

The impact on ovarian reserve after laparoscopic ovarian cystectomy versus three-stage management in patients with endometriomas: a prospective randomized study

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Objective: To investigate the effect of two different laparoscopic methods on ovarian reserve in patients with ovarian endometriomas.

Design: Prospective, randomized clinical trial.

Setting: Endoscopy unit of a university hospital.

Patient(s): Twenty women with endometriomas.

Intervention(s): Patients were randomly selected to undergo either laparoscopic cystectomy for endometrioma (group 1) or the "three-step procedure" (group 2). Before and 6 months after laparoscopy all patients were evaluated, and 12 months postoperatively they underwent ultrasound scan examination.

Main Outcome Measure(s): The primary end point was ovarian reserve damage based on the alterations of anti-Müllerian hormone (AMH). Secondary end points were the changes of antral follicle count and serum concentration of FSH, LH, E₂, and inhibin B.

Result(s): Mean serum AMH was reduced significantly from 3.9–2.9 ng/mL in group 1 compared with the reduction from 4.5–3.99 ng/mL in group 2.

Conclusion(s): Ovarian reserve determined by AMH is less diminished after the three-step procedure compared with cystectomy of endometriomas. (Fertil Steril® 2010;94:71–7. ©2010 by American Society for Reproductive Medicine.)

Key Words: Endometrioma, laparoscopic stripping, laparoscopic laser vaporization, ovarian reserve, anti-Müllerian hormone

Endometriosis is a common but still enigmatic disease affecting 3%–43% of reproductive-age women. The disease is usually manifested by pelvic pain and infertility in symptomatic patients. Endometrioma is defined as the formation of a cyst with ectopic endometriotic lining within the ovary. Endometriomas are the third most common manifestation of endometriosis after Douglas peritoneum and uterosacral ligament endometriosis, and represent 35% of benign ovarian cysts requiring surgery. They are associated with advanced stage of endometriosis and increased morbidity (1).

Although several theories and mechanisms have been proposed since the "retrograde transplantation theory" described by Sampson in 1927, the pathogenesis of endometriosis is still controversial (2). According to epidemiological, surgical, and pathological data, the most contemporary theory suggests that ovarian endometriosis, peritoneal endometriosis,

and adenomyotic nodules of the rectovaginal septum are considered different entities of a single disease. Recently, it has been proposed that ovarian endometriomas, in most cases (90%), are formed by invagination of the ovarian cortex and metaplasia of the coelomic epithelium (3).

The complexity of the disease and the limited progress in identifying its exact cause explain the reason for existence of so many controversies in the literature regarding the most effective modality to treat endometriomas.

Operative laparoscopy compared with laparotomy has been established as the gold standard surgical approach in the treatment of endometriomas in terms of reduced postoperative pain, analgesic requirement, hospitalization, and lower incidence of de novo adhesion formation (4).

Despite the limited number of prospective trials and their drawbacks, excisional surgery for endometriomas seems to be more beneficial than drainage and ablation techniques, if the end points are recurrence of endometriomas and symptoms. To the best of our knowledge, no retrospective or prospective studies were found in the literature to address the issue of laparoscopic stripping versus drainage and ablation of endometriomas on ovarian function (5). Taking into consideration several pathology studies, stripping of the cyst

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wall may result in ovarian reserve damage due to the removal of healthy ovarian cortex and thermal destruction of ovarian follicles by excessive use of bipolar coagulation for hemostatic purposes (6, 7).

To investigate the extent of ovarian reserve damage, anti-Müllerian hormone (AMH) has been recently acknowledged as the most useful, reliable, and sensitive hormonal serum marker of the ovarian primordial follicle pool compared with other known serum markers (8). Furthermore, serum AMH levels are strongly correlated to early antral follicle count (AFC) measured by ultrasound (9).

This relationship was documented more reliable by AMH than those obtained with serum levels of inhibin B, E₂, FSH, and LH (10). In addition, the AMH level represents a stronger independent marker of ovarian reserve without significant fluctuation during the menstrual cycle, which progressively decreases with age (11, 12).

This prospective randomized study focused on the difference in ovarian reserve impairment between laparoscopic stripping of endometriomas and the “three-step procedure” based on AMH and AFC changes.

MATERIALS AND METHODS

This prospective study was conducted in “Papageorgiou” University Hospital of Thessaloniki in Greece between January 2005 and March 2007. Due to the lack of related published literature, a pilot study was conducted to define the sample size needed. It was estimated that inclusion of 10 patients in each group is sufficient to achieve statistical power of 80% with an $\alpha = 5\%$, considering a difference of 0.48 ng/mL for AMH. Thirty-seven consecutive women of reproductive age (22–40 years old) were examined in the outpatient department and a diagnosis of endometrioma with diameter of at least 3 cm was determined. These women were considered eligible for the study. The exclusion criteria were as follows: patients’ refusal to participate, pregnancy, previous surgery for benign ovarian cysts, body mass index (BMI) more than 30 kg/m², history of cancer, suspected malignancy, presurgical evidence of premature ovarian failure (POF), and use of estrogen (E)-suppressive drugs, such as oral contraceptives, GnRH analogues, progestins, or danazol in the preceding 6 months. Finally, 20 of 37 patients accepted to participate in the study and gave written informed consent after being aware of the two methods of laparoscopic treatment. Randomization was performed by choosing 1 of the 20 files and allocating them in proportion 1:1 either to group 1 (one step—stripping procedure) or group 2 (three step—ablation procedure). In all cases, histologic examination confirmed the preoperative and intraoperative diagnosis of ovarian endometriotic cyst. No patient dropped out and all were adequately followed up.

Demographic data and symptoms, such as dysmenorrhea, dyschezia, chronic pelvic pain, dyspareunia, or presence of infertility, were documented in each patient. The primary out-

come of our study was the impact on ovarian reserve determined by AMH after the application of the two laparoscopic techniques for the treatment of ovarian endometriomas. Secondary end points were the changes of AFC and serum concentration of LH, FSH, E₂, and inhibin B.

In all study patients, on days 3–6 during their spontaneous cycle preceding the operation and 6 months after the operation, AMH was assayed in duplicate using a commercial ELISA kit (The DSL ACTIVE MIS/AMH ELISA; Diagnostic System Laboratories, Webster TX) according to the manufacturer’s protocol. The detection limit of AMH was 0.006 ng/mL and the intra-assay and interassay coefficients of variation (CV) were less than 10% and 7%, respectively. Also, inhibin B was assayed using a commercial ELISA kit (DSL-ACTIVE Inhibin B ELISA, Diagnostic System Laboratories). The sensitivity of inhibin B assay was 7 pg/mL and the intra-assay and interassay CV were less than 8% and 11%, respectively.

In addition, concentrations of FSH, LH, and E₂ were measured by commercial solid-face, two-site chemiluminescent immunometric assay kits (AxSYM FSH Kit; Abbott Laboratories, Abbott Park, IL) and interassay CV were 0.1 mIU/mL and less than 3% and 5%, respectively, for FSH and LH. For E₂, functional sensitivity was 20 pg/mL and intra-assay and interassay CV were 7% and 9%, respectively.

Except for hormonal evaluation, all patients preoperatively and 6 months during their follow-up underwent transvaginal ultrasound examination (5–7.5 Mz transvaginal transducer) in the early proliferative phase of the cycle (days 3–6) to record the dimension of endometrioma AFC, ovarian volume, and to rule out functional or malignant suspected cysts. For cyst diameter, the mean diameter of the three perpendicular dimensions of the ovary was considered. Antral follicle count was estimated as the total number of follicles with a diameter less than 9 mm. Furthermore, ovarian and cyst volume were estimated using the formula $\frac{4}{3} \times \pi \times (d/2)^3$ where d is the mean diameter. All ultrasound examinations were performed by the same investigator.

Operative laparoscopy was performed during the late proliferative phase of the cycle through insertion of a 10-mm subumbilical trocar and three 5-mm trocars in the lower abdomen. In all patients the preoperative diagnosis of endometrioma was confirmed at laparoscopy. All endoscopic procedures were performed by the same endoscopist (G.P.) and assistant (D.T.) and followed the same protocol during the diagnostic phase of laparoscopy. This included inspection of pelvic and peritoneal organs, peritoneal washings, staging of endometriosis, and adhesiolysis to fully release the adhesive ovaries from the surrounding structures. If the ovarian cyst remained unruptured despite the manipulations during adhesiolysis, it was punctured to drain and aspirate its chocolate content. Further extension of the incision into the antimesenteric edge facilitated meticulous inspection of the inner cyst’s wall for exclusion of possible suspicious areas. Endometriosis was staged according to the revised American Society for Reproductive Medicine (ASRM) classification.

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