Decline of serum antimüllerian hormone levels after laparoscopic ovarian cystectomy in endometrioma and other benign cysts: a prospective cohort study

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Objective: To identify the most important factor in predicting ovarian reserve after laparoscopic ovarian cystectomy and to evaluate whether there is any difference in the postoperative decline of ovarian reserve between women with endometrioma and those with other benign ovarian cysts.
Design: Prospective cohort study.
Setting: University hospital.
Patient(s): A total of 100 women who had undergone laparoscopic ovarian cystectomy for endometrioma (n = 68) or other benign ovarian cysts (n = 32).
Intervention(s): Serum antimüllerian hormone (AMH) levels measured by enzyme immunoassay preoperatively and at 3 months after surgery.
Main Outcome Measure(s): Rate of AMH decline after surgery and follicle numbers retained in cystectomy specimens.
Result(s): Serum AMH levels were obviously decreased at 3 months after the surgery (4.97 ± 2.83 vs. 3.33 ± 2.08 ng/mL, mean ± standard deviation). Adjusting for several parameters, we could see that bilaterality of the ovarian cyst was the only significant factor in predicting the rate of postoperative decline of AMH levels. The rate of AMH decline did not differ between the endometrioma group and the other benign ovarian cyst group.
Conclusion(s): Bilaterality of the ovarian cyst is the only significant factor in predicting the rate of decline of AMH level after laparoscopic ovarian cystectomy. The rate of decline of AMH levels after surgery was similar between the endometrioma group and the other benign ovarian cyst group. (Fertil Steril® 2014;101:435–41. ©2014 by American Society for Reproductive Medicine.)
Key Words: antimüllerian hormone, endometrioma, endometriosis, ovarian cystectomy, ovarian reserve

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Ovarian reserve can be defined as the size and quantity of the remaining ovarian follicular pool at any given time. Although there is no single ideal estimate to measure functional ovarian reserve in women of reproductive age, antimüllerian hormone (AMH) has been shown to be a better marker in predicting ovarian response after controlled ovarian hyperstimulation as compared with age or levels of basal follicle-stimulating

hormone (FSH), estradiol, or inhibin (1). Antimüllerian hormone is a dimeric glycoprotein and belongs to the transforming growth factor-β family (2). It is secreted by granulosa cells in preantral and antral follicles, and the serum levels of AMH are mainly influenced by antral follicles (1). Because AMH levels are independent of the menstrual cycle and are not affected by the use of gonadotropin-releasing hormone (GnRH) agonists or oral contraceptives, serum AMH measurement has been widely used in clinical practice for assessment of ovarian reserve (3).

Evidence is accumulating that AMH levels are severely decreased after excision of an ovarian endometrioma (4–9). A recent meta-analysis of eight eligible studies comprising 237 patients with endometrioma has shown that AMH levels are significantly reduced (38%) after cystectomy (10). In another recent meta-analysis, Somigliana et al. (11) also confirmed the presence of surgery-related damage to the ovarian reserve after surgical excision of endometriomas. They suggested that further evidence to confirm this finding is no longer a research priority and proposed that a larger study is necessary to clarify the risk factors for damage to the ovarian reserve after surgery. Indeed, because several studies using multivariate analysis have suggested various risk factors to be the most important determinants of AMH reduction, it is still unclear what the most important risk factor is for the prediction of ovarian reserve after ovarian cystectomy (7–9). It is also unclear whether there are any differences in the decline of ovarian reserve after ovarian cystectomy between women with endometrioma and those with other benign ovarian cysts. Although several studies have shown that AMH reduction is milder in nonendometriotic benign ovarian cysts compared with endometriomas (4, 7), further studies are necessary because the number of cases in these reports was too small. Another previous study described serious injury to the ovarian reserve in nonendometriotic benign ovarian cysts (12).

Our prospective cohort study clarified the most important factor for predicting ovarian reserve after laparoscopic ovarian cystectomy, and also evaluated whether there is any difference in the decline of the ovarian reserve after laparoscopic ovarian cystectomy between women with endometrioma and those with other benign ovarian cysts. To the best of our knowledge, our study includes the largest number of patients to date in whom changes of serum AMH levels were analyzed after laparoscopic ovarian cystectomy.

MATERIALS AND METHODS

Patients and Surgery

The present prospective cohort study recruited a total of 100 women who underwent laparoscopic ovarian cystectomy due to endometrioma (n = 68) or a nonendometriotic benign ovarian cyst (n = 32) from February, 2011 to January, 2013 at the Department of Obstetrics and Gynecology of Asan Medical Center in Seoul, Korea. All the women had regular menstrual cycles, and their ages ranged from 18 to 45 years (31.1 $\pm$ 5.9, mean $\pm$ standard deviation [SD]). None of the patients had a history of adnexal surgery, had received any hormone treatment during the previous 6 months, had evidence of any other endocrine disorders, or had a malignancy. All the patients in the endometrioma group were confirmed by histologic report to have endometriosis. All the patients in the other benign ovarian cyst group were confirmed by laparoscopy as having nonendometriotic lesions. The histologic diagnoses of women in the other benign ovarian cyst group were mature cystic teratoma (n = 15), follicular or luteal cyst (n = 9), and mucinous or serous cystadenoma (n = 8). The institutional review board of our institute approved the study, and all patients provided written, informed consent.

After a 1.5–2.5 cm vertical intraumbilical skin incision and rectus fasciotomy, an Alexis wound retractor (Applied Medical) was inserted into the peritoneal cavity through the umbilical incision. We fixed a surgical glove to the outer ring of the Alexis retractor, and inserted a 12-mm trocar as well as another 5-mm or 12-mm trocar after making incisions in the fingertip portion of the glove. After insufflation of 2 L of carbon dioxide gas, a 10-mm 0° laparoscope and an operating instrument were inserted through the trocars. Another 5-mm trocar was inserted in the suprapubic area to assist the surgical procedure. After adhesiolysis and mobilization of the ovary, the contents of the cyst was aspirated, and the outer wall of the cyst was incised from the ruptured orifice if the cysts were ruptured during the procedures. If the cyst was not ruptured during the adhesiolysis and mobilization, the normal ovarian cortical tissues on the cysts were incised to the level of the cyst capsule. Every effort was made to remove the cyst without spilling the content in case of preoperative diagnosis of mature cystic teratoma.

After identifying the cleavage plane between the cyst capsule and the adjacent normal ovarian tissue, the cyst wall was stripped from the normal ovarian tissue by traction and countertraction using two atraumatic grasping forceps. Hemostasis was performed using a monopolar tip or bipolar forceps as little as possible to prevent serious thermal damage to normal ovarian tissue. The ovarian defect was sutured with a 2-0 Vicryl after hemostasis.

All the operations in this study were performed by two gynecologists who have had over 10 years' experience in laparoscopic ovarian cystectomy (83 surgeries were performed by Dr. S.H. Kim, and 17 surgeries were performed by Dr. D.Y. Kim). In the endometrioma group, the extent of disease was staged according to the American Society for Reproductive Medicine (ASRM) criteria (13). For the postoperative medical treatment of endometriosis, a GnRH agonist or oral contraceptive was administered to 55 and 1 patients, respectively; 12 patients had no medication.

Hormonal Measurements and Histologic Reviews on Cystectomy Specimens

The serum samples were collected preoperatively and at 3 months after the surgery from each patient. There were no cases lost to the 3 months follow-up evaluation after surgery. The serum AMH concentration was measured by an enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions (AMH Gen II ELISA; Immunotech). The intra-assay and interassay coefficients of variation for the AMH assay were both below 10%. The lowest amount