





# Sonographic Assessment of Ovarian Endometrioma Recurrence Six Months After Laparoscopic Cystectomy in Patients with Endometriosis

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## Abstract

**Background:** The high risk of recurrence of ovarian endometrioma after laparoscopy is a major challenge.

**Objectives:** In this study, we measured recurrence of endometriosis six months after laparoscopic surgery and evaluated its risk factors in these patients.

**Methods:** In this cross-sectional study, patients with endometrioma (based on the pathologic report) who underwent laparoscopic cystectomy in Rasool-Akram Hospital, Tehran, from April 2015 to August 2016, were evaluated by ultrasonography six months after the surgery. Endometriosis surgery was done by a team of expert surgeons. The demographic information of patients, number, size, and location of cysts, disease stage, and medical treatment taken after the surgery were recorded in the study checklist. The pre-operative endometriosis-related symptoms, including pelvic pain, dysmenorrhea, dyspareunia, dyschezia, and dysuria were recorded by visual analogue scale and compared with related symptoms six months after the surgery.

**Results:** Seventy-nine patients completed the study with the mean age of  $31.38 \pm 5.98$  years. The mean cysts' size was  $69.2 \pm 2.76$  mm: 44.3% had multiple cysts and 39.2% bilateral endometrioma. In 53.1% deep infiltrative endometriosis (DIE) was recorded. After six months, 13.9% had a recurrence with the mean size of  $37.2 \pm 13.3$  mm. There was a statistically significant correlation between recurrence and a previous surgery ( $P = 0.001$ ) and infertility ( $P = 0.02$ ). All endometriosis-related symptoms significantly decreased six months after the surgery.

**Conclusions:** The recurrence rate, compared to the previous report, indicated that patients with a previous surgery and infertility should be closely monitored for the risk of recurrence. Possibly, damages in the previous surgery and cellular and molecular abnormalities that encountered more deeply in endometriosis-associated infertility predispose the patients to more recurrence rate, which can be further investigated.

**Keywords:** Endometriosis, Recurrence, Ultrasonography, Cystectomy

## 1. Background

Endometriosis is a common benign gynecological disorder associated with dysmenorrhea, pelvic pain, and subfertility that leads to disability in women of reproductive age (1). Several treatments, including medical and surgical approaches have been suggested for the treatment of endometriosis (2) and several factors, including genetic, anatomic, immunologic, and environmental factors have been associated with the risk of endometriosis (3-5). The ectopic endometriotic tissue may be implemented at any site in the abdominal cavity, particularly the ovaries, result-

ing in the presence of endometrial glands, stroma, or glandular epithelium with hemosiderin within the ovary (6, 7). Ovarian endometriomas are one of the most frequent adnexal masses in premenopausal women and predispose the patients to ovarian malignancies, especially clear cell carcinoma and endometrioid adenocarcinoma (7-9).

Several treatments are suggested for the management of ovarian endometrioma and excisional surgery is recommended a better approach than drainage and ablation for treating patient's pain and infertility, as well as the risk of malignancy; meanwhile, each surgical approach has its own complications (10). Laparoscopic cystectomy is the

treatment of choice for endometriomas  $\geq 3$  cm, due to low morbidity, high tolerance, and overall low costs (11, 12); however, it may decrease the ovarian reserve and function, particularly in bilateral endometriomas with  $\geq 5$  cm diameter (13, 14). Furthermore, the recurrence of endometrioma and the symptoms, especially pain, dyspareunia, dysmenorrhea, and pelvic pain are still the main challenges (15). As the complete cure of endometriosis is not possible and owing to the high risk of recurrence after medical therapy and surgery, it is suggested that the most appropriate treatment approach should be individually selected for each patient (16).

Several risk factors have been associated with a higher recurrence rate (17-19) and recent studies suggest administration of oral contraceptive (OCP), synthetic progestins, or selective progesterone receptor modulators to optimize the efficacy of the surgery and reduce the recurrence rate (20). Nonetheless, the risk of recurrence, estimated about 40% - 50% five years after surgery, is still a major challenge (21).

## 2. Objectives

Few studies have been conducted on the recurrence of endometriosis in Iran and Rasool-Akram Hospital is a referral center for endometriosis equipped with laparoscopy facility. Therefore, in this study, we measured the recurrence of endometriosis six months after laparoscopic surgery and evaluated its risk factors in these patients.

## 3. Methods

We conducted a cross-sectional study to evaluate the recurrence rate of endometrioma after six months in 79 patients with endometriosis who underwent laparoscopic cystectomy in Rasool-Akram Hospital, Tehran, from April 2015 to August 2016. The protocol of the study was approved by the Research Committee of Iran University of Medical Sciences (Ethics Committee number: IR.IUMS.REC 1394.9211290005).

The diagnosis of endometriosis was confirmed by pathologic reports of the center's gynecologist, based on the patients' chief complaint, physical examination, and the result of ultrasonography. The researcher explained the research objectives and phases to patients who had the inclusion criteria and asked them to read and sign the written informed consent. They were ensured that their information will be kept confidential and they are free to leave the study, whenever they did not wish to continue the research. Patients went on oophorectomy during the laparoscopy were excluded from the study.

The information recorded in the researcher-designed checklist included age, marital status, age at menarche

and marriage, body mass index (BMI), family history of endometriosis, personal history of surgery or medical treatment for endometriosis and infertility were extracted from medical records or asked from the patients. Also, intraoperative information, including number, size, and location of cysts, and disease stage was recorded.

For all patients, laparoscopy was done by direct trocarization and CO<sub>2</sub> insufflation, using a standard four-port method as follows: one 11 mm port through the umbilicus for telescope insertion and the other two 5.5 mm ports through outer upper margins of bilateral rectus muscles, and an 11 mm suprapubic trocar. The gas pressure was set at 12 - 16 mmHg during the procedure. After comprehensive abdominal and pelvic exploration and with visualization of endometrioma, cystectomy was performed by the separation of cyst wall from the ovarian tissue beginning at the thinnest part of the cyst and was continued very carefully to complete the procedure. Then bleeder points were sutured and hemostasis was performed by minimal application of bipolar electrocautery in the case of bleeding. Next, the rest of the operation would have been performed by standard methods. In deep infiltrative endometriosis (DIE) cases, the excision of endometriosis lesions and associated adhesive diseases were done.

The patients were contacted to refer for sonographic assessment six months after the laparoscopy. Married women underwent transvaginal sonography (TVS) using a vaginal probe IC 5 - 9 Voluson 730 pro (GE, USA) and single women underwent abdominal ultrasonography. Recurrent endometrioma was defined as the presence of an ovarian cyst with typical ultrasonographic criteria of endometrioma with minimum diameter of 20 mm, unilocular or multilocular cyst, with homogeneous low-level echogenicity or ground glass echogenicity of the cyst fluid.

Any medical treatment taken after the surgery was recorded in the study checklist. Postoperative medical therapy selection was based on the patient's desire for conception. Endometriosis-related symptoms, including pelvic pain, dysmenorrhea, dyspareunia, dyschezia, and dysuria were recorded by a 10-point visual analogue scale (VAS) before the surgery and six months after the surgery.

### 3.1. Statistical Analysis

The results of the quantitative variables were presented as mean  $\pm$  standard deviation (SD) and that of categorical variables were summarized by frequency (percentage). The results of one-sample Kolmogorov-Smirnov test showed that the data were not normally distributed ( $P < 0.05$ ). Therefore, nonparametric methods were used for data analysis. Continuous variables were compared using Mann-Whitney U-test and categorical variables using chi-square test. The VAS scores for the symptoms before and after the surgery were compared using Wilcoxon ranks test.

Logistic regression analysis was used to evaluate the recurrence rate and possible risk factors. For the statistical analysis, the statistical software IBM SPSS Statistics for Windows version 21.0 (IBM Corp. 2012. Armonk, NY: IBM Corp.) was used. P values less than 0.05 was considered statistically significant.

#### 4. Results

Of 100 patients with the inclusion criteria who were contacted, 79 patients referred for sonographic examination. The mean  $\pm$  SD of the patients' age was  $31.38 \pm 5.98$  years, the mean  $\pm$  SD of the patients' age at menarche was  $13.37 \pm 1.53$  years, and the mean  $\pm$  SD of the patients' age at marriage was  $22.23 \pm 5.30$  years. Fifty-five women (69.62%) were married. There were 7 patients (8.86%) with a positive family history of endometriosis, 13 patients (16.45%) with a positive personal history of surgical treatment for endometriosis and 20 patients (25.31%) with a positive history of infertility. The mean  $\pm$  SD of cysts' size of the patients on ultrasonography was  $69.20 \pm 2.76$  mm. Thirty-five patients (44.30%) had multiple cysts, 31 cases (39.24%) had bilateral endometrioma, and 42 patients (53.16%) were in the DIE stage. Fifty-one patients (64.55%) had received medical treatment before the surgery and 27 cases (34.17%) used OCP or GnRH agonist after the laparoscopic cystectomy.

Six months after the laparoscopy, 11 cases (13.92%) had a recurrence. The mean size of the recurrent cysts was  $37.18 \pm 13.34$  mm. There was no significant difference in terms of the mean age, age at menarche or marriage. There was a statistically significant correlation between the recurrence and the history of surgery ( $P = 0.001$ ) and infertility ( $P = 0.02$ ), but no correlation was found between the recurrence and BMI, a positive family history of endometriosis (Table 1). Moreover, there was no correlation between the recurrence and characteristics of endometrioma, including DIE, the number of cysts, and treatments received before or after the surgery (Table 2).

Using a logistic regression model, the only predicting factor, namely the history of the surgery for endometriosis was significantly associated with lower odds ratio of the recurrence (OR = 0.007, P value = 0.012) and the odds ratio of the recurrence was slightly higher in the group with a positive surgery history in comparison to the others (Table 3). Comparing the severity of symptoms by VAS score indicated that all symptoms significantly decreased six months after the surgery (Table 4).

#### 5. Discussion

Our study showed a recurrence rate of 13.9% for endometrioma six months after the laparoscopic cystectomy.

Many studies have evaluated the risk of recurrence after surgery (17, 22, 23), but a great variation is observed among different studies. The review study, reporting a range of 11% to 35% for a recurrence rate of postoperative ovarian endometrioma, mentioned that the main reason for this discrepancy could be related to the different definitions of endometrioma, as some have only considered ovarian endometrioma  $> 3$  cm (24). Another review study reported the variation in the recurrence rate (ranging from 6% to 67%) in different studies is due to the different criteria used for diagnosis and duration of follow-up (25). Hayasaka et al. investigated 175 patients and reported a recurrence rate of 45% for endometrioma up to one year after laparoscopic excision (17). Koga et al. investigated the recurrence of ovarian endometrioma in 224 patients 2 years after laparoscopic excision and reported a recurrence rate of 30.4%, considering ultrasonographic mass of  $> 2$  cm (22). A meta-analysis of 23 studies reported the average 2-years' recurrence rate at 19.1%, but reported significant heterogeneity among studies (21). The recurrence rate in these studies is higher than that of ours, but are not exactly comparable, due to different diagnostic criteria, study design, and follow up period. According to the results of the study by Muzii et al., a minimum of three to six months was reported to be appropriate for studying the ultrasonographic evidence of endometrioma recurrence (23); therefore, we selected six months for follow-up. Nevertheless, most studies have focused on longer follow-up periods. One other pitfall is that studies have not reported whether the recurrence appeared in the ipsi- or contra-lateral ovary. Although researchers have reported that more than 85% of recurrence occurs on the operated ovary, the rest may appear on the contralateral untreated ovary (26, 27). Meanwhile, most studies have only reported the general entity of the recurrence and have not defined the ovary's side. Another important factor is that all these studies have used TVS as the diagnostic tool (17, 21-27), while a percentage of our patients were not married and should have undergone abdominal ultrasonography because their hymen should not damage. Furthermore, the differences in the surgical techniques used could affect the recurrence rate (28). The difference in the accuracy of sonographic methods could also be attributed to the difference in the recurrence rates. Despite these variations among studies (17, 21-25), the results of all these studies confirm that of the present study on the high risk of recurrence of endometrioma after surgery, which is of great importance and has to be considered by gynecologists.

Studying a wide range of demographic characteristics in this study showed that none of the factors, including age, age at menarche or marriage, BMI, or family history affected the rate of recurrence, although some have determined younger age as a significant risk factor (27, 29). The

**Table 1.** Comparison of the Demographic Characteristics in the Groups of Patients with or Without Endometrioma Recurrence Six Months After Laparoscopy<sup>a</sup>

	Total	No Recurrence	Recurrence	P Value
Age, y	31.38 ± 5.98	31.62 ± 6.15	29.91 ± 4.76	0.43 <sup>b</sup>
Age at menarche, y	13.37 ± 1.53	13.37 ± 1.62	13.40 ± 0.84	0.97 <sup>b</sup>
Age at marriage, y	22.23 ± 5.30	22.57 ± 5.43	19.67 ± 3.44	0.24 <sup>b</sup>
<b>Body mass index category</b>				0.66 <sup>c</sup>
Underweight	12	11 (91.7)	1 (8.3)	
Normal weight	42	35 (83.3)	7 (16.7)	
Overweight	19	16 (84.2)	3 (15.8)	
Obese	6	6 (100)	0 (0)	
<b>Family history</b>				0.80 <sup>c</sup>
Positive	7	6 (85.7)	1 (14.3)	
Negative	72	62 (86.1)	10 (13.9)	
<b>Previous surgery</b>				0.001 <sup>c</sup>
Positive	13	7 (53.8)	6 (46.2)	
Negative	66	61 (92.4)	5 (7.6)	
<b>Infertility</b>				0.02 <sup>c</sup>
Positive	20	15 (75)	5 (25)	
Negative	35	34 (97.1)	1 (2.9)	

<sup>a</sup>Values are expressed as mean ± SD or No. (%).<sup>b</sup>The results of Mann-Whitney U-test.<sup>c</sup>The results of chi-square test.**Table 2.** The Correlation Between the Recurrence and Characteristics of Endometrioma

	Total	No Recurrence, No. (%)	Recurrence, No. (%)	P Value <sup>a</sup>
<b>Deep infiltrative endometriosis</b>				0.74
Positive	42	37 (88.1)	5 (11.9)	
Negative	37	31 (83.8)	6 (16.2)	
<b>Number of cysts</b>				0.95
1	44	38 (86.4)	6 (13.6)	
2	28	24 (85.7)	4 (14.3)	
3	4	3 (75)	1 (25)	
4	1	1 (100)	0 (0)	
5	2	2 (100)	0 (0)	
<b>Treatment before surgery</b>				0.92
None	28	24 (85.7)	4 (14.3)	
Oral contraceptive	48	41 (85.45)	7 (14.6)	
GnRh agonist	3	3 (100)	0 (0)	
<b>Treatment after surgery</b>				0.12
None	52	47 (90.4)	5 (9.6)	
Oral contraceptive	16	13 (81.3)	3 (18.8)	
GnRh agonist	11	8 (72.7)	3 (27.3)	

<sup>a</sup>The results of chi-square test.

two factors, including positive infertility and a history of surgery for endometrioma were significantly higher in the

group of patients with recurrence after 6 months. Previous surgery was reported as a predictive risk factor of the

**Table 3.** Predicting Factors for Endometrioma Recurrence Using a Logistic Regression Model with Enter Approach

Factors	B	SE	P Value	OR	95% CI for OR	
					Lower	Upper
Age	-0.080	0.158	0.611	0.923	0.677	1.258
Age of marriage	-0.374	0.322	0.245	0.688	0.366	1.294
BMI	0.963	1.498	0.521	2.619	.139	49.389
Family history of endometriosis (positive = 1, negative = 2)	-2.268	2.529	0.370	0.104	0.001	14.723
Pre-surgery history of infertility (positive = 1, negative = 2)	-256.642	204.46	0.990	0.003	0.000	1.016
DIE (positive = 1, negative = 2)	-0.715	2.302	0.756	0.489	0.005	44.567
Pre surgery treatment (negative = 1, positive = 2)	-0.326	1.614	0.840	0.722	0.031	17.072
Post-surgery treatment (negative = 1, positive = 2)	0.079	0.998	0.937	1.082	0.153	7.649
Laparoscopy/laparotomy history for endometriosis (positive = 1, negative = 2)	-5.015	2.000	0.012	0.007	0.000	0.334

**Table 4.** Comparison of Mean Scores of Endometriosis-Related Symptoms Before and After Surgery Using Wilcoxon Ranks Test<sup>a</sup>

	Before Surgery	After Surgery	P Value <sup>a</sup>
Pelvic pain	4.97 ± 3.93	1.06 ± 2.06	< 0.001
Dysmenorrhea	7.96 ± 2.42	3.15 ± 2.53	< 0.001
Dyspareunia	1.77 ± 3.02	0.41 ± 1.21	< 0.001
Dyschezia	0.73 ± 1.97	0.15 ± 0.62	0.002
Dysuria	0.47 ± 1.70	0.19 ± 1.00	0.014

<sup>a</sup>Values are expressed as mean ± SD.

recurrence in several studies (15, 24). Infertility and previous surgery may indicate the presence of anatomical abnormalities and adhesions, but may also refer to the severity of disease that caused a higher risk of the recurrence. However, the results of the present study indicated that the disease stage (the presence of DIE) and cyst's size were not associated with the recurrence of endometrioma. In the study by Porpora et al., deep lesions and cyst's size were not associated with recurrence (15), which is consistent with the results of our study. The study by Liu et al. also reported that patients' age, number, and size of cysts were no longer associated with the risk of the recurrence, after adjustment for COX-2 overexpression, suggested as an important etiology of endometrioma recurrence (30). These results are in line with the results of our study; meanwhile, some researchers have reported the size and stage of the disease as significant risk factors for the recurrence of endometrioma (22, 31), which is contradictory to the results of the present study. Exacoustos et al. stated that the size of the recurrent endometrioma, even if associated with the risk of recurrence, is not as important as the patients' symptoms and the choice of reoperation should be determined

based on the severity of patients' symptoms rather than the cyst's size (26).

The choice of medical treatment after surgery is also controversial. In the present study, we did not perform any intervention in this regard, but recorded any treatment the patients received during this period and the results showed that 34.1% used OCP or GnRH agonist after laparoscopic cystectomy, but medical treatment was not associated with increasing or decreasing the risk of recurrence. Other researchers have reported that previous medical treatment had no effect on the recurrence of endometrioma (17, 18), which confirm the results of the present study. On the contrary, the results of the study by Dimitrijevic and colleagues showed later recurrence in patients using GnRH analog treatment. Seracchioli et al. also reported that long term use of OCP (24 months) could reduce the risk of endometrioma recurrence (32) and Vercellini et al. reported lower recurrence rate in patients using OCP after 28 months (29). The difference in the results of these studies with that of ours could be due to the shorter follow-up in our study and OCP might show protective effects in longer follow-up periods. Hence, even if long term OCP has a protective effect on the recurrence of endometrioma, its usage will be challenging, as many patients suffered from infertility and are suggested to conceive after surgery. As evidence shows, pregnancy has a protective effect on the risk of recurrence of endometrioma (17). Therefore, the choice of pregnancy or long term use of OCP is an important issue that should be chosen individually for each patient (33).

The present study evaluated the rate and risk factors of endometrioma recurrence at a tertiary medical center; however, this study could also have some limitations. The most important limitation was the limited follow-up pe-

riod and sample size; meanwhile, after six months, some patients didn't refer for the follow up.

In conclusion, the results of the present study showed a recurrence rate of 13.9% for endometrioma six months after laparoscopic cystectomy, significantly associated with infertility and previous surgery for endometrioma. Possibly, damages in the previous surgery and Cellular and molecular abnormalities that encountered more deeply in endometriosis-associated infertility predispose the patients to more recurrence rate, which can be further investigated. Studying the mechanism of this association can help the diagnosis of the etiology underlying this high recurrence rate and appropriate treatments for the prevention of endometrioma recurrence.

## Footnotes

**Conflict of Interests:** The authors have no conflicts of interest.

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