)	<i>Z</i> , <i>P</i>	Med (IQR)	<i>Z</i> , <i>P</i>
Dysmenorrhoea								
Baseline	8 (7-8.5)	-3.6,	8 (7–9)	-3.8,	9 (7–9)	-3.8,	9 (7-10)	-4.8,
2–5 years	2 (0-6)	< 0.0001	4.5 (2-6.5)	< 0.0001	3.5 (1-7)	< 0.0001	2 (0-8)	< 0.0001
Non-menstrual pelvic pain								
Baseline	6 (5-8)	-2.1,	6 (5.5–8)	-3.7,	6 (5.5–8)	-1.9,	7 (5.5–8)	-4.7,
2–5 years	3 (1-5.8)	0.036	3.3 (0-5.5)	< 0.0001	2.9 (0-6.3)	0.046	2.4 (0-5)	< 0.0001
Dyspareunia								
Baseline	7 (6-8)	-3.1,	5.5 (2-8)	-2.8,	6 (1.5-8)	-2.9	5 (2-6.5)	-4.3,
2–5 years	2.6 (0-6)	0.002	1.7 (0-4.2)	0.005	0 (0-2.5)	0.004	0 (0–5)	< 0.0001
Dyschesia								
Baseline	6 (1.5-8.5)	-2.1,	6 (0-8)	-2.7,	4 (0-7)	-1.5,	5 (0-9)	-3.1,
2–5 years	3.1 (0-6)	0.035	2.7 (0-5)	0.006	0 (0-3.5)	0.12	2 (0-6)	0.002

Values are median visual analogue scores).

Med = median; IQR = interquartile range.

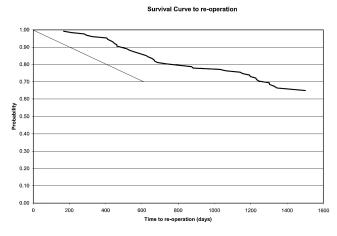


Figure 1. Survival curve estimating the time to re-operation projected to 5 years.

hysterectomy and bilateral salpingo-oophorectomy, anterior rectal resection and reimplantation of her left ureter due to ureteric obstruction secondary to endometriosis.

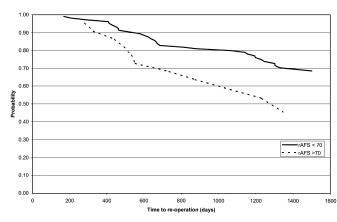
Of the 24 women who did not have hysterectomy, five had no visible or histological evidence of endometriosis, four had stage I disease, six stage II disease, four stage III disease and five stage IV disease resected at the time of their second surgery. One woman in this group had an anterior resection and ureteric reimplantation of the left ureter due to obstruction caused by endometriosis.

### Quality of life outcome

The results of the long-term outcome for the EQ-5Dindex and EQ-5Dvas are shown in Table III. The baseline values indicate a marked impairment in quality of life compared with the 'normal population'. Laparoscopic excision of endometriosis significantly improved these quality of life measures up to 5 years after surgery, though the values do not reach those of the normal population.

The results of the SF-12 are summarized in Table IV. This shows an improvement in the scores from baseline to 5 years,

Survival Curve rAFS <70 versus rAFS >70



**Figure 2.** Survival curve estimating the time to re-operation projected to 5 years for women with a revised American Fertility Society (rAFS) score of <70, compared with women with a rAFS score of >70.

though this does not reach statistical significance. The increase in the physical component is greater than the mental component of the score.

Table V summarizes the results of the sexual activity questionnaire. For sexual activity, there is a significant improvement in pleasure and habit, and a decrease in discomfort with intercourse that is maintained up to 5 years.

### Discussion

In 1776, a Scottish physician described endometriosis by saying: 'Bodily illness is an inevitability when it comes to this disease' (Brotherson, 1776). Over two centuries later, 'bodily illness' remains an integral part of this disease and continues to cause impairment to quality of life due to pain and/or infertility (Burns and Schenken, 1999).

This study indicates that at up to 5 years follow-up, there is a highly significant improvement in all parameters of pain measured. These findings are consistent with those we

Parameter	Score, mean (SD)	Population normal	t-Test	$P^{\mathrm{a}}$
EQ-5Dvas				
Baseline	68.8 (19)	86.3 (14.8)	10.1	< 0.0001
2–5 years	74.9 (21)	86.3 (14.8)	6.4	< 0.0001
Baseline versus 2-5 years			2.1	0.031
EQ-5Dindex				
Baseline	0.6 (0.31)	0.916 (0.15)	11.3	< 0.0001
2–5 years	0.7 (0.29)	0.916 (0.15)	8.4	< 0.0001
Baseline versus 2-5 years			2.7	0.008

<sup>a</sup>Student's *t*-test.

### Table IV. Short-Form 12 scores

	Score, median (IQR)	Population normal	P value
Physical component score			
Baseline	43.5 (36.3-51.2)	52.8 (44.3-56.0)	< 0.0001ª
2–5 years	47.6 (38.2–54.1)	52.8 (44.3-56.0)	$< 0.0001^{a}$
Baseline versus 2–5 years			0.12 <sup>b</sup>
Mental component score			
Baseline	46.7 (34.8-53.6)	51.9 (43.8-56.9)	$< 0.0001^{a}$
2–5 years	47.0 (38.6–55.4)	51.9 (43.8-56.9)	$< 0.0001^{a}$
Baseline versus 2-5 years		· /	0.14 <sup>b</sup>

<sup>a</sup>Mann–Whitney *U*-test. <sup>b</sup>Wilcoxon rank sum test.

IQR = interquartile range.

Table V. Sexual activity questionnaire				
Parameter	Median (IQR)	Baseline versus 2–5 years <sup>a</sup>		
		Z score	P value	
Pleasure				
Baseline	10 (5-12)	3.1	0.001	
2-5 years	12 (9–16)			
Habit				
Baseline	1 (0-1)	2.5	0.012	
2-5 years	1 (1-1)			
Discomfort				
Baseline	3 (1.5–5)	3.2	0.001	
2-5 years	2 (1.5–3)			

<sup>a</sup>Wilcoxon rank sum test.

IQR = interquartile range.

Pleasure is scored to a maximum of 18, habit maximum 3 and discomfort maximum 6.

previously reported in a preliminary short-term study (Garry *et al.*, 2000) and confirm the effectiveness of laparoscopic excision of endometriosis that is reported by others (Bianchi *et al.*, 1999; Anaf *et al.*, 2000; Wright, 2000; Chapron *et al.*, 2001).

In this current study, many women had previously been treated for symptoms of endometriosis, prior to having surgical excision. It is possible that this may bias the outcome, with women being pre-selected to have previous failed therapy. This highlights two important points. The first is that the perfect treatment is yet to be arrived at, with all current available treatments having a significant 'failure rate' as noted by recurrence of pain and the desire for further treatment. The second point is that in this study during the follow-up period to 5 years, two-thirds of the patients avoided further surgery. Additional treatments were used in a minority of women, and overall more than half the women studied required no further treatment for endometriosis-associated pain. No randomized trial has been performed to compare medical and excisional surgery as treatments for endometriosis, but such a trial would be helpful to indicate the most efficacious and cost-effective treatment.

In this study 59% of women wishing to become pregnant did so. Medical therapy in the form of ovulation suppression is not effective. A recent Cochrane review looking at the effectiveness of ovulation suppression in the treatment of endometriosis-related infertility concluded that given the significant period of amenorrhoea, the lack of treatment benefits and the adverse effects commonly associated with such drugs, ovulation suppression cannot be recommended as standard therapy for endometriosis-associated infertility (Hughes *et al.*, 2000).

It has been reported that there is a poor correlation between the extent of endometriosis and pain symptoms (Kistner, 1979; Buttram and Reiter, 1985; Crosignani *et al.*, 1996; Garry *et al.*, 2000). We agree with this finding, as many women with minimal disease in this study reported significant pain and a decrease in their quality of life. The results from sub-analysis examining pain scores by stage suggest that there was a reduction in pain for all four parameters examined, independent of stage. We found that dysmenorrhoea remained the most common symptom following surgery with pain scores being higher than for the other parameters.

We investigated factors predisposing to the need for further surgery and the only significant finding was that the group with very advanced disease (delineated arbitrarily by the 'half-way point' in the traditional rAFS system and indicating the combination of deeply infiltrating ovarian disease, cul-de-sac obliteration and adhesions) were at significantly greater risk of re-operation.

It is possible that the results from this study may be affected by the 23% of women who did not respond to the follow-up questionnaire. We performed a sensitivity analysis based on the stage of disease, the rAFS score and the follow-up time. These variables were not significantly different for responders and non-responders. Based on this analysis it is unlikely that the results would be significantly altered by women who were not included in the follow-up cohort.

Of women who had further surgery, almost one-third of them had no evidence of endometriosis, either macroscopically or histologically at the time of re-operation. This signifies that the aphorism 'once endometriosis, always endometriosis' is not always true. We have clearly demonstrated that some women who had excision of histologically confirmed endometriosis could subsequently present with similar pain but which on a second occasion was not associated with deposits of the disease. It is therefore also possible that endometriosis may not have been the cause of pelvic pain at the time of presentation, despite it being present and surgically excised.

We also recognize that endometriosis can recur in a very aggressive manner. In one woman with stage IV disease, symptoms recurred within 6 months of surgery and extensive disease causing ureteric obstruction and rectal infiltration required subsequent very radical surgery including a pelvic clearance, reimplantation of the ureter and rectal resection. In another woman desirous of fertility, severe disease required ureteric reimplantation and rectal resection, though her uterus was left intact. She conceived spontaneously 1 year later and delivered a normal healthy infant at term.

Nearly one-half of the women who had further surgery had a hysterectomy. Pain was not always a feature and endometriosis was demonstrated in just over half of these cases. Of the women without endometriosis, five had neither endometriosis nor adenomyosis, though the remaining four were found to have adenomyosis.

In summary, laparoscopic excision significantly reduces pain and improves quality of life and sexual function in women with all stages of endometriosis for up to 5 years follow-up. Women with endometriosis have an impaired quality of life, which, despite treatment, may not return to levels enjoyed by women without disease. The chance of requiring further surgery after laparoscopic excision in a tertiary referral teaching hospital is 36%. Endometriosis is not found in onethird of women who undergo further surgery.

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