Laparoscopic Stripping of Ovarian Endometriosis in Relation to Ovarian Response and Reserve

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Abstract

Objective: To evaluate the changes in ovarian reserve and response after laparoscopic stripping for ovarian endometrioma.

Patients and Method: Forty infertile women in reproductive age were submitted to laparoscopic cystectomy and stripping for symptomatic ovarian endometrioma(s) of at least 30mm in diameter. The evaluated parameters were follicle-stimulating hormone (FSH), Estradiol (E2), serum anti-Müllerian hormone (AMH), as well as ovulation and pregnancy rates.

Results: Three months after laparoscopy, preoperative antral follicle count (AFC) significantly increased ($p<0.001$), with a significant reduction in ovarian volume ($p<0.001$). The levels of AMH at 3 months reduced significantly ($p=0.02$), with non-significant changes in serum FSH and E2.AMH was significantly increased in bilateral lesions. There was a significant reverse correlation between preoperative AMH and age after laparoscopy. A significant positive correlation between AMH and AFC was detected preoperatively and after 3 months. The ovulation rate was 52.5% at 3 months, with a pregnancy rate of 42.5%.

Conclusion: Laparoscopic stripping of ovarian endometriomas may be associated with worsen ovarian reserve.

Keywords: *Ovarian endometriosis, infertility, laparoscopic cystectomy, ovarian reserve, ovarian response.*

Introduction

Endometriosis has been estimated witha prevalence of 11% among women in reproductive age [1]. Even mild endometriosis can impair fertility, and severe disease can lead to tubal adhesions, reduced ovarian reserve and oocyte and embryo quality, and poor implantation[2-4]. Laparoscopic excision of ovarian endometrioma is performed on infertile women of reproductive age. However, residual ovarian function after the procedure remains an important yet inadequately researched topic.[5,6]

Multiple clinical and biochemical indicators can evaluate ovarian reserve including antral follicle count (AFC), ovarian volume, Follicle-stimulating hormone (FSH), Estradiol (E2) and serum anti-Müllerian hormone (AMH)[7,8]. The aim of this study is to evaluate whether a change take place in ovarian reserve laparoscopic stripping of ovarian endometrioma, using ultrasonographic parameters and biochemical markers.

Patients and Method

This prospective study included 40 patients submitted to laparoscopic excision of ovarian endometrioma(s) at department of Obstetrics and Gynecology, Faculty of Medicine, Minia University. The study was conducted

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after an institutional approval and a formal consent taken from all patients. The study included infertile women in reproductive age with symptomatic endometriosis and an endometrioma diameter of at least 30mm. We excluded patients when there were refusal to participate, pregnancy, previous surgery for benign ovarian cysts, pre-surgical evidence of premature ovarian failure, body mass index (BMI) ≥ 30 kg/m^2, therapy with estrogen or suppressive drugs, suspicion or history of malignancy, mural irregular lesions or septations, cystic lesions compatible with dermoid cyst, and extensive pelvic adhesions.

The antral follicle was defined on ultrasound as a small fluid filled sac that contains immature egg measuring 2-10 mm in diameter. AMH, FSH, E2 levels were measured by ELISA on the third day of the menstruation before the surgery, and three month after the procedure. The main steps of laparoscopic procedure were incision on the ovary at antimesentric border away from ovarian hilum, incision of the ovarian cyst, aspiration of the cyst by repeat irrigation suction which help to separate cyst wall from the ovarian parenchyma, followed by stripping of the cyst using two atraumatic grasping forceps by traction and countertraction after identification of correct cleavage plane so healthy ovarian tissue was not removed.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software version 18.0. Independent groups of continuous data were compared using Student t-test or Mann-Whitney for non-parametric data, while categorical data were compared using Chi-square or Fisher exact test. Intra-group comparisons were performed using paired t-test or Wilcoxon test for non-parametric data. Pearson's test was used to assess correlations. Significant p-values were defined at the level of 0.05.

Findings: Table 1 represents demographic, clinical, and operative characteristics of the studied 40 patients. The ultrasonographic and biochemical parameters before and three months after laparoscopic surgery are shown in (Table 2). Three months after laparoscopy, preoperative AFC significantly increased ($p<0.001$), with a significant reduction of ovarian volume ($p<0.001$). The levels of AMH reduced significantly ($p=0.02$) after 3 months, with non-significant decrease in serum levels of FSH and non-significant increase of E2 levels.

Bilateral lesions showed significantly higher preoperative AFC than unilateral lesions ($p=0.03$), with non-significant differences in ovarian volume, AMH, FSH, or E2 between unilateral and bilateral lesions (Table 3). At 3 months of laparoscopy, AFC significantly increased and ovarian volume significantly reduced regardless to the laterality of the lesion. The levels of serum AMH at 3 months were significantly higher than preoperative levels only in bilateral lesions.

There was a significant reverse correlation between preoperative AMH and age of the patient, which became non-significant three months after surgery, reflecting that the influence of stripping on ovarian reserve is not dependent on age (Figure 1, A and B).On the other hand, there was a significant positive correlation between AMH and AFC preoperatively, and three months after surgery, reflecting the significant association of improved AFC with improved levels of AMH (Figure 1, C and D).

Table 1: Demographic, clinical, and operative characteristics of the studied patients

Variables	Patients (n=40)
Age (years)	30.45±2.36
BMI (kg/m^2)	23.93±2.15
Primary infertility	23(57.5%)
Chronic pelvic pain	31(77.5%)
Parity	0.90±0.84
Menstrual cycle, days	27±1.81
Uni-/Bilateral lesions	30 (75%)/10 (25%)
Operative duration, min	90.03±28.11
Operative blood loss, mL	77.25±38.36

Data are expressed as mean±SD or number and percent. BMI: Body mass index.

Table 2: Ultrasonographic and biochemical parameters for ovarian reserve, before and three months after laparoscopic stripping of ovarian endometrioma.

Variables	Preoperative	3 months	P-value
AFC	5.53±2.34	7.28±2.84	<0.001*
Ovarian volume (ml)	13.1 ± 1.55	6.63 ± 2.46	<0.001*
AMH (ng/ml)	2.87 ± 0.24	2.66 ± 0.55	0.02*
FSH (mIU/l)	6.50 ± 2.69	5.90 ± 2.25	0.28
E2 (pg/ml)	118.65±70.86	112.50±46.29	0.34

Data are expressed as mean±SD. AFC: Antral follicle count. AMH: Anti mullerian hormone. FSH: Follicular stimulating hormone. E2: Estradiol. *Significant difference.

Table 3: Comparison of ultrasonographic and biochemical parameters in patients with unilateral and bilateral lesions

Variables	Unilateral (n=30)	Bilateral (n=10)	P-value
AFC: Preoperative	6±2.36	4.10±2.13	0.03*
AFC:3 months	7.43±2.93 #	6.90±2.81 #	0.61
Ovarian volume (ml): Preoperative	13.17±1.66	12.90±1.20	0.59
Ovarian volume (ml):3 months	6.50±2.39 #	7±2.75 #	0.62
AMH (ng/ml):Preoperative	2.87±0.25	2.85 ±0.23	0.82
AMH (ng/ml):3 months	2.72±0.55	2.47±0.52 #	0.21
FSH (IU/l):Preoperative	6.73±2.90	5.80±1.87	0.25
FSH (IU/l):3 months	6±2.41	5.6±1.78	0.58
E2 (pg/ml):Preoperative	119.33±66.61	116.60±86.37	0.93
E2 (pg/ml):3 months	107.90±43.78	99.30±55.21	0.66

Data are expressed as mean±SD. AFC: Antral follicle count. AMH: Anti mullerian hormone. FSH: Follicular stimulating hormone. E2: Estradiol. # Significant with baseline preoperative value, *Significant inter-groups comparison.

The ovulation rate was 52.5% (21/40) at 3 months after laparoscopy, while the pregnancy rate was 5% (2/40) for biochemical pregnancy, 10% (4/40) for ongoing pregnancy, and 27.5% (11/40) for clinical pregnancy, with a total pregnancy rate of 42.5% (17/40) (Figure 2).

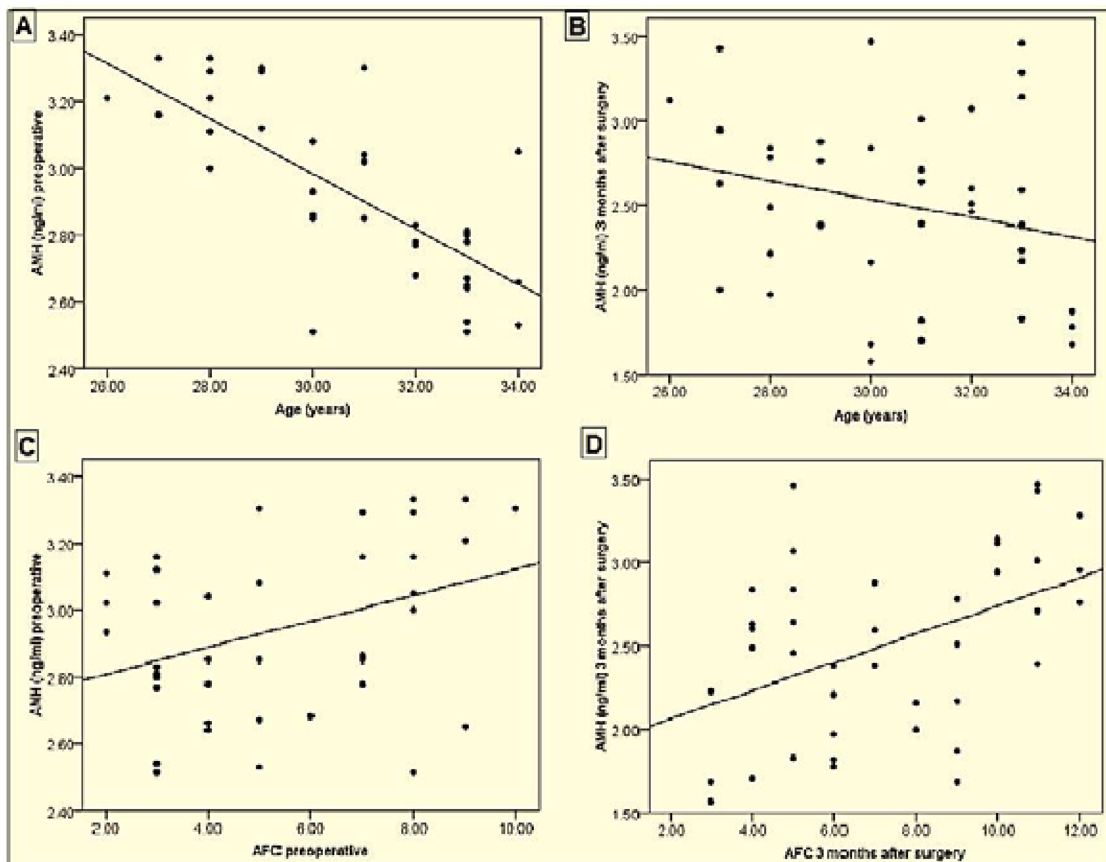

Fig. 1: Correlations: (A) between serum anti-Mullerian hormone (AMH) and age before laparoscopic stripping of ovarian endometriomas, r-value = -0.769, p-value <0.001; (B) between serum AMH and age, three months after laparoscopic stripping of ovarian endometriomas, r-value = -0.241, p-value = 0.12; (C) between serum AMH and antral follicle count (AFC) before surgery, r-value = 0.375, p-value = 0.01; (D): between serum AMH serum concentrations and AFC three months after laparoscopic stripping of ovarian endometriomas, r-value = 0.445, p-value = 0.001.

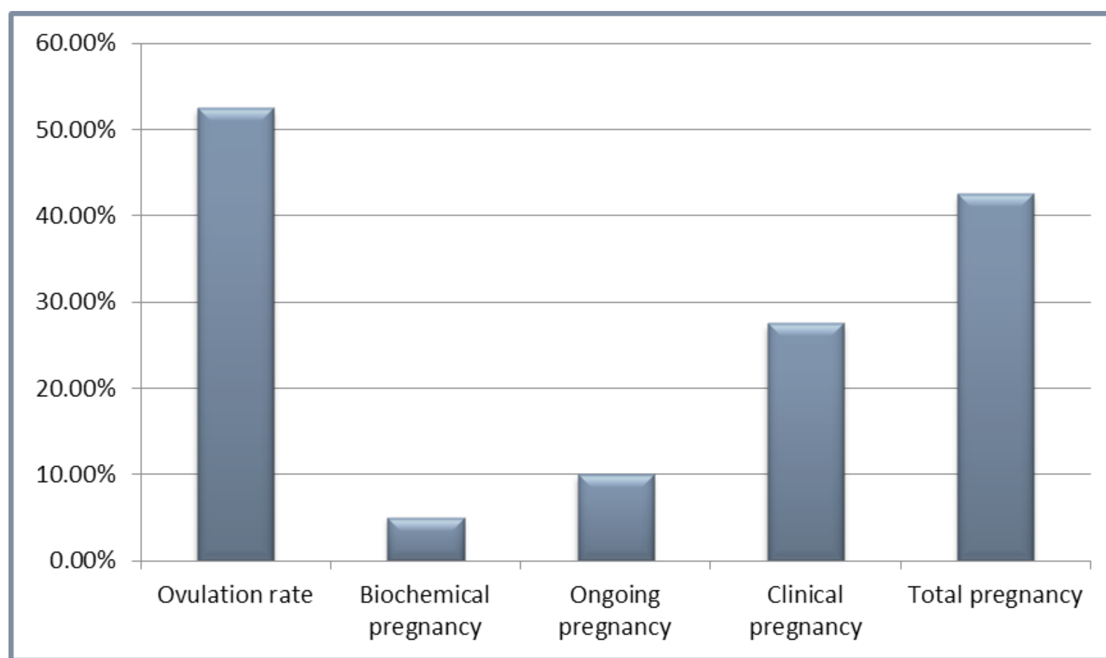

Fig. 2: Ovulation and pregnancy rates after laparoscopic stripping in 40 patients with for ovarian endometriosis

Discussion

Laparoscopic cystectomy is recommended for symptomatic ovarian endometrioma because of higher pregnancy rate and lower recurrence rate[9, 10]; however the ovarian reserve may be negatively affected due to removal of normal ovarian tissue[7]. In our study, AFC was significantly increased 3 months after cystectomy with a significant decrease in ovarian volume, which is consistent with other studies[11,12]. In contrary, other authors reported that AFC is similar or apparently increased after surgery with non-significant changes which can be explained by difficult and inaccurate estimation of AFC in the presence of the anatomical alteration caused by an endometrioma[13,14]. Moreover, there may be a paradoxical increase in AFC in the postoperative period as a consequence of undercounted preoperative AFC beyond the ovarian lesion or due to a reactive response of ovarian parenchyma after surgery[11].

The levels of AMH is probably the most reliable tool to assess ovarian reserve, being synthesized in the pre-antral and small antral follicles[15], AMH provides information about the number of follicles relocated from the quiescent pool of primordial follicles to the pool of activated ones[13]. The significant reduction of AMH after surgery while FSH and E2 did not, may be explained by the higher sensitivity of AMH to ovarian damage and by the existence of a selective damage caused by surgery on the primordial and small antral follicle pool (secreting AMH) that are hosted in the tissue near the cyst, with a rare detection of more developed ovarian follicles secreting inhibin, E2, and hence FSH near an endometrioma[13].These findings may confirm that basal FSH and E2 have low sensitivity for early decrease in the ovarian reserve[16]. However, some studies reported that FSH levels were decreased after three months follow-up, which showed a good ovarian reserve[17,18].

The significant inverse correlation between age and AMH concentrations that the present study and other studies observed before surgery lost significance after the operation[13, 19], suggesting that the surgical damage on healthy ovarian tissue is independent of age and can lower ovarian reserve in the same way in both young and older women. The finding of the significant positive correlation of postoperative serum AMH level with AFC three months postoperatively reflects the high sensitivity of both measurements for ovarian reserve.

The positive correlation between AMH and AFC, in addition to the significant postoperative increase in AFC with a significant reduction in AMH reflects a significant

reduction in ovarian reserve after laparoscopic stripping for ovarian endometrioma, which may be related to pre-surgery negative effects of the cyst, unintentional removal of a considerable amount of healthy tissue[20], direct damage from electrosurgical coagulation[21], damage to ovarian vasculature, or an inflammation-mediated injury[22].

In the present study, bilateral ovarian lesions associated with a significant decrease of preoperative in AMH three months after surgery, which was not reported with unilateral lesions. Other studies demonstrated that bilateral ovarian cystectomy is a significant factor associated with the decline of serum AMH concentrations after cystectomy for ovarian endometriomas[20, 23-25]. The declines in the post-surgical serum AMH concentrations of patients who underwent bilateral cystectomy could be explained by a lower rate of recovery or a continuous decrease in AMH concentration because of the extended ovarian ischemia resulting from the bilateral surgery [25].

The pregnancy rate in our patients is consistent with the reported pregnancy rates after surgery and laparoscopy for ovarian endometerosis which range from 24% to 67%, with an overall mean of about 50% [26-28]. It has been indicated that laparoscopic removal of an ovarian endometrioma can improve pregnancy outcome in infertile patients[29]. The findings of reduced ovarian reserve may add a disadvantage of a consequent reduction of the response to ovarian stimulation [30, 31], however, it has been demonstrated that laparoscopic cystectomy may reduce the frequency of ovulation in the operated ovary, but it maintains the pregnancy rate per ovulation[32].

Conclusion

The laparoscopic stripping of ovarian endometriomas may further worsen ovarian reserve. Serum AMH could be a delicate marker to provide surgical impact on ovarian reserve. Larger studies could be recommended to clarify the relation between the change of serum AMH and actual loss of ovarian reserve.

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Ethical Clearance: Taken from Faculty of Medicine, Minia University committee

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