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Laparoscopic Surgery for Endometriosis: A Long Term Follow-Up

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Abstract

Objective: To investigate if complete resolution of endometriosis by laparoscopic surgery is beneficial to postoperative fecundity, dysmenorrhea and dyspareunia.

Design: An observational comparative study on the outcome of laparoscopic surgery.

Patients: Laparoscopically-treated symptomatic women with endometriosis (total n = 236); complete (n = 185) and incomplete (n = 51) surgery groups.

Measurements: Postoperative fecundity and symptom reduction.

Results: With whole populations, no surgical completeness-related difference was observed in cumulative pregnancy rates during the postoperative days 0–400 (cycle fecundity rate = 0.0319). Further accumulation of pregnant cases was followed in the complete surgery group (final cumulative pregnancy rate = 80%), but not in the counterpart group (p = 0.003). The similar result was obtained when only r-AFS classification stages III and IV were compared (p = 0.007). No r-AFS stage-related difference was observed in cumulative pregnancy rates when only patients of complete surgery were selected for comparison. The surgery reduced dysmenorrhea (84.7%) and dyspareunia (80.0%).

Conclusions: Laparoscopic conservative surgery for endometriosis, especially when it is complete, increases fecundity and reduces disease-related symptoms, such as dysmenorrhea and dyspareunia.

Key words: laparoscopic surgery, endometriosis, fecundity, dysmenorrhea, dyspareunia

Introduction

Meta-analysis studies have postulated that conservative surgeries for endometriosis, including laparoscopic and laparotomic procedures, enhance postoperative fecundity in infertile women having endometriosis.[1,2] This implies that endometriosis is one of the generating factors of impaired fecundity and the removal of endometriosis creates a favorable condition for future pregnancy. In addition, laparoscopic removal of endometriosis reduces pelvic pains and dysmenorrhea.[3]

It is, therefore, reasonable to provide a surgical intervention to endometriotic women with symptoms such as infertility and/or pelvic pains and to remove endometriotic foci and related pathologies as completely as possible. However, this cannot be always completed partly because of surgeon's skill. Endometriosis can, for in-

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stance, involve a large area of alimentary tract and other vital organs. Removal of this type of endometriosis under laparoscopy is of great difficulty and it is not advisable to go across the border for most laparoscopic surgeons with the limited skill level. Such endometriosis may, therefore, reside untouched.

The purpose of this study is to investigate the influence of residual endometriosis, if any, on postoperative fecundity and pain recurrence. We surveyed all the women having symptomatic endometriosis and being treated laparoscopically through the years 1992 and 1998 in our institution. The collected data were statistically analyzed.

Materials and Methods

The subjects enrolled in the present study were 236 women having symptomatic endometriosis and being laparoscopically treated in our hospital with an informed consent through the years 1992 and 1998; *i.e.*, 176 infertile women having regular ovulatory cycles, having adequate frequency of intercourse and normal semen analysis in all of their partners, 203 women having dysmenorrhea, and 105 women having dyspareunia.

Laparoscopic procedures we employed were direct puncture of the first 10-mm trocar, CO_2 pneumoperitoneum, laparoscopically guided placement of two additional 5-mm trocars in each side of the suprainguinal region, aspiration of serosanguinous fluid out of the pouch of Douglas, KTP-laser evaporation of peritoneal superficial endometriosis, excision of deep endometriosis, removal of ovarian endometriomas, adhesiolysis, chromotubation, and pelvic lavage. Chromotubation revealed tubal patency of at least one side in all the women. Endometriosis was scored and staged according to the revised American Fertility Society (r-AFS) classification.[4] Endometriosis and related pathologies were completely resolved in 198 women (complete surgery group). In the remaining 38 women the complete resolution was impossible due to the site, the depth, and/or the spread of endometriosis (incomplete surgery group). Most of the women were hospitalized for 2 postoperative days. The rest had one or 2 more days of hospital stay because of patients' condition or personal inquiry. All the daily activities were allowed following the hospital discharge.

They were requested to be interviewed by us every third month or when pregnancy ensued. No intensive treatments for fecundity increase were applied to them and those willing to receive such treatments, *i.e.*, assisted reproductive technologies, were excluded from the present study at this point. All of them were requested to record basal body temperature (BBT) chart and to show it to us at each interview. Pregnancy was diagnosed by elevated urinary hCG levels and a prolonged high BBT phase. The day of BBT rise was documented to be the day of conception.

Dysmenorrhea was scored with a scoring system as follows; scores 0 for those having no dysmenorrhea, 1 for those having dysmenorrhea but needing no analgesics, 2 for those having dysmenorrhea and needing analgesics, and 3 for those having dysmenorrhea severe enough to limit daily activities even with analgesics. Dyspareunia was scored with a scoring system as follows; scores 0 for those having no dyspareunia, 1 for those having dyspareunia but no impairment in their sexual activity, and 2 for those having severe dyspareunia inducing limitation in their sexual activity. Dysmenorrhea and dyspareunia were scored with the above scoring systems at pre- and postoperative interviews. For those who desired reduction of dysmenorrhea and/or dyspareunia was allowed taking oral tablets or rectal suppositories of prostaglandin synthetase inhibitor at necessity.

All the accumulated data were statistically analyzed with a computer-aided analyzing system using Statistica 4.1 J, Microstat. When a probability was less than 0.05, the comparison was documented to be significant.

Results

Table 1 reveals the distribution of the patients in terms of r-AFS classification stages and their basic characteristics. The mean age was greater in r-AFS classification stage IV than in other stages. No between-group difference was observed in the mean infertile period. Between-group difference was highly significant as to surgical completeness. While endometriosis could be resolved completely in all the patients belonging to r-AFS classification stages I and II, proportions of incomplete surgery increased as the disease progressed ($p = 0.000$).

Of 176 infertile women 94 (53.4%) conceived spontaneously during the postoperative follow-up. The pregnancies produced 86 full term deliveries, 6 spontaneous abortions during the first trimester, and 2 ectopic pregnancies. When they were subgrouped in terms of surgical completeness, 138 and 38 women entered in complete and

Table 1. Distribution of patients in terms of r-AFS classification stages and their basic characteristics

r-AFS stage	*n*	Age (years) (Mean ± SD)	Infertile period (years)* (Mean ± SD)	Complete/incomplete surgery
I	61	28.9 ± 4.5	3.1 ± 2.9	61/0
II	44	28.9 ± 5.8	3.4 ± 3.1	44/0
III	57	29.5 ± 5.3	3.8 ± 3.7	45/12
IV	74	31.2 ± 5.3	3.3 ± 2.8	35/39
p		0.043	0.828	0.000

* Infertile period was calculated only for women of infertility (n = 176).

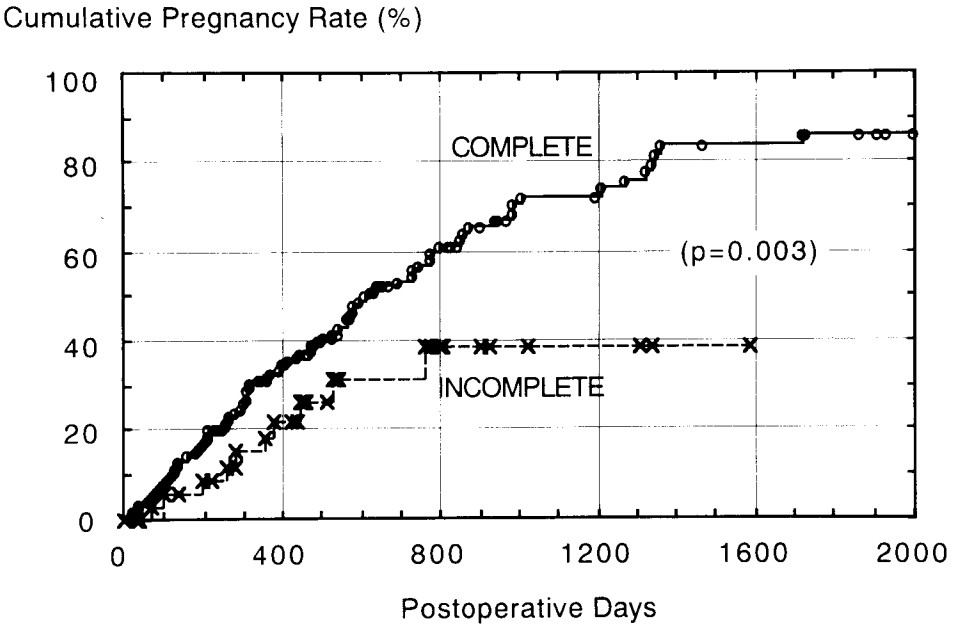

Fig. 1. Cumulative pregnancy rates in complete and incomplete surgery groups (whole populations). Cumulative pregnancy rates are identical during the postoperative days 0–400. Thereafter, more and more pregnant cases accumulated in the complete surgery group, reaching a final cumulative pregnancy rate of 80%. This type of accumulation was not observed in the incomplete surgery group.

incomplete surgery groups, respectively. Of the 94 pregnant women 84 and 10 women entered in the respective groups, giving pregnancy rates of 60.9 and 26.3%. In order to clarify the influence of surgical completeness on postoperative fecundity, cumulative pregnancy rates were compared between the 2 groups with the Kaplan-Meyer technique (Fig. 1). The cumulative pregnancy rates at the postoperative day 400 were not different between the groups, being approximately 30% in the both groups. The cycle fecundity rate during the initial 400 postoperative days was calculated to be 0.0319. During the subsequent postoperative days, in contrast, considerable numbers of pregnant cases accumulated in the complete surgery group but not in the incomplete surgery group. The final cumulative pregnancy rates reached 80 and 40% in the complete and incomplete surgery groups, respectively, giving a statistical significance (p = 0.003).

Since, as shown in Table 1, all the women of incomplete surgery belonged to the category of advanced endometriosis, there might be a case-selection bias in interpretation of the results coming from the whole populations. To avoid this bias, only women belonging to r-AFS classification stages III and IV were extracted and subjected to cumulative pregnancy rate analysis. The complete and incomplete surgery groups consisted of 55 and 38 women, respectively. The Kaplan-Meyer technique was employed to compare cumulative pregnancy rates in the 2 groups (Fig. 2). The result was similar to that coming from the whole populations. After reaching 30% of comparable cumulative pregnancy rates at the postoperative day 400 in the both groups, more preg-

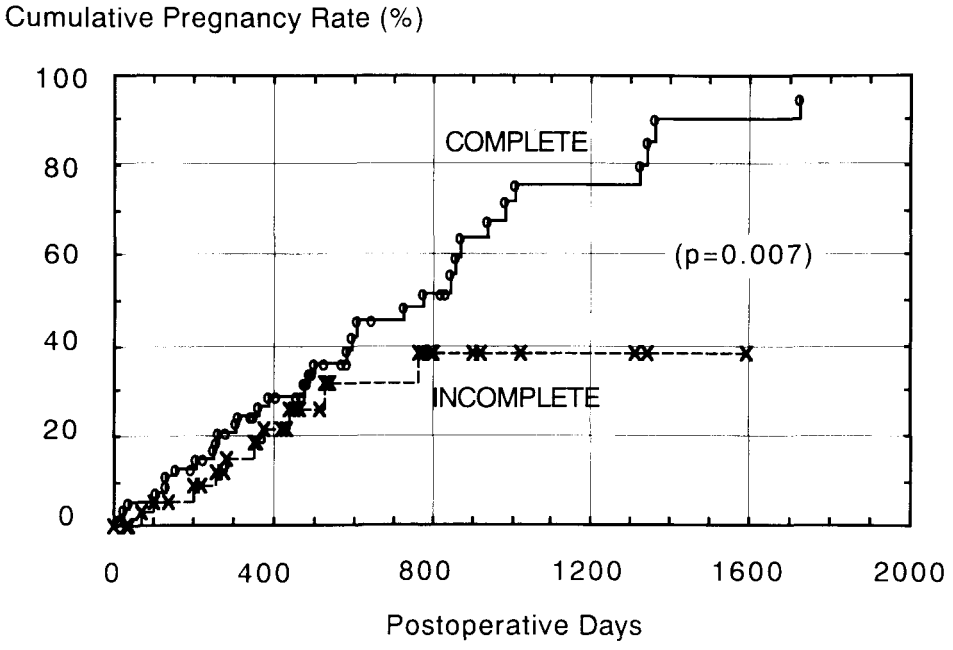

Fig. 2. Cumulative pregnancy rates in complete and incomplete surgery groups (r-AFS classification stages III and IV). Time-related accumulations of pregnant cases in the both groups are similar to that seen in Fig. 1.

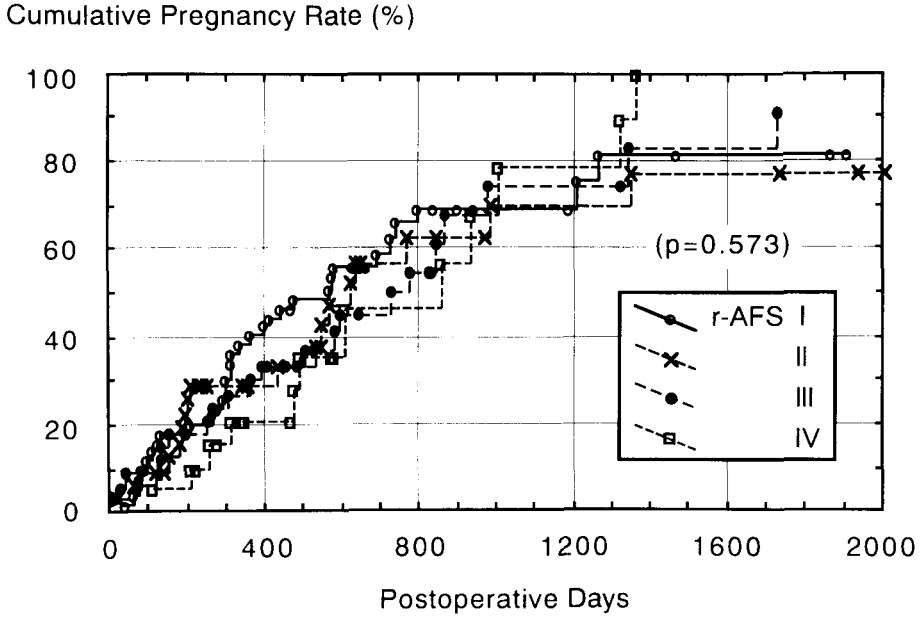

Fig. 3. Cumulative pregnancy rates in various r-AFS classification stages with the proviso that the laparoscopic surgery was complete. Preoperative conditions of endometriosis do not influence postoperative fecundity, as far as the surgery completely removes endometriosis and successfully restores the pelvic conditions.

nant cases accumulated in the complete surgery group but not in the incomplete surgery group. The final cumulative pregnancy rates were 90 and 40% in the respective groups ($p = 0.007$).

Another Kaplan-Meyer analysis was performed within the complete surgery group ($n = 138$) to analyze the influence of the stages of endometriosis on postoperative fecundity when the surgery completely removed endometriosis and related pathologies. The candidate women were subgrouped in terms of preoperative r-AFS classification stages I–IV ($n = 51$, 32, 35 and 20, respectively). Of them, 33 (64.7%), 18 (563%), 21 (60.0%) and 12 (60.0%) women, respectively, con-

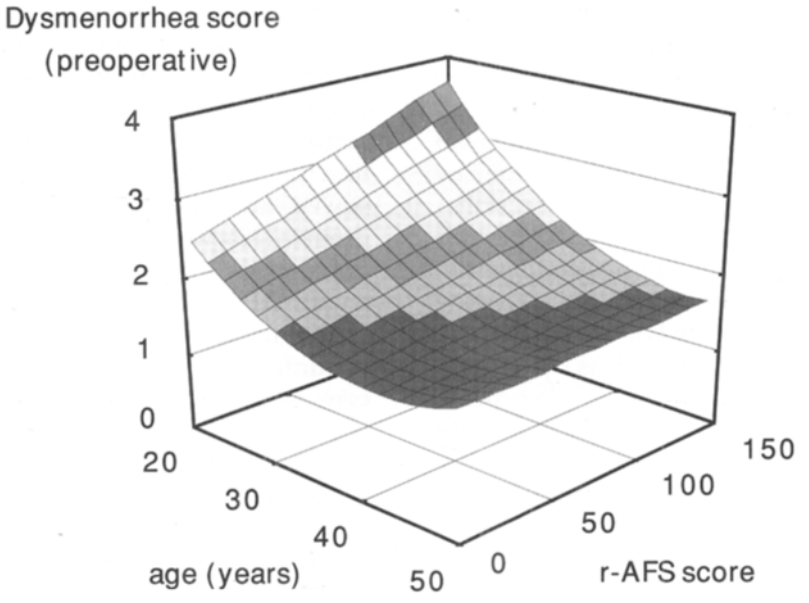

Fig. 4. Relationship between preoperative dysmenorrhea score, age and r-AFS classification score. Dysmenorrhea is more potent in the younger than in the older populations. Advanced endometriosis produces more potent dysmenorrhea than non-advanced endometriosis in the younger populations. Dysmenorrhea in the older populations is rather low and independent of r-AFS classification scores.

Table 2. A contingency table as to dysmenorrhea scores before and after the laparoscopic surgery

Postoperative dysmenorrhea score		0	1	2	3
Preoperative dysmenorrhea score	1	35	17	0	0
	2	37	22	9	0
	3	23	27	28	5

Table 3. A contingency table as to dyspareunia scores before and after the laparoscopic surgery

Postoperative dyspareunia score		0	1	2
Preoperative dyspareunia score	1	38	18	0
	2	26	20	3

ceived spontaneously after the surgery. The Kaplan-Meyer analysis revealed no between-group difference (Fig. 3).

A step-wise regression analysis was performed to analyze the relationship between preoperative conditions of endometriosis and the intensity of dysmenorrhea. Parameters listed up as contributing factors on dysmenorrhea were age ($p = 0.000$) and preoperative r-AFS scores ($p = 0.009$). The relationship between these 3 parameters was visualized in three-dimensional least square-fitted curved surface (Fig. 4). Preoperatively, 203 women had dysmenorrhea of various intensities. As shown in Table 2, 172 (84.7%) of the 203 women having painful periods reported enlightened dysmenorrhea postoperatively. No statistical relationship was disclosed between pain relief and surgical completeness ($p = 0.694$). Dysmenorrhea recurred in 34 (19.8%) women with a mean recurrence interval of 422.9 days.

Out of 105 women having dyspareunia preoperatively, 84 (80.0%) documented enlightened symptom postoperatively (Table 3). Since the number of women to be analyzed was not large enough, no further statistical analysis was attempted.

Discussions

Endometriosis is a disease occurring in women of reproductive age and causes various symptoms, *i.e.*, impaired fecundity and pelvic pains such as dysmenorrhea and dyspareunia. Endometriosis has the nature of progression with dynamic remodeling in baboons[5–7] and also in humans.[8,9] Therefore, endometriosis is a target of treatment when it is symptomatic.

Among a variety of treatment modalities for endometriosis, one of the most favorable ones is laparoscopic surgery with preservation of fecundability. It is shown that laparoscopic surgery is efficacious in promoting postoperative fecundity[1,2] and also in reducing dysmenorrhea.[3] The goal of laparoscopic surgery is to remove endometriosis and related pathologies and to restore normal pelvic conditions with minimal sur-

gical invasiveness. However, this is not always accomplished. For instance, endometriosis may involve large areas of the alimentary tract and other vital organs. Laparoscopic removal of such endometriosis may increase surgical invasiveness and the risk of complication when done by laparoscopic surgeons of limited technical skills.

Our current philosophy on laparoscopic surgery for endometriosis is to remove endometriotic lesions as completely as possible with keeping minimal surgical invasiveness. In cases where additive invasive procedures such as laparotomy are recommended, the procedures are, in general, not performed immediately and postponed until the performance is really needed. Therefore, we have sometimes, especially during the early days of laparoscopic experience, had to make a compromise and produced women of incomplete laparoscopic surgery. We accumulated these cases and compared the outcome of them to that of women in whom laparoscopic surgery removed endometriosis and related pathologies completely.

Although the present study is not randomized or double-blind, a Kaplan-Meyer analysis produced interesting results as to postoperative fecundity by comparing the 2 groups, complete and incomplete surgery groups. During the postoperative days 0–400, the cumulative pregnancy rate in the complete surgery group was comparative, though appearing slightly higher in Fig. 1, to that in the incomplete surgery group, reaching 30% at the day 400. The cycle fecundity rate during this period was 0.0319. This figure is comparable to that appearing in the literature which came from 172 infertile women having minimal or mild endometriosis and being surgically treated under laparoscope.[10] This initial accumulation of pregnant cases, the laparoscopy effect, is not dependent on surgical completeness. Even in women of incomplete surgery most endometriotic lesions were eliminated during our laparoscopic surgery. It is, therefore, feasible to speculate that the residual endometriosis is not large enough to produce negative influence on fecundity. In addition, it could be hypothesized that the laparoscopy effect is partly owing to removal of serosanguinous fluid and pelvic lavage during the surgery. Serosanguinous fluid of infertile women with endometriosis contains soluble factors interfering with fecundity, such as an ovum capture inhibitor[11,12] and others. The similar phenomenon can be seen in the expectant management, where endometriosis is not removed but aspiration and rinsing are performed as well, and where postlaparoscopic fecundity is increased.[13]

Being noticed is the difference in cumulative pregnancy rates after the postoperative day 400. In the complete surgery group pregnant cases accumulated more and more, reaching the final cumulative pregnancy rate of 80%. In contrast, it stayed low (40%) in the incomplete surgery group. This was so not only when the whole populations were analyzed but also when women of r-AFS classification stages III and IV were analyzed (Figs. 1 and 2). Therefore, it is likely that the difference is perfectly dependent on surgical completeness. The fact that the laparoscopy effect is abolished in the incomplete surgery group after the day 400 implies progression of the lesions left behind and/or new accumulation of the conception-interfering soluble factors. The delayed accumulation of pregnant cases as seen in the complete surgery group provides an interesting hypothesis as to the natural history of endometriosis. It appears that, once endometriosis is completely removed, *de novo* development of the disease is seldom to occur in women aged 25 years or more. In other words, endometriosis, if occurs, develops as early as during adolescence.

This hypothesis is supported by the findings as follows. Redwine's report[14] says that the mean age of women having endometriosis increases from 21.5 years for those with clear papules only, via 26.3 years for those with red lesions, to 31.9 years for those with black lesions. Clear papules cannot be seen in women over the age of 31 years. We have recently obtained the similar results by reviewing snap shot pictures of laparoscopic findings, being recorded in CD-ROMs during the operation, coming from 307 women of symptomatic endometriosis (unpublished data). Clear papules, an early appearance of endometriosis, were very frequent in women aged 12–20 years (90.0%). The incidence rapidly declined as the age increased and clear papules were almost exceptional in women aged 31 years or more. Red lesions, of high activity, were most frequent in women aged 21–25 years (75.5%) and steadily decreased as the age increased. Black lesions, old and of less activity, were very scarce in women aged 12–20 years (5.0%). The incidence increased as forming a peak in women aged 26–30 years (68.0%) and then gradually decreased. Assuming that the clear papules are the early lesions of peritoneal endometriosis, they undergo dynamic changes in appearance and also in function to red active lesions and finally to black inactive lesions.

It is interesting that preoperative conditions of endometriosis do not influence on postoperative

fecundity, as far as the surgery completely removes endometriosis and successfully restores the pelvic conditions (Fig. 3). With the proviso that the surgery is complete, women of endometriosis-associated infertility can wait for future pregnancy for at least 2 postoperative years with the probability as high as 60%. This evidence encourages laparoscopic surgeons to perform such an operation that endometriosis should be resolved as completely as possible.

The present study also produced interesting results as to dysmenorrhea. In younger populations dysmenorrhea is more potent than in older populations. While it is not completely perceived how dysmenorrhea occurs in endometriosis, bioactive substances, such as prostaglandins and/or cytokines, are the candidates of pain-generating factors.[15] Young women with dysmenorrhea have the largest proportion of red active lesions.[14,16] Red endometriotic lesions seem to be the most active producers of prostaglandins when compared to other lesions.[17] As the age increases, dysmenorrhea becomes less potent even in women having endometriosis of high r-AFS scores. The findings would support the hypothesis mentioned previously, *i.e.*, endometriosis develops during the younger ages, fulminates and finally regresses leaving adhesions and/or scars behind, being one of the producers of high r-AFS classification scores.

The results of postoperative relief of dysmenorrhea and its recurrence in the present study are comparable to those appearing in the literature.[3,18–20] Complete surgery showed no superimposing effect on pain reduction obtained by incomplete surgery. This is partly because we removed most of endometriotic lesions and related pathologies even in women of incomplete surgery. It can be assumed that the residual disease was not large enough to produce symptoms postsurgically, although the present study did not include no-treatment group to compare with.

Dysmenorrhea recurred in 34 (19.8%) women with a mean recurrence interval of 422.9 days. Again, no difference was disclosed between the complete and incomplete surgery groups as to recurrence of dysmenorrhea. The underlying mechanism is not known.

It could be concluded that laparoscopic surgery, especially when it completely resolves endometriosis and restores normal pelvic conditions, increases fecundity and reduces endometriosis-associated pelvic pains such as dysmenorrhea and dyspareunia. It is extremely important to recognize all the endometriotic lesions under laparoscope in order to perform complete surgery, since we can not touch invisible lesions. Our future progress on laparoscopic surgery should be directed toward a goal where all the endometriotic lesions are under our controls.

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