

## GENERAL GYNECOLOGY

# Recurrence of ovarian endometrioma after second-line, conservative, laparoscopic cyst enucleation

Mi-La Kim, MD, PhD; Joo Myoung Kim, MD, PhD; Seok Ju Seong, MD, PhD; Soo Yoon Lee, MD, MS; Myoungseok Han, MD, PhD; Yeon Jean Cho, MD, PhD

**OBJECTIVE:** We sought to evaluate the cumulative recurrence rate of endometrioma after a second-line, conservative, laparoscopic endometriotic cyst enucleation and to analyze the factors that influence the recurrence of endometrioma.

**STUDY DESIGN:** A multicenter retrospective cohort study was performed at 3 gynecologic surgery centers from January 2000 through December 2010. Patients surgically treated by laparoscopic enucleation of endometriotic cysts on 2 previous occasions were selected. All patients were aged <40 years at the time of the primary surgery and were followed up for at least 6 months. Endometrioma recurrence was considered when transvaginal sonography indicated a cystic mass with a diameter of  $\geq 20$  mm.

**RESULTS:** In total, 183 patients were followed up for  $33.2 \pm 27.7$  months (range, 6–121 months). Thirty-eight (20.8%) patients experienced recurrence after the second-line surgery and 24 (13.1%)

patients underwent a third surgery. The median time to recurrence was  $24 \pm 3.36$  months (SEM) (range, 3–72 months). The cumulative recurrence rates per patient at 12, 24, 36, and 60 months after the second-line surgery were 7.7%, 13.7%, 21.3%, and 37.5%, respectively. After multivariate analysis and analysis of covariance, the revised American Fertility Society score and stage were significantly higher in patients who experience a third recurrence of endometrioma.

**CONCLUSION:** The cumulative recurrence rate of ovarian endometrioma after a second-line surgery appears to be correlated to the duration of follow-up. Severe endometriosis at the second-line surgery seems to be a factor associated with a high recurrence risk. Physicians should be cautious with regard to the postoperative management of these patients.

**Key words:** conservative surgery, endometrioma, endometriosis, recurrence rate, second-line surgery

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Endometriosis, defined as the presence of endometrial tissue beyond the uterine cavity, is a chronic and recurrent disease that negatively influences patient quality of life.<sup>1</sup> The prevalence of endometriosis is approximately 10-20%

among women of reproductive age,<sup>2</sup> and it is 2-5 times higher in women with infertility.<sup>3</sup> The need for subsequent surgery after the initial conservative surgical treatment for endometriosis was 21.6%, 46.7%, and 55.4% at 2, 5, and 7 years after the previous surgery, respectively.<sup>4</sup> A higher recurrence rate is reported in younger patients, in those with an advanced disease stage,<sup>5-7</sup> and in patients who underwent incomplete removal of endometriotic lesions.<sup>7,8</sup>

Several studies have reported endometriosis recurrence following primary surgery.<sup>6,9-11</sup> The recurrence rate varies with the definition of recurrence, type of endometriosis, surgical methods, postoperative medical intervention, and the surgeons' technical competency. Recurrence of endometriosis following surgical and/or medical therapy is one of the most challenging aspects of this condition. Recent literature showed that the long-term probability of pain recurrence after repeat conservative surgery for endometriosis varies between 20-40%.<sup>12</sup>

However, little is known about the recurrence rate of ovarian endometrioma in patients who underwent second-line conservative surgery. Long-term data regarding the need for a third surgical intervention in women with recurrent endometriosis are scarce, but these data are essential to provide patients with adequate information regarding this disease. In cases where endometriosis recurrence develops after second-line conservative surgery, the third-line surgery may either be conservative or destructive, depending on the need to preserve fertility. Repeated endometrioma excision may cause decreased ovarian reserve or premature ovarian failure (POF).<sup>13</sup> Therefore, in the current study, we aimed to evaluate the recurrence rate of endometrioma following the second-line conservative surgery for endometriosis and to analyze the preoperative, intraoperative, and postoperative factors that may influence the recurrence of endometrioma. We also described the operative characteristics of

From the Departments of Obstetrics and Gynecology, CHA Gangnam Medical Center, CHA University (Drs M.-L. Kim and Seong), and Cheil General Hospital and Women's Healthcare Center, Kwandong University College of Medicine (Drs J. M. Kim and Lee), Seoul, and Dong-A University Medical Center, Dong-A University College of Medicine, Busan (Drs Han and Cho), Republic of Korea.

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Reprints: Yeon Jean Cho, MD, PhD, Department of Obstetrics and Gynecology Dong-A University School of Medicine, Dongdaeshindong 3 Ga-1, Seo-gu, Busan, 602-715, Korea.

[jeanjane@naver.com](mailto:jeanjane@naver.com).

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patients who underwent the third reoperation as well as POF rate and indicated the surgical method used when a third recurrence was detected.

## MATERIALS AND METHODS

A total of 7662 women with endometriosis were surgically treated by laparoscopy at 3 gynecologic surgery centers from January 2000 through December 2010. Among these patients, 267 patients underwent surgical management for endometriosis on at least 2 previous occasions. Only the patients who underwent laparoscopic enucleation of endometriotic cysts on 2 previous occasions were considered for this analysis. The exclusion criteria were: (1) patients aged  $\geq 40$  years at the time of the primary surgery ( $n = 7$ ); (2) those who underwent semiradical procedures, such as hysterectomy ( $n = 55$ ) or oophorectomy ( $n = 37$ ); and (3) those who were followed up  $< 6$  months after the second-line surgery ( $n = 9$ )—these patients were considered as follow-up loss because most of them revisited the clinic only once. Thus, a total of 183 patients were included in the current study. Disease staging was based on the revised American Fertility Society (rAFS) classification of endometriosis.<sup>14</sup> The study protocol was approved by the institutional review board on the use of human subjects in research.

The medical charts of all of the patients were reviewed to collect data on demographics, age at surgery, age at menarche, body mass index, surgical method used (conservative or semiradical), reports of dysmenorrhea (if any), number of previous abortions, parity (if any), use of preoperative medication for endometriosis treatment, size of the endometrioma (defined as the diameter of the largest cyst in centimeters), presence of adhesions, rAFS score and stage, use of postoperative medications, and time to recurrence. The time to recurrence was defined as the time in months from the second-line surgery until the detection of a new endometrioma. Endometrioma recurrence was considered when transvaginal sonography (TVS) indicated the presence of a rounded cystic mass with a minimum

diameter of 20 mm, thick walls, irregular margins, homogenous low echogenic fluid content with scattered internal echoes, and the absence of papillary proliferations.<sup>15</sup> If a patient had 2 endometriomas that were  $< 20$  mm and the sum of their diameters was  $> 20$  mm, the patient was considered to have endometrioma recurrence. This cutoff size was obtained from the results of previous studies.<sup>5,16-19</sup>

Conservative surgery was performed only by using mechanical instruments and electrosurgery. Laparoscopic cyst enucleation was performed by applying the classic technique: sharp cortical incision was made, a cleavage plane was identified, and the entire cyst was enucleated and stripped from the normal ovarian tissue, using traction, water pressure, and/or sharp dissection. Hemostasis was achieved by selective application of bipolar current. All the patients underwent clinical postoperative follow-up at intervals ranging from 3–12 months or when medical evaluation was needed. At every follow-up visit, a TVS examination was performed, and symptoms, medical treatment, and clinical data were recorded.

Statistical analysis was performed using software (SPSS, version 12.0; IBM Corp, Armonk, NY). The  $\chi^2$  and Fisher exact tests were used for analysis of categorical variables, in cases where the variables showed a normal distribution. Quantitative variables were compared by means of Student *t* test. Univariate, multivariate regression analyses and analysis of covariance were performed to compare the clinical characteristics between patients with and without recurrence of endometrioma. The Kaplan-Meier method was used to calculate the cumulative probability of recurrence and the comparison between the curves was performed using the log rank test. A *P* value of  $< .05$  was considered statistically significant.

## RESULTS

In total, 183 patients were followed up for  $33.2 \pm 27.7$  (mean  $\pm$  SD) months (range, 6–121 months). At the time of the second-line conservative surgery, the mean age of the patients was

$32.3 \pm 4.9$  years. The baseline clinical and surgical characteristics of the patients who were followed up after the second-line conservative surgery are shown in Table 1. The mean cyst size was  $5.8 \pm 2.1$  cm; 64.5% of patients had stage IV endometriosis. Dysmenorrhea was the most common symptom prior to the second-line surgery, and was reported in 104 (53.6%) patients. Bilateral ovarian involvement was noted in 57 (31.1%) cases. The type of postoperative therapy was chosen on the basis of individual characteristics; approximately 65.6% of patients were treated with medications such as gonadotropin-releasing hormone agonists (85.6%), oral contraceptive pills (7.2%), progesterone agents (5.8%), and danazol (1.6%).

According to the definition of recurrence, 38 patients (20.8%) experienced recurrence after the second-line surgery and 24 patients (13.1%) underwent a third surgery. The median time to recurrence was  $24 \pm 3.36$  months (SEM) (range, 3–72 months). The cumulative recurrence rates by Kaplan-Meier analysis per patient at 12, 24, 36, and 60 months after the second-line surgery were 7.7%, 13.7%, 21.3%, and 37.5%, respectively (Figure). There was no difference in the cumulative recurrence rate according to patient age (those aged 20–29 years vs 30–39 years;  $P = .25$ , log rank test) at the time of the second-line surgery.

The laterality of the surgical site is illustrated in Table 2. There was no difference in the overall frequency of the surgical site. After the second-line surgery, the ipsilateral cyst, contralateral cyst, and repeated bilateral cyst recurrence rates were 17.5% (right  $\rightarrow$  right and left  $\rightarrow$  left), 4.7% (right  $\rightarrow$  left and left  $\rightarrow$  right), and 12.3%, respectively. The rate of bilateral cyst recurrence after unilateral conservative surgery was 12.8%, whereas that of unilateral cyst recurrence after bilateral cystectomy was 15.8%.

The possible risk factors for endometrioma recurrence are presented in Table 3. There was no difference in body mass index, cyst diameter, resection of the cul-de-sac lesion, postoperative medication, laterality, and history of

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