Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci
August 2023; 9(3): 542-549

RESEARCH ARTICLE
DOI: 10.19127/mbsjohs.1266532

# Surgical Removal of Endometriomas Adversely Affects Ovarian Reserve: Comparison of Serum FSH, AMH and AFC Before and After Cystectomy

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Received: 16 March 2023, Accepted: 26 July 2023, Published online: 31 August 2023


## Abstract

**Objective:** Surgical removal of endometriomas, even if performed in experienced hands, leads to a decrease in ovarian reserve in varying degrees depending on age. This study was designed to determine the pre- and post-surgical changes of ovarian reserve markers in patients who underwent endometrioma cystectomy.

**Methods:** Gözde Akademi Hospital gynecology outpatient clinic with the diagnosis of symptomatic ovarian endometrioma was included in the study. Fourteen normal-ovulatory women aged between 21-36 were included in the study. In addition to serum anti-Mullerian hormone (AMH), follicle-stimulating hormone (FSH), and estradiol levels, antral follicle count (AFC) was evaluated before and 3 months after cystectomy. Ovarian damage was avoided as much as possible during endometrioma surgery.

**Results:** After endometrioma cystectomy, serum AMH levels were significantly decreased (3.21 ± 1.1 ng/mL vs 1.9 ± 0.6 ng/mL; p= 0.02). There was no significant change in serum FSH (5.97 ± 1.6 mIU/mL vs 7.34±0.55 mIU/mL, p=0.08) and estradiol (37.8 ±9.44 pg/mL vs 32.9 ±10.7 pg/mL, p=0.56) values measured three months after surgery. Similarly, there was no significant change in AFC values before and after surgery (4.12 ± 2.80 vs 4.89 ±3.06, p=0.24).

**Conclusion:** Endometrioma cystectomy leads to a significant decrease in AMH levels, which is the main ovarian reserve marker, but does not affect AFC and FSH values.

**Keywords:** Endometrioma, Cystectomy, AMH, FSH, Estradiol.

**Suggested Citation:** Tanılır Çağıran F, .Kali Z, Surgical removal of endometriomas adversely affects ovarian reserve: Comparison of serum FSH, AMH and AFC before and after cystectomy Mid Blac Sea Journal of Health Sci, 2023;9(3):542-549.

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## INTRODUCTION

Endometriosis is an important reproductive tract disease with a frequency of approximately 10% in women of reproductive age, accompanied by pelvic pain and subfertility. Although it can be treated to some extent with conservative approaches in single women, it is very difficult to manage in infertile couples. Ovarian endometrioma is an important complication of endometriosis and there is no general consensus on its treatment (1,2). Endometrioma is a blood-filled pseudocyst formation that occurs due to close contact between the endometrial foci in the peritoneum and the ovarian surface epithelium (3,4). Retrograde menstruation, small invaginated cysts, and corpus luteum metaplasia have also been implicated in the formation of endometrioma (5). The location of endometriomas close to the ovarian cortex may cause damage to the primordial follicles in this area. The most important feature that keeps endometrioma on the clinician's agenda is its harmful effects on ovarian reserve. Since endometrioma occupies a place in the ovarian cortex, it both restricts the location of the follicles and can reduce the ovarian reserve by disrupting its blood supply. The fact that the ovarian cortex of patients with endometrioma contains fewer follicles than healthy individuals or the opposite ovary is important evidence that these cysts cause follicle damage (6,7). Increased cortical fibrosis and follicular atresia in areas close to endometrioma are further evidence that endometrioma itself negatively affects ovarian reserve (1,2).

If an ovarian endometrioma causes a decrease in ovarian reserve, surgical removal should lead to recovery of the reserve. However, clinical studies and observational data have not led to a consensus that endometrioma surgery fully restores ovarian reserve. While some studies have reported that ovarian reserve improves after endometrioma cystectomy (8), others have suggested that cystectomy has no clear effect on reserve or is harmful (1,2). In light of recent meta-analyses, it has been emphasized that both endometrioma and endometrioma surgery lead to a decrease in ovarian reserve (9). Endometrioma reduces the reserve by restricting the location of the follicles and impairing oxygenation. Endometrioma surgery disrupts the reserve by removing healthy cortical tissue (1,2).

Serum and ultrasonographic markers can be used alone or in combination to detect ovarian reserve. Serum anti-müllerian hormone (AMH), FSH, and estradiol are considered the

most reliable biomarkers (10). Ultrasonographically measured antral follicle count (AFC) is another important ovarian reserve marker (11). AMH and AFC are more sensitive in determining ovarian reserve than other markers. This study was planned to determine the changes in serum (AMH, FSH, estradiol) and ultrasonographic (AFC) markers of ovarian reserve before and after endometrioma cystectomy in patients with uni- or bilateral symptomatic endometrioma.

## METHODS

Fourteen patients who applied to Gözde Akademi Hospital gynecology outpatient clinic with the diagnosis of symptomatic ovarian endometrioma were included in the study. All participants exhibited different symptoms related to endometrioma (pelvic pain, subfertility, etc.). Therefore, a decision was made for laparoscopic ovarian endometrioma cystectomy. The ages of the patients ranged from 21 to 36. The BMI values of the participants were taken into account (24.8 ± 10.6 kg/m2) to prevent possible dilutional changes in serum AMH levels. Endometrioma diagnosis was made by transvaginal USG. It was recorded whether the cyst was uni- or bilateral. To measure serum AMH, FSH and estradiol levels, blood samples were taken from all patients before and three months after surgery in the follicular phase of the cycle. After an overnight fast, cubital venous blood was collected from all participants in a sitting position. Serum AMH, FSH and estradiol levels were measured by electro-chemiluminescence immunoassay (ECLIA) method with Roche Cobas e602 (Roche Diagnostics GmbH, Germany) immunoassay analyzer. AFC was calculated in the early follicular phase and with TV-USG. Follicles larger than 2-6 mm in both ovaries were counted and recorded. Patients with BMI values >30 kg/m2, those with concurrent non-endometriotic ovarian cysts, PCOS patients, those who had previous ovarian or pelvic surgery, and those who used hormonal therapy in the last 6 months were excluded from the study.

***Endometrioma Cystectomy:*** Laparoscopy was performed under general anesthesia using the four-port laparoscopy technique. The contents of the endometrioma were aspirated through a small cautery incision made by the antimesenteric side. The endometrioma capsule was removed by grasping forceps. If there was no bleeding, cauterization was not performed. Bipolar cautery was used in patients with bleeding. Endometriosis foci detected in the peritoneum and on the ligaments were cauterized or excised. During the surgical procedure, care was taken not to damage the healthy ovr tissue. The removed cyst components were sent to the pathology.

***Statistical Analysis:*** Statistical Package for Social Sciences version 21.0 (SPSS, Chicago, IL, USA) was used for the analysis of all

collected data. Whether the data were normally distributed was tested with Shapiro-Wilk. Normally distributed data were analyzed with paired samples t-test, and parameters that were not normally distributed were analyzed with Wilcoxon test. The correlation between ovarian reserve markers and demographic data was calculated using Spearman's test. While the results were presented as mean+ SD, $p<0.05$ was considered statistically significant.

**Table 1:** Patients characteristics

| ***Demographic features**** | ***Participants (n=14)*** |
|---|---|
| **Age (years)** | 32.4±11.2 |
| **BMI (kg/m$^2$)** | 25.8±10.6 |
| **Application complaint** | |
| **Severe dysmenorrhea, n (%)** | 6 (42.8%) |
| **Subfertility/infertility, n (%)** | 5 (35.7%) |
| **Dysmenorrhea + subfertility, n (%)** | 3 (21.4%) |
| **Laterality** | |
| **Unilateral, n (%)** | 10 (71.4%) |
| **Bilateral, n (%)** | 4 (28.5%) |
| **Endometrioma size (mm)** | 43.6 ± 9.32 (34-52) |
| **AMH (ng/mL)** | |
| **Before surgery** | 3.21 ± 1.1 |
| **After surgery** | 1.9 ± 0.6 |
| **FSH(mIU/mL)** | |
| **Before surgery** | 5.97 ± 1.6 |
| **After surgery** | 7.34±0.55 |
| **AFC** | |
| **Before surgery** | 4.12 ± 2.80 |
| **After surgery** | 4.89 ±3.06 |
| **Estradiol (pg/mL)** | |
| **Before surgery** | 37.8 ±9.44 |
| **After surgery** | 32.9 ±10.7 |
| **Values was presented as mean ± SD, or n (%).** | |

## RESULTS

Endometrioma cystectomy was successfully performed in all participants without serious complications. Of the 14 participants, 4 had bilateral (28.5%) and 10 had unilateral endometrioma (71.4%). The patients were discharged after one day of observation. No menstrual irregularity was detected in the early postoperative period and at the end of 3 months. Three patients gave a history of spotting vaginal bleeding on the first and second postoperative days. Demographic data and pre-postoperative ovarian reserve marker values of the patients are shown in Table 1. After endometrioma cystectomy, serum AMH levels were significantly decreased (3.21 ± 1.1 ng/mL vs 1.9 ± 0.6 ng/mL; p= 0.02). There was no significant change in serum FSH (5.97 ± 1.6 mIU/mL vs 7.34±0.55 mIU/L, p=0.08) and estradiol (37.8 ±9.44 pg/mL vs 32.9 ±10.7 pg/mL, p=0.56) values measured three months after surgery. Similarly, there was no significant change in AFC values before and after surgery (4.12 ± 2.80 vs 4.89 ±3.06, p=0.24).

The AFC value on the endometrioma side was lower than the ovarian AFC on the healthy side (4.12 ± 2.80 vs 5.66 ±2.30, p<0.01). The

change in AFC values was similar at the postoperative third month. A positive and significant correlation was found between AMH values and AFC both before (r=0.467, p=0.03) and after surgery (r=0.490, p=0.02). No significant correlation was found between other parameters.

## DISCUSSION

Although many hypotheses regarding the formation of endometrioma have been put forward, a common consensus has not been established so far. The unclear etiology of endometrioma has also led to heterogeneous results regarding its effects on reproductive outcome. While some studies report that the ovary on the endometrioma side responds less to ovarian stimulation than the healthy ovary, there are also studies reporting that there is no difference between the ovaries (1,2). In another study, it was reported that women with endometrioma had lower AMH levels than those without endometrioma in the same age group (2). The bilateral and severe stage of endometrioma leads to a more significant decrease in ovarian reserve markers. However, the low AFC and AMH values may vary depending on the size of the cyst and the severity of the disease. In addition, it has been emphasized that AFC may show a false-negative decrease (1,2) since the cyst distorts the ultrasonographic appearance.

In the presence of endometrioma, decreased area for follicle placement in the ovarian cortex and low blood flow may decrease AMH and AFC levels. Indeed, the presence of fibrosis, inflammation and low blood flow in the cortical area adjacent to the cyst may lead to a decrease in the follicle pool and decrease in AFC, especially AMH (12,13). If subfertility due to endometrioma is due to the space-occupying effect of the lesion, surgical removal of the cyst should lead to recovery of ovarian reserve. To test this, we evaluated the main ovarian reserve markers, AMH, FSH, E2, and AFC, before and three months after surgery in patients who underwent endometrioma cystectomy. If the space-occupying effect of the cyst is the main cause of subfertility, AMH, E2, and AFC should increase and FSH should decrease after surgery. However, our results did not fully meet our expectations. After endometrioma cystectomy, serum AMH levels decreased, but there was no significant change in AFC, FSH, and estradiol levels. Post-surgery AMH reduction may be an indication that cystectomy leads to deterioration in ovarian reserve. Removal of healthy cortex tissue during cystectomy may lead to a decrease in AMH. The presence of cortical tissue and preantral follicles in cystectomy material is evidence of surgery's damage to healthy ovarian tissue (1,2). However, the absence of a significant change in AFC led us to question the space-occupying effect of the cyst. Similarly, the fact that FSH and estradiol values remained the same in the postoperative period did not support

the idea that cystectomy had a negative effect on ovarian resection.

We can list the possible reasons why the AFC remains stable despite the decrease in AMH value after endometrioma cystectomy. The disappearance of the compression effect of the endometrioma on the preantral follicles in the post-cystectomy period may have allowed them to become functional. The re-functioning of follicles released from pressure after surgery suggests that the AFC pool is not seriously affected by surgery (2). Although the follicle under the pressure of endometrioma maintains its vitality, these follicles may not be able to fulfill their AMH secretion task. We believe that surgery should not be delayed due to the risk of losing the vitality of the follicles in endometriomas that have not undergone surgery for a long time. Since changes in FSH and estradiol levels are long-term effects of endometriomas, it may be accepted as normal for their levels to remain unchanged after surgery. The positive correlation between AMH and AFC is evidence that these two markers work in coordination. No matter how experienced the surgeon is, a decrease in reserve can occur. Cauterization of unpredictable bleeding, the presence of accompanying peritoneal and deep endometriosis, and bilaterality may be the reason for the discrepancy in AMH and AFC results. AMH reduction can be minimized thanks to the necessary care and attention to be shown during cystectomy. In addition, since the age range of the participants is variable, AMH and AFC mismatch may have occurred. In a recent study (14), it was reported that laparoscopic endometrioma resection increased FSH levels while decreasing serum AMH levels. The FSH results of this study are inconsistent with ours. We measured FSH levels at the third-month post-cystectomy. The other study measured it three days after surgery. The reason for the inconsistency may be the difference in FSH measurement times. Decreased estradiol levels due to early cautery damage may have led to an increase in FSH. After three months, histomorphological and functional improvement in the ovary may have normalized FSH levels. The lack of international standardization of AMH values does not allow us to make a clear discussion about whether there is a decrease in post-surgical levels (15). On the other hand, the fact that AMH has a stronger effect in determining the response to ovarian stimulation compared to basal FSH concentrations weakens the clinical significance of unchanged FSH levels after endometrioma surgery (16).

Despite the small number of cases and the short follow-up period, our study showed that endometrioma cystectomy did not cause a significant change in AFC, despite a decrease in serum AMH levels. If the number of AFCs is sufficient, the decrease in AMH may not mean much. Whether there is a decrease in AFC in

long-term follow-up should be investigated extensively. We did not evaluate ovarian reserve marker changes according to whether the endometrioma is unilateral or bilateral. This can be a handicap. However, since the distribution of patients into groups was not homogeneous, statistical analysis results would not be very objective. However, we can expect a further decrease in AMH values in bilateral cases. By including cyst size and individual ovarian reserve, it will be possible to interpret ovarian reserve marker changes more objectively in bilateral endometriomas. In conclusion, in symptomatic endometriomas, the clinician should decide in light of treatment guidelines and based on the patient's past clinical and fertility history.

**Ethics Committee Approval:** Ethics Committee Approval: Ethics approval for this study was obtained from the Diyarbakır Gazi Yaşargil Education and Research Hospital Clinical Research Ethics Committee (ethics committee date: 09/12/2022, ethics committee number:254).

**Author Contributions:** Concept: FTÇ, Design: FTÇ, Supervision: FTÇ, ZK, Data Collection and/or Processing: ZK, Analysis and/or Interpretation: ZK, Writing: FTÇ.

**Acknowledgments:** We would like to thank Zercan Kalı for his/her contribution to our study.

***Conflict of Interest:*** No conflict of interests

***Financial Disclosure:*** No financial support

**Peer-review:** Externally peer-reviewed.

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