

Second surgery for recurrent unilateral endometriomas and impact on ovarian reserve: a case-control study

Simone Ferrero, Ph.D., Carolina Scala, M.D., Annalisa Racca, M.D., Luana Calanni, M.D., Valentino Remorgida, M.D., Pier Luigi Venturini, M.D., and Umberto Leone Roberti Maggiore, M.D.

Obstetrics and Gynecology Unit, IRCCS San Martino Hospital and National Institute for Cancer Research, University of Genoa, Genoa, Italy

Objective: To investigate the impact on ovarian reserve of second laparoscopic surgery for recurrent unilateral endometriomas.

Design: Case-control study.

Setting: University teaching hospital.

Patient(s): This study included patients who underwent stripping of endometriomas (diameter ≥ 4 cm) and were followed-up at our institution. Case subjects had second surgery for recurrent unilateral endometriomas ($n = 18$); control subjects had no recurrence and no second surgery ($n = 18$).

Intervention(s): This case-control study was based on a retrospective analysis of a prospectively collected database including patients who underwent surgery for endometriomas at our institution.

Main Outcome Measure(s): The primary outcome of the study was to assess the changes in antimüllerian hormone (AMH) levels in each study group and between the two study groups. The secondary outcomes of the study were to assess the changes in basal FSH, antral follicle count (AFC), and ovarian volume in each study group and between the two study groups.

Result(s): In both study groups, primary surgery decreased AMH, increased basal FSH, and decreased the AFC of the operated ovary. Before second surgery, case subjects had AMH, basal FSH, and AFC similar to control subjects. After second surgery, case subjects had lower AMH, higher basal FSH, and lower AFC of the affected ovary than before surgery; the volume of the operated ovary was lower than that of the contralateral ovary.

Conclusion(s): The laparoscopic stripping of recurrent ovarian endometriomas is associated with a high risk of ovarian reserve damage and ovarian failure.

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Key Words: AMH, antral follicle count, endometriosis, laparoscopy, ovarian reserve

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The laparoscopic stripping of the cyst capsule is the most commonly used surgical technique to treat endometriomas. The stripping technique has been shown to be associated with lower risk of recur-

rence compared with other techniques (such as fenestration and vaporization of the capsule) (1, 2); however, there are concerns that this procedure may damage ovarian function. Two systematic reviews showed that the

surgical excision of endometriomas is associated with an impairment of ovarian reserve as demonstrated by the decreased levels of serum antimüllerian hormone (AMH) after surgery (3, 4). In line with these observations, women treated for bilateral endometriomas are at increased risk of premature ovarian failure (5). The damage caused to the ovarian reserve during surgery seems to be higher in cases of larger cysts (main diameter >4 cm) (5–7) and bilateral cysts (5), in older patients (8), and when surgery is performed by less experienced surgeons (9), whereas it

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Reprint requests: Simone Ferrero, Ph.D., Obstetrics and Gynecology Unit, IRCCS San Martino Hospital and National Institute for Cancer Research University of Genoa, Largo Rosanna Benzi 1, 16132, Genoa, Italy (E-mail: simone.ferrero@unige.it).

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seems to be independent from the method used to obtain hemostasis on the ovary (bipolar coagulation or laparoscopic suturing) (10).

One of the major challenges in the management of endometriomas is their recurrence after surgery (11, 12). In a pooled analysis of 23 published studies, Guo reported that the recurrence rate of endometriomas after primary surgery is 19.1% at 2 years and 40%–50% at 5 years (11). The recurrence rate of endometriomas after surgery varies accordingly to stage of endometriosis (13), age at primary surgery (14), surgical techniques (1), administration of postoperative medical therapies (15–19), and surgeon's technical competency (20). Endometrioma recurrence may be associated with a recurrence of pain symptoms, and, therefore, these patients may undergo further surgery for its management.

Surprisingly little attention has been given to the function of ovaries with recurrent endometriomas (21) and to the impact on ovarian reserve of second surgery for endometriomas (22). The aim of the present study was to investigate the changes in ovarian reserve after laparoscopic excision of recurrent unilateral endometriomas.

MATERIALS AND METHODS

This case-control study was based on a retrospective analysis of a prospectively collected database including all consecutive patients who underwent surgery for endometriomas at our institution (IRCCS San Martino Hospital and National Institute for Cancer Research University of Genoa) from January 2007 to November 2013. It was registered at [Clinical trial.gov](https://clinicaltrials.gov/ct2/show/study/NCT02047838) (NCT02047838).

Study Population

The study included patients who had second surgery for recurrent unilateral endometrioma in the previously operated ovary (case subjects; $n = 18$) and patients who had no recurrence of endometrioma and therefore did not undergo second ovarian surgery (control subjects; $n = 18$).

The patients fitting the following criteria were considered for the study: reproductive age; single unilateral endometrioma with largest diameter of the endometrioma ≥ 4 cm, treated by standardized laparoscopic stripping technique (10); histologic diagnosis of ovarian endometrioma; surgery and follow-up performed at our institution; and complete assessment of ovarian reserve at routine follow-up at our institution. Patients with the following characteristics were excluded from the study: age ≥ 40 years at the time of primary surgery; surgical procedures on the contralateral ovary; unilateral oophorectomy; previous salpingectomy or hysterectomy; ultrasonographic diagnosis of persistent endometrioma after first surgery (at 1 month follow-up); additional nonhormonal treatments for endometriomas (e.g., aspiration and ethanol sclerotherapy) during follow-up; additional surgical treatment for other ovarian diseases during follow-up; hormonal treatment within 3 months from ovarian reserve and ovarian volume assessment; and follow-up < 3 months after second surgery.

The criteria for inclusion among the case subjects were: recurrent unilateral endometrioma with diameter ≥ 4 cm in the previously operated ovary; second surgery for recurrent endometrioma performed by means of the laparoscopic stripping technique at our institution; and histologic diagnosis of recurrent ovarian endometrioma. The criteria for inclusion among the control subjects were: reproductive age at the time of ovarian reserve assessment and no recurrence of endometrioma (on the previously operated ovary or on the contralateral ovary).

All cases fitting these criteria were included in the analysis. Control subjects were selected from the database as the first patient operated on after the case with the same age (within 1 year), with similar diameter of the endometrioma (within 1 cm), and with available assessment of ovarian reserve at a follow-up period similar to that of the case subject before second surgery (within 1 year; Fig. 1).

Patients included in the database used for the study gave written informed consent to the use of their clinical data for scientific purposes. Ethics Committee approval was not requested, because this was a retrospective analysis of data prospectively collected for the clinical follow-up of patients.

Outcomes of the Study

The primary outcome of the study was to assess the changes in AMH levels between the two study groups (after primary and second surgery). The secondary outcomes of the study were to assess: changes in basal FSH between the two study groups; changes in the antral follicle count (AFC) and ovarian volume between the operated and the contralateral ovary in each study group and between the two study groups.

Diagnosis of Endometriomas and Assessment of Ovarian Reserve

The ultrasonographic criteria for the diagnosis of endometriomas were: round cystic mass with thick walls, regular margins, homogeneous low echogenic fluid content with scattered internal echoes, and no papillary projections with no or poor vascularization of capsule (23). For the diagnosis of endometrioma, the cyst had to be present on at least two consecutive ultrasonograms performed with an interval of ≥ 1 month.

At our institution, ovarian reserve (serum markers and AFC) is routinely assessed within 3 months before surgery for endometriomas, 3 months after surgery, at yearly follow-up, and, in case of second surgery, within 3 months before laparoscopy and 3 months after surgery. As previously stated, patients using hormonal therapies in the 3 months before ovarian reserve assessment were excluded from the study.

The presence and the characteristics of endometriomas were evaluated by means of ultrasonography at each follow-up. The volume of the ovaries and the volume of the endometriotic cysts were estimated with the use of virtual organ computer-aided analysis (VOCAL; GE Healthcare) as previously described (23). Briefly, the VOCAL technique was used to obtain a sequence of 20 sections of each ovary/ovarian endometriotic cyst around a fixed axis, each section after 9° rotation from the previous section. The contour of each

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