Factors affecting surgery-related decline in ovarian reserve in women with endometriomas

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Abstract

Background: Endometriosis is a main cause of female infertility. Surgical treatment of ovarian endometriomas raised great concerns about future fertility and the possible decline in ovarian reserve.

Objective: Evaluate factors associated with the decline in ovarian reserve after surgical excision of the endometriomas.

Study design: This cross-sectional study was conducted in tertiary hospital from 1/11/2020 to 31/7/2022. We recruited eligible patients during the study duration according to predetermined inclusion and exclusion criteria. Eligible patients were subjected to ultrasound examination to diagnose ovarian endometrioma, its diameter, and the AFC of the affected. The AMH was also withdrawn. Patients were prepared for laparoscopic cystectomy. After three months, patients were subjected to reevaluation, including recurrence of the cyst, AFC, AMH levels, and patient satisfaction using the endometriosis treatment satisfaction questionnaire.

Results: Sixty patients were recruited throughout the study duration. The mean age was 30.33 ± 7.95. The recurrence rate was 19/60 (31.7%). There was a significant reduction in the cyst diameter, AFC, and AMH after surgical excision (p-value <0.001). Only preoperative AFC and AMH levels were significant predictors for each marker individually (p<0.001). There was a significant increase in all domains of the endometriosis treatment satisfaction questionnaire and the total score (p-value <0.001).

Conclusion: Surgical removal of endometriomas was associated with a significant decline in ovarian reserve. The decline in AFC and AMH was independent of other patient-related factors but for preoperative AMH, which affected post-operative AMH levels significantly.

Keywords: Ovarian reserve; Endometriosis; Surgery; Predictors; Satisfaction.

Introduction:

Endometrioma is a cystic lesion in the ovary developed due to the presence of ectopic endometrial cells. It occurs in 17-44% of patients with endometriosis (1). Different management options are available, with surgical excision representing the mainstay treatment (2). However, several concerns were raised about the deleterious effect of surgical excision on ovarian reserve. This was rendered to the concomitant removal of healthy ovarian tissue (3). The ovarian reserve is a reflection of the reproductive capacity of women (4). Its markers included antral follicle count (AFC) and anti-mullerian hormone (AMH) (5). Endometriomas result in decreased ovarian reserve due to inadequate blood supply caused by the pressure effect of the endometriomas on the capsule and the local inflammatory reaction destroying the follicles (6). The AFC, although reliable, has some limitations as inter-cycle variation and the difficulty in obtaining accurate results because of the presence of endometriomas (7). The AMH is a reliable one without the limitations above (8). It has been noted that endometriomas managed conservatively lead to decreased ovarian reserve, and surgical excision leads to further decline (9). Other factors implicated in reducing ovarian reserve included age, size of the endometrioma, removal of ovarian tissue, the surgeon's expertise, and the endometrioma's site (3, 10, 11). Accordingly, this study was conducted to evaluate possible factors associated with reducing the ovarian reserve in women undergoing surgical excision of ovarian endometriomas.

Methods

This cross-sectional study was conducted in the obstetrics and gynecology department at a tertiary hospital from 1/11/2020 to 31/7/2022. We recruited eligible patients during the study duration according to predetermined inclusion and exclusion criteria. Inclusion criteria: a) unilateral endometrioma, b) unilocular endometrioma of any size, c) age 18-45 years, d) regular cycles, e) no previous history of ovarian operations, and f) patients undergoing surgical excision of the endometrioma by laparoscopy. Exclusion criteria: a) suspected or confirmed malignancy, b) women within two years of menarche, c) women on progesterone only

or combined hormonal contraception, d) women refusing to participate in the study, and f) women preferring medication for the management of endometriomas.

After a detailed explanation of the study's aim and procedure, informed consent was obtained from all eligible study participants. Eligible patients were subjected to the following:

1. Complete personal and medical history.
2. Ultrasound examination, either transabdominal for virgins or transvaginal for sexually active women, to diagnose ovarian endometrioma. It was diagnosed as a unilocular cystic lesion with a ground glass echogenicity of the fluid and a regular thick wall (12). The AFC was evaluated on days 2-3 of the cycle by determining the number of follicles measuring 2-10 mm (13). The AFC of the affected ovary was considered for pre- and post-therapy evaluation.
3. Routine preoperative laboratory investigations such as complete blood count, coagulation profile, and liver function test was withdrawn. The AMH was also withdrawn.
4. Patients were prepared for laparoscopic cystectomy. Bipolar cauterization was used to achieve hemostasis.
5. After three months, patients were subjected to reevaluation, including recurrence of the cyst, AFC, and AMH levels.
6. Patient satisfaction was evaluated after intervention using an endometriosis treatment satisfaction questionnaire. The questionnaire included six questions that evaluated patient satisfaction after surgical excision of the endometrioma regarding endometriosis-related pain before or during periods, during or after sexual activity, endometriosis-related pain, any bleeding or spotting, tolerability, and overall satisfaction. Each question has seven scales to answer, ranging from extremely satisfied to extremely dissatisfied, with scores of 6 to 0. A higher score indicates a more remarkable improvement (14).

Ethical approval

This study was conducted after approval of the research ethics committee of the faculty of medicine, Suez Canal University, on 26/4/2021, with a reference number of 4538#.

Statistical analysis

Data were statistically described as mean and standard deviation, frequencies (number of cases), and percentages when appropriate. P values of less than 0.05 were considered statistically significant. All statistical calculations were done using the computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA), release 23 for Microsoft Windows. Wilcoxon Wallis test was used to evaluate the difference between ovarian reserve markers before and after surgery.

Results

Sixty patients were recruited throughout the study duration. The mean age was 30.33 ± 7.95. The study population was either virgins or married/divorced/widowed equally. The mean parity of the married/divorced/widowed patients was 1.27 ± 0.69 **(Table 1)**.

The recurrence rate after excision was 12/60 (20%). There was a significant reduction in the cyst diameter, AFC, and AMH after surgical excision (p-value <0.001) **(Table 2)**.

Age, parity, history of infertility, and endometrioma diameter did not affect the ovarian reserve after cystectomy. Only preoperative AFC and AMH levels were significant predictors for each marker individually (p<0.001) **(Table 3)**.

There was a significant increase in all

domains of the endometriosis treatment satisfaction questionnaire as well as the total score (p-value <0.001) **(Table 4)**.

Discussion

Surgical excision of ovarian endometriomas is cornerstone management; however, the decline in ovarian reserve represented a challenge. Variable methods were reported as fenestration and irrigation, cyst wall ablation, cystectomy, and other methods in combination (15). The current study evaluated possible factors contributing to the decline in ovarian reserve after cystectomy.

The mean age of the recruited patients was 30.33 ± 7.95. This was similar to previous results (16, 17), as endometriomas affect women in their childbearing years (18). After surgical excision, recurrence was noted in 20 % of the participants. The recurrence rate after endometrioma excision was reported to be high. It ranged from 29-56% after 2 years while after 5 years it was 43% (19) without post-operative medical treatment. Another study reported a recurrence rate of 6.4% (20). The current study provided no medical treatment after surgery, while the follow-up period was only three months. Immune cells and extracellular matrix metalloproteinase lead to the proliferation and survival of endometriotic cells, explaining recurrent endometriosis (21).

There was a significant decline in the AFC and AMH levels after surgical excision. A meta-analysis reported no change in the AFC after cystectomy. However, the detailed analysis reported decreased AFC in the operated ovary than the normal one (22). This was rendered to compression of the ovarian capsule by the endometrioma leading to underestimation of the AFC (23), limiting its reliability in evaluating the ovarian reserve (24). Another reported a significant decline in AMH levels after the excision of unilateral endometriomas (3). Although conflicting results were reported, the eventual conclusion pointed to AMH reduction (11). An earlier study reported a persistent decline in AMH levels at 1 and 6 months after excision. Although some increase was noted at six months, the results were below those obtained at baseline (25). This was explained by the accidental removal of healthy ovarian tissue during the operation (8).

Age, parity, history of infertility, and endometrioma diameter did not affect the ovarian reserve after cystectomy. Preoperative AMH and AFC were significant predictors for the decline in each marker individually. It has been reported that age and endometrioma size were not related to the decreased AMH levels (3, 11). Another factor that contributed to the decline in AMH was the laterality (8); however, we recruited patients with unilateral endometriomas only. Also, preoperative AMH correlated significantly with the decrease noted postoperatively. Women with increased AMH reported more decline post-operative. This was due to the presence of primordial follicles in large numbers in the ovarian tissue that was removed inadvertently (26, 27). An additional contributing factor is the method of hemostasis used during excision. Hemostasis would be achieved using sutures or bipolar cauterization. The current study depended on bipolar cauterization in all cases. Suturing leads to increased intraovarian pressure and ischemia due to suture tightening, which might affect the ovarian reserve (28). However, bipolar cautery was associated with tremendous damage to ovarian reserve (29, 30).

There was a significant improvement in patients' satisfaction after the operation. There was an improvement in all pain aspects. The mean ETSQ score increased significantly from 12.65 ± 3.31 to 21.22 ± 2.93. This agreed with previous results, where 42.5% and 45.2% were satisfied and very satisfied with endometriosis treatment at three months (31). Similar results were reported by an earlier one (32). However, the former used gonadotropin-releasing

hormone agonists (GnRHa) and combined oral contraceptives (COC) after the operation in their recruited patients, which might affect pain scores. Also, they reported a minor change in dysmenorrhea, contradicting the current results. This would be due to other pelvic pathologies such as adenomyosis (31). As surgery didn't impact the pathogenesis of endometriosis, recurrent symptoms were the cause of declining satisfaction at 12 months (32).

Strength and limitations

This study adopted a fixed technique for endometrioma removal performed by the same surgical team. Follow-up was for three months only. When possible, we resected pelvic endometriotic lesions, which might affect the pain scores. Dyspareunia scores were excluded among non-sexually active participants to avoid bias.

Conclusion

Surgical removal of endometriomas was associated with a significant decline in ovarian reserve. The decline in AFC and AMH was independent of other patient-related factors but for preoperative AMH, which affected post-operative AMH levels significantly. Patients were satisfied after the intervention.

Conflict of interest: None.

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Table 1: Basic demographic data of the studied population (N= 60)

Age (years) (Mean ± SD)		30.33 ± 7.95
Occupation N (%)	Not working	29 (48.33%)
	Working	31 (51.67%)
Residence N (%)	Urban	28 (46.67%)
	Rural	32 (53.33%)
Marital status N (%)	Virgin	30 (50%)
	Married/Divorced/Widowed	30 (50%)
Parity (Mean ± SD)		1.27 ± 0.69

Table 2: Comparison of the ovarian reserve before and after intervention

Group	Before	After	P-value
Cyst diameter (cm) (Mean ± SD)	5.39 ± 1.62	0.4 ± 0.7	**<0.001a**
Anti-Mullerian hormone (ng/ml) (Mean ± SD)	1.77 ± 0.4	1.52 ± 0.43	**<0.001a**
Antral follicular count (Mean ± SD)	5.33 ± 2.13	3.4 ± 1.63	**<0.001a**

[a]Wilcoxon Wallis test

Table 3: Factors affecting the ovarian reserve after surgical excision.

AFC			
	Beta	**95% confidence interval**	**P value**
Constant	3.612	-0.121- 7.346	0.057
Age	0.013	-0.082- 0.108	0.783
Parity	0.180	-0.860- 1.221	0.724
Infertility	-0.313	-1.694- 1.068	0.645
Endometrioma diameter	-0.190	-0.639- 0.258	0.390
AFC (preoperative)	0.546	0.405- 0.687	<0.001
AMH			
Constant	1.186	0.227- 2.144	0.017
Age	-0.001	-0.026- 0.023	0.921
Parity	0.105	-0.163- 0.372	0.428
Infertility	0.158	-0.197- 0.512	0.368
Endometrioma diameter	0.039	-0.076- 0.154	0.488
AMH (preoperative)	-0.139	0.937- 1.109	<0.001

Table 4: Patient satisfaction after surgical excision of the endometrioma

Variable	PRE	POST	P value
Endometriosis-related pain before or during periods	1.93 ± 1.23	3.43 ± 1.13	<0.001a
Endometriosis-related pain during or after sexual activity	2.03 ± 1.46	3.43 ± 1.2	<0.001a
Endometriosis related pain	2.33 ± 1.37	3.68 ± 1.14	<0.001a
Any bleeding or spotting	2.13 ± 1.37	3.8 ± 1.2	<0.001a
Tolerability	1.88 ± 1.37	3.33 ± 1.05	<0.001a
Overall satisfaction	2.33 ± 1.4	3.53 ± 1.19	<0.001a
ETSQ total score	12.65 ± 3.31	21.22 ± 2.93	<0.001b

[a] Wilcoxon Wallis test, b Paired sample t-test.