



## Full length article

## The age-related recurrence of endometrioma after conservative surgery



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## ARTICLE INFO

## Article history:

Received 1 July 2016

Received in revised form 20 October 2016

Accepted 15 November 2016

## Keywords:

Ovarian endometrioma

Postoperative medical treatment

Endometrioma recurrence

Age-related recurrence

Conservative surgery

## ABSTRACT

**Objective:** As endometrioma frequently recurs after conservative surgery, long-term postoperative medical treatment for the prevention of recurrence is necessary. However, it has not been elucidated whether long-term postoperative medical treatment is crucial to all patients until menopause. Thereupon, this study was conducted to evaluate the age-related recurrence patterns after conservative surgery for endometrioma.

**Study design:** A retrospective cohort study was performed on a total of 420 reproductive-aged women who underwent conservative surgery for endometrioma between January 2000 and December 2010. Ultrasonography was used during the follow-up period to detect endometrioma recurrence. Patients were classified into two groups according to the use of postoperative medications. The first group was observation only, while the second received gonadotropin releasing hormone agonists followed by cyclic oral contraceptives. The cumulative recurrence rate of endometrioma was compared according to the age at surgery (20–29 years, 30–39 years, 40–45 years) within each group. Subgroup analysis was performed according to the age between the two groups.

**Results:** The median follow-up duration after surgery was 29.0 months (range 6–159 months) for all patients. After adjusting for parity, size and bilaterality of cyst, and stage with American Society for Reproductive Medicine classification of endometriosis which was statistically different, within the group of no treatment, the cumulative recurrence rate in 40–45 years (10.2%) was significantly lower compared with those in 20–29 years (43.3%; hazard ratio (HR) = 0.04; 95% confidence interval (CI) = 0.01–0.52) and 30–39 years (22.5%; HR = 0.19; 95% CI = 0.04–0.92). However, there were no differences within the group of postoperative medical treatment. When we compared between the two groups, the cumulative recurrence rate was significantly different in 20–29 years (8.1 vs 43.3%;  $p < 0.001$ ) and 30–39 years (5.4 vs 22.5%;  $p = 0.007$ ), but there was no difference in 40–45 years (4.5 vs 10.2%;  $p = 0.901$ ).

**Conclusions:** Our preliminary results demonstrate that the risk of endometrioma recurrence decreases with age. After the age of forty, the recurrence rate does not differ according to the use of postoperative medication. Based on our results, postoperative medical treatment may be individualized according to the patient's age at the time of surgery. Further studies are needed to identify patients who may benefit from postoperative medication.

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## Introduction

One of the most common manifestations of endometriosis is the presence of an ovarian mass arising from the growth of ectopic endometrial tissue in the ovary. This ectopic tissue in the ovary is called an ovarian endometrioma, or chocolate cyst. Between 17 and

44% of patients with endometriosis have ovarian endometriomas [1,2].

Laparoscopic conservative surgery is considered the gold standard treatment for ovarian endometrioma [3,4]. However, endometrioma frequently recurs after surgery [5]. Since repeated surgery can cause significant ovarian damage [6,7], postoperative medical treatment is essential to prevent recurrence. Previous studies have demonstrated that long-term postoperative medical treatment has a protective effect against the recurrence of ovarian endometrioma, which vanishes rapidly after treatment is discontinued [8–12]. Although it was suspected that the endometrioma recurrence rate might differ according to the age at surgery

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[9,13–15], this issue has never previously been clearly elucidated. Therefore, this study was conducted to evaluate the recurrence patterns after conservative surgery for ovarian endometrioma according to age at the time of surgery and the use of postoperative medications.

## Materials and methods

### Patients

All reproductive-aged women who underwent laparoscopic surgery for ovarian endometrioma and were followed at Samsung Medical Center between January 2000 and December 2010 were considered for inclusion in this retrospective study.

The inclusion criteria were as follows: (1) the diagnosis of endometrioma was confirmed by pathologists; (2) ultrasonography was conducted in order to determine endometrioma recurrence from least 6 months after surgery; and (3) patients were observed without postoperative medications or were treated with postoperative gonadotropin releasing hormone agonists (GnRHa) injections every 28 days for 6 cycles, followed by oral contraceptive (OC) treatment.

The exclusion criteria were as follows: (1) age was <20 or >45 years; (2) patients underwent oophorectomy or hysterectomy; (3) patients were treated with other types of postoperative medical treatment (such as progestins or an intrauterine device); (4) patients had a history of previous pelvic surgery for endometriosis; and (5) patients had a history of preoperative hormonal treatment.

Initially, 827 women were screened. Among them, 407 women who did not meet inclusion and exclusion criteria were excluded, and finally, 420 women were selected for statistical analysis: 189 reproductive-aged women who were observed after surgery and 231 who received postoperative medical treatment (GnRHa followed by cyclic OC) (Fig. 1). In the treatment group, 72 women discontinued OC or were lost to follow up. Most common cause of OC discontinuation was desire of pregnancy ( $n = 38$ ).

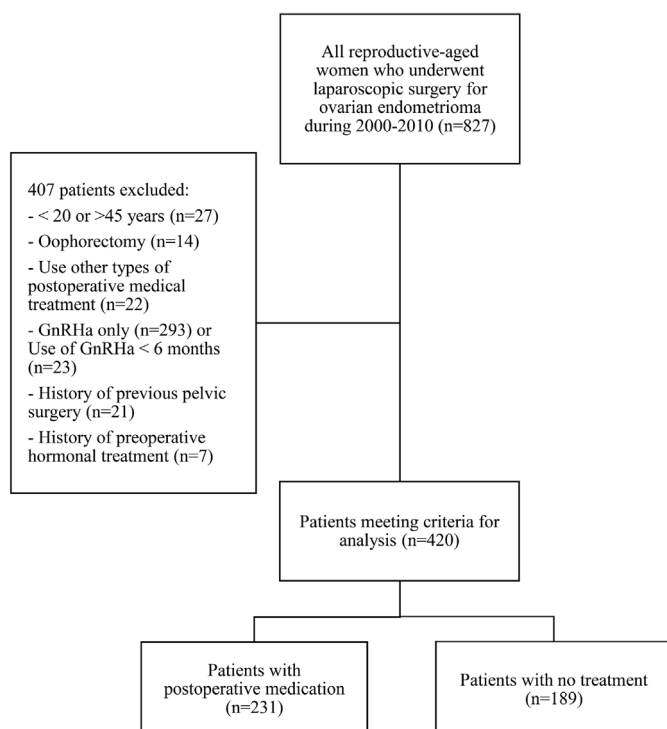


Fig. 1. Flow diagram of patient selection process.

Within each group, the cumulative recurrence rate of endometrioma was compared according to age at the time of surgery (20–29 years, 30–39 years, 40–45 years). Subgroup analysis was also performed according to age between the two groups. This study was approved by the institutional review board at Samsung Medical Center.

### Treatment and measurement

Patients were offered 6 months of postoperative treatment with GnRHa (3.75 mg of leuprolide acetate) and add back therapy (estradiol 1 mg or equivalent with progestogen), followed by cyclic, low-dose, monophasic OCs. All patients were advised to use OCs to prevent the recurrence of endometrioma, as long as possible. OCs (ethinyl estradiol plus desogestrel or drospirenone) were selected based on the availability and patient's or doctor's preference. Patients who refused to receive postoperative medical treatment were followed without any treatment. Endometrioma recurrence was determined using ultrasonography. Recurrence was defined as the presence of a persistent ovarian cyst with a thin wall (with a diameter of at least 2 cm), regular margins, and a homogenous low echogenic fluid content with scattered internal echoes, but no papillary projections [16]. All patients were followed every 3–6 months. Pelvic ultrasounds were performed for patients with postoperative medications annually and for patients with no treatment twice per year.

### Surgery

On the basis of management guidelines for endometriosis [17], all patients with ovarian endometriomas of  $\geq 3$  cm in diameter underwent laparoscopic ovarian cystectomy as followings regardless of pain or infertility, although many patients had varying degrees of pain: first, the pelvis, abdomen, and external surface of the cyst were inspected for endometriosis staging. The endometriosis was staged according to the classification of the American Society for Reproductive Medicine (ASRM) [18]. Adhesions were dissected using laparoscopic scissors. Both ovaries were then completely mobilized. A sharp cortical incision was made into the cyst, and a cleavage plane was identified. Atraumatic forceps and counter traction were used to strip the endometrioma from the ovarian parenchyma. Hemostasis was achieved by the selective application of bipolar coagulation. After the endometriomas were removed, all remaining, visible endometriotic lesions were excised or fulgurated. Anatomical restoration was then achieved.

### Statistical analyses

Statistical analyses were performed using the Statistics Package for Social Sciences Version 20.0 (SPSS Inc., Chicago, IL, USA). The baseline characteristics and cumulative recurrence rate was compared according to the age at the time of surgery (20–29 years, 30–39 years, 40–45 years) within each group. In addition, subgroup analysis was performed according to age between the two groups. Quantitative variables were compared using *t*-tests and ANOVA with Bonferroni's correction for multiple testing. Fisher's exact or chi-square tests were used to analyse qualitative variables. Proportional hazards assumption for Cox proportional hazard model was tested using graphical approach and Schoenfeld residual [19]. Cox proportional hazard model was used to quantify the difference in recurrence rate according to use of postoperative medication or age at the surgery, after adjusting for parity, size and bilaterality of cyst, and ASRM stage. The Kaplan-Meier method was used to calculate the cumulative probability of endometrioma recurrence. The curves were compared with the log rank test. *P*-values < 0.05 were considered statistically significant.

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