

# Ovarian cystectomy versus laser vaporization in the treatment of ovarian endometriomas: a randomized clinical trial with a five-year follow-up

Francisco Carmona, M.D., M. Angeles Martínez-Zamora, M.D., Aintzane Rabanal, M.D., Sergio Martínez-Román, M.D., and Juan Balasch, M.D.

Institut Clínic of Gynecology, Obstetrics, and Neonatology, Faculty of Medicine, University of Barcelona, Hospital Clínic-Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain

**Objective:** To investigate the effect of two laparoscopic techniques for treatment of ovarian endometriomas on recurrence rate.

**Design:** Prospective randomized clinical trial.

**Setting:** University teaching hospital.

**Patient(s):** Ninety women with ovarian endometriomas.

**Intervention(s):** Patients were randomly selected to undergo either laparoscopic cystectomy (group 1) or laser vaporization (group 2) of ovarian endometrioma.

**Main Outcome Measure(s):** Recurrence, evaluated by ultrasound scan examination, was assessed at 12 and 60 months of follow-up.

**Result(s):** Endometrioma recurrence rate was higher, though not significantly different, in group 2 at 60 months of follow-up. Nevertheless, at 12 months of follow-up recurrences were statistically higher in group 2.

**Conclusion(s):** The comparison between laparoscopic laser ablation and laparoscopic cystectomy for ovarian endometriomas after long-term follow-up showed earlier recurrences and a higher recurrence rate in the laser group, although at 5 years of follow-up there were no statistically significant differences. (Fertil Steril® 2011;96:251–4. ©2011 by American Society for Reproductive Medicine.)

**Key Words:** Ovarian endometrioma, laparoscopic surgery, endometriosis, cystectomy, laser vaporization, ovarian reserve, recurrence

One of the most frustrating aspects of treating endometrioma is disease recurrence after surgery, which varies between 10% and 50% after 2–5 years depending on the surgical approach and the time of follow-up (1–7). Excisional surgery of endometriomas reportedly seems to be more beneficial than ablative techniques in this respect (8–11). However, laser vaporization has also been proposed as the best method to preserve ovarian function (12, 13). A randomized comparison of laser vaporization with cystectomy has recently been published evaluating the impact of both types of surgery on ovarian reserve, but recurrences were not evaluated (13).

To date, no randomized prospective or comparative studies have compared laser vaporization versus cystectomy to assess long-term recurrences after the laparoscopic treatment of endometriomas.

Therefore, we provide the first report on the rate of long-term recurrence after laser vaporization and cystectomy.

## MATERIALS AND METHODS

Ninety patients undergoing laparoscopy for adnexal mass with the diagnosis of endometrioma(s) were enrolled in this prospective randomized clinical trial at the Hospital Clínic of Barcelona. Each of the patients gave informed consent to participate in the study, which was approved by the hospital Ethics Committee. Inclusion criteria were: age between 18 and 40 years, uni- or bilateral symptomatic endometriomas  $\geq 3$  cm, and no counterindication for the use of GnRH-agonists. The exclusion criteria were: previous pelvic surgery, history of cancer, suspected malignancy, presurgical suspicion or evidence of deep endometriosis, presurgical suspicion or evidence of premature ovarian failure, and the use of estrogen suppressive drugs, including oral contraceptives (OC), GnRH-agonists, progestins, or danazol in the preceding 6 months. We excluded patients with suspicion of deep endometriosis according to an extensive preoperative work-up (including magnetic resonance imaging when necessary) routinely performed in such patients.

Patients, when surgery was proposed, were randomly allocated according to a computer-generated randomization list generated using the method of simple randomization to undergo either endometrioma cystectomy (group 1) or drainage and laser coagulation of the inner lining (group 2; Fig. 1). Group 2 was treated for 2 months with intramuscular doses of triptorelin (3.75 mg), as previously recommended (12). Concealment of treatment allocation was achieved with the use of sealed opaque envelopes,

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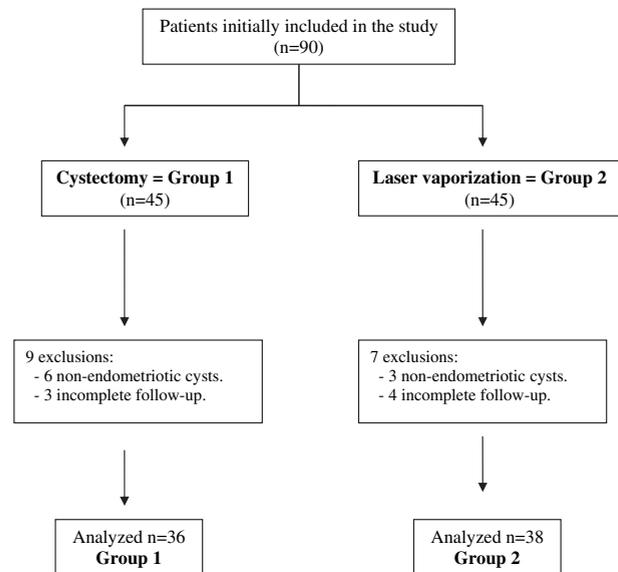
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Reprint requests: Francisco Carmona, M.D., Institut Clínic de Ginecologia, Obstetrícia i Neonatologia, Hospital Clínic de Barcelona, Villarroel, 170, 08036 Barcelona, Spain (E-mail: fcarmona@clinic.ub.es).

**FIGURE 1**

Flow chart of the patients included and excluded/lost to follow-up.



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each containing a unique study number, and prepared independently by a secretary. Envelopes were opened at diagnosis. Histologic examination was performed in all cases to confirm the preoperative and intraoperative diagnosis of ovarian endometrioma. Forty-five patients were enrolled in each group. A total of 16 patients were excluded (Fig. 1).

Operative laparoscopy was performed through insertion of a 12-mm umbilical trocar and two or three 5-mm ancillary trocars in the lower abdomen. All interventions were performed by the same team of surgeons who had a wide experience in both techniques, having performed such surgical operations  $\geq 2$ –3 times per week over the preceding 5 years. The same protocol was used during the diagnostic phase of laparoscopy. Standard laparoscopic instruments and 0-degree video laparoscope were used in all procedures (Olympus Europe Holding). Endometriosis was staged according to the revised American Society for Reproductive Medicine classification (ASRM) (14).

After identification of the cleavage plane in group 1, the wall of the cyst was stripped from the healthy surrounding normal ovarian tissue and sent for histologic examination. Patients in group 2 underwent drainage of the cyst content and irrigation and inspection of its inner wall. A biopsy of the cyst wall was sent for routine histologic examination to confirm the diagnosis of endometriosis. Vaporization of the internal wall was performed using a CO<sub>2</sub> laser at a power density of 30 W/cm<sup>2</sup>. No sutures were placed after surgery.

Patients without gestational desire received OC after surgery throughout the follow-up (10/36 [28%] in group 1 and 14/38 [36%] in group 2;  $P=NS$ ). Patients were followed with standard gynecologic examination and transvaginal ultrasound exploration at 6, 12, 18, 24, 36, 48, and 60 months after surgery, or earlier if symptoms related to possible recurrence were reported. Recurrence was defined as an endometrioma  $\geq 3$  cm in the operated ovary. The same investigators performed all ultrasonic scans with the use of an endovaginal probe. Antral follicle count (AFC) and basal (menstrual cycle days 3–5) FSH serum levels were determined in all patients at 5 years of follow-up according to methods previously reported (15, 16).

Data analysis was performed with the SPSS 15.0 software. The chi-square or Fisher exact test was used for comparison of categorical variables. The Student *t* test and the Mann-Whitney test were used for comparison of continuous variables. Comparison of cumulative recurrence and pregnancy rates was conducted with the use of Kaplan-Meier test. Results are presented as mean  $\pm$  SD.  $P < .05$  was considered to be statistically significant.

**TABLE 1**

Baseline clinical characteristics and ultrasonographic findings of the two groups of patients with ovarian endometriomas.

Characteristic	Group 1 (n = 36)	Group 2 (n = 38)	P value
Age (y)	32.5 $\pm$ 6	32.3 $\pm$ 5.9	NS
Diameter of the larger endometrioma (mm)	54.7 $\pm$ 14.1	53.6 $\pm$ 16.3	NS
Mean diameter of all endometriomas (mm)	62.8 $\pm$ 17.2	62.5 $\pm$ 16.8	NS
Bilateral endometrioma	8 (22.2)	12 (31.6)	NS
Nulliparous	27 (75)	29 (76.3)	NS
Infertility	7 (19.4)	13 (34.2)	NS
Dysmenorrhea	25 (69.4)	22 (57.9)	NS
Chronic pelvic pain	4 (11.1)	6 (15.8)	NS

Note: Values are mean  $\pm$  SD or number of patients (%). NS = not significant.

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**RESULTS**

The baseline clinical characteristics and ultrasonographic findings of the two study groups were similar regarding age, mean cyst diameter, bilaterality, mean diameter of all endometriomas, nulliparity, infertility, dysmenorrhea, and chronic pelvic pain, as shown in Table 1. There were no conversions to laparotomy or complications during or after surgery in either group. Similarly, the operative time, length of hospitalization, and follow-up time were also similar between the two groups (Table 2). The endometriosis stage according to the revised ASRM classification showed no differences between groups (Table 2).

The endometrioma recurrence rate was higher, though not statistically different, in group 2 than in group 1 at 60 months of

**TABLE 2**

Surgical characteristics, follow-up, and sonographic recurrence rate of the two groups of patients with ovarian endometriomas.

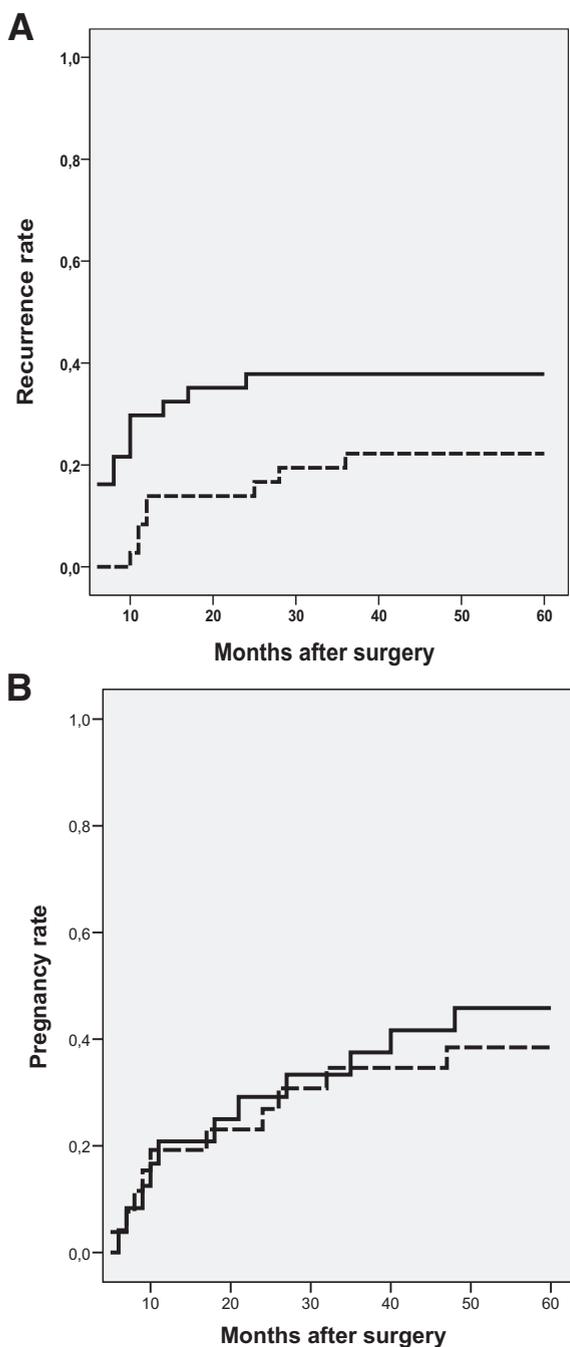
Characteristic	Group 1 (n = 36)	Group 2 (n = 38)	P value
Median rAFS score (range)	27 (19–96)	28 (20–94)	NS
Mean operating time (min)	72 $\pm$ 33	65 $\pm$ 39	NS
Hospital stay (d)	1.6 $\pm$ 0.6	1.5 $\pm$ 0.7	NS
Follow-up (mo)	64.8.7 $\pm$ 13.3	63.1 $\pm$ 17.6	NS
Recurrence at 12 mo			
Per patient	4/36 (11)	12 (31)	.04
Per endometrioma	4/44 (9)	4/50 (8)	.1
Recurrence at 60 mo			
Per patient	8 /36 (22)	14/38 (37)	.2
Per endometrioma	8/44 (18)	14/50 (28)	.4
Time of recurrence (mo)	18.1 $\pm$ 10.1	7.5 $\pm$ 4.3	< .003

Note: Values are mean  $\pm$  SD or number of patients (%). NS = not significant; rAFS = revised American Fertility Society.

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**FIGURE 2**

(A) Survival analysis of the interval between operation and recurrence of ovarian endometrioma. Vertical axis: cumulative recurrence rate; horizontal axis: number of months after surgery. Cystectomy is shown by the dashed line, laser vaporization by the solid line. Endometrioma recurrence at 12 months of follow-up:  $P = .04$ ; endometrioma recurrence at 60 months of follow-up:  $P = NS$ . (B) Overall 60-month probability of becoming pregnant after surgery among patients with pregnancy desire (26 in group 1 and 24 in group 2). Vertical axis: cumulative pregnancy rate; horizontal axis: number of months after surgery. Cystectomy is shown by the dashed line, laser vaporization by the solid line. Pregnancy rate at 12 months of follow-up:  $P = NS$ ; pregnancy rate at 60 months of follow-up:  $P = NS$ .



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follow-up. Nevertheless, we observed earlier time of recurrence in group 2; thus, the recurrence rate at 12 months of follow-up was statistically higher in group 2 (Table 2; Fig. 2A). The recurrence rate at 12 and 60 months was similar in groups 1 and 2 when considering the total initial number of endometriomas. Recurrence rates at 60 months of follow-up were similar in patients receiving OC after surgery (7/24, 29%) or not (15/50, 30%;  $P = NS$ ). Two patients in group 1 and four in group 2 required subsequent surgery. Pathologic examination confirmed endometriosis in all of these cases.

There were no differences in pregnancy rates in the patients desiring pregnancy (26 in group 1 and 24 in group 2) at 12 months (19.2% in group 1 vs. 20.8% in group 2;  $P = NS$ ) or 60 months (38.1% in group 1 vs. 44.4% in group 2;  $P = NS$ ) of follow-up. The total cumulative pregnancy rate at 60 months in patients with gestational desire was similar in both treatment groups (Fig. 2B). Two and three pregnancies in groups 1 and 2, respectively, were obtained after in vitro fertilization treatment. The remaining were spontaneous gestations.

## DISCUSSION

The overall recurrence rate of 29.7% reported here is in line with other studies reporting a long-term recurrence rate of endometriomas (1–7). The present study shows that the recurrence rate was higher, though not significantly, in the laser group, perhaps owing to the low number of cases, a finding which, to our knowledge, has not been previously described.

Earlier reports have shown that the trend in the cumulative recurrence rate of endometrioma depends on the months elapsed since surgical treatment and that it increases over time (4, 5, 17). This stresses the importance of long-term follow-up to assess the recurrence rate after the surgical treatment of endometriomas. Nonetheless, it has recently been reported that OC use may be protective against recurrence (18). According to patients receiving OC in both groups and the results observed, this does not seem to be a confounding factor in the current study.

According to a recent Cochrane review (11) only two randomized controlled trials have compared cystectomy and drainage with ablation by electrosurgery in terms of recurrence (10, 19). To the best of our knowledge, the present study is the first randomized clinical trial comparing cystectomy and vaporization to treat endometriomas with the longest follow-up described to date. Although this study included a limited number of patients, the sample size is in line with earlier studies on the subject (10, 13, 19, 20). Considering the difference in recurrence rates between the two treatment arms at 5 years, a sample size of 312 patients per group would be necessary to provide a statistical power of 80% to avoid a type II error and a 5% chance of making a type I error.

Sample size planning for a clinical study is based on an estimate from prior information and performed to ensure the ability to detect a difference in outcome (21, 22). Nevertheless, providing definitive answers in the face of low event rates and small-to-moderate treatment effects necessitates sample sizes in the thousands or tens of thousands. Therefore, even very large trials seldom provide definitive answers (23). The scientific community has appropriately accepted that only systematic reviews and meta-analyses combining high-quality evidence from many RCTs will yield robust answers. Individual trials are best viewed as providing important information that contributes to the larger body of evidence (23). As the first report on the rate of long-term recurrence after vaporization and cystectomy, the present study lacked previous information on the subject at study planning. Therefore, this study should be considered as a preliminary clinical trial where the number of

patients recruited was probably small from a biometric point of view, but it is intended to stimulate future larger, adequately powered, probably multicenter, trials or other investigators to address this issue and provide a larger basis for eventual meta-analysis of small randomized trials to help clarify the value of the approach investigated.

Only a few retrospective studies have attempted to study endometrioma recurrence after laser ablation (12, 24, 25). Our study provides further support indicating earlier recurrence in endometrioma patients treated with laser (24).

The use of GnRH agonists before surgery is controversial. We used them in the present study because this has been considered a standard practice when treating endometriomas with CO<sub>2</sub> laser but not with cystectomy (12). In our experience, the effect of 2-month GnRH agonist treatment on endometrioma size preceding surgery is small and clinically irrelevant. Thus, in the present study the mean reduction in the size of the cyst at the time of surgery in patients in group 2 was 18 ± 9 mm (*P*=NS, comparing endometrioma size before and after 2-month treatment). Therefore, this may not represent a bias in our study.

Surgical management of endometriomas and its effect on ovarian reserve remain controversial (13, 24, 26–28). We measured FSH serum levels and AFC at 60 months of follow-up to compare postsurgical ovarian reserve between the two groups. Basal FSH (8.9 ± 10.2 mIU/mL in group 1 vs. 6.8 ± 3.4 mIU/mL in group 2; *P*=NS) and AFC (6.1 ± 3 in group 1 vs. 5.4 ± 2.0 in group 2; *P*=NS) showed no statistical differences between groups. The finding of similar postoperative FSH levels and AFC between the two groups seems to disagree with earlier data showing larger damage to ovarian reserve after cystectomy than with vaporization (21). Remarkably, however, according to our experience (15, 29), AFC measurement in both treatment groups was suggestive of poor ovarian reserve. Therefore, long-term follow-up studies to analyze postsurgical results in patients with endometriomas treated with different surgical techniques are warranted.

In conclusion, the present study shows there are early recurrences in the laser group and more recurrences during long-term follow-up in the laser group compared with the cystectomy group, although the differences were not statistically significant at 60 months of follow-up.

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