

IMPACT OF LAPAROSCOPIC OVARIAN CYSTECTOMY ON OVARIAN VOLUME, ANTRAL FOLLICLE COUNT (AFC) AND OVARIAN DOPPLER VELOCIMETRY

By

Mohamed Salah Sayed Saadawy, Emad Maarouf Abd El-Latif and Mofeed Fawzy Mohamed

Department of Obstetrics and Gynecology, Faculty of Medicine- Al-Azhar University

***Correspondence author:** Mohamed Salah Sayed Saadawy,

E-mail: m.salah_86@yahoo.com

ABSTRACT

Background: Ovarian cysts are common in reproductive-aged women. Most cysts are normal functional cysts that typically resolve spontaneously and do not require treatment. However, pathologic cysts such as endometriomas and dermoids may require surgical intervention.

Objective: To evaluate the impact of laparoscopic ovarian cystectomy on ovarian reserve regarding ovarian volume, antral follicle count (AFC) and ovarian doppler velocimetry.

Patients and Methods: A prospective observational study was conducted at 15 May Specializes Hospital on 80 women, less than 35 years old, with single unilateral ovarian cyst (endometriotic or non-endometriotic) ovarian cysts. Presence of ovarian cyst was diagnosed by preoperative transvaginal ultrasound (TVUS) scan which was confirmed at laparoscopy. All laparoscopic ovarian cystectomies were performed under general anesthesia.

Results: There was a statistically significant decrease in ovarian volume (OV) volume and AFC in operated side than contralateral side while no statistically significant difference found between them regarding resistive index (RI).

Conclusions Laparoscopic ovarian cystectomies were risk factors for decreased ovarian reserve and may impair the future fertility.

Keywords: Antral follicle count, Transvaginal ultrasound, laparoscopic ovarian cystectomies.

INTRODUCTION

Ovarian cyst is commonly discovered in women of reproductive age generally as well as in those undergoing work-ups for infertility. The differential diagnosis of an ovarian cyst discovered in women of reproductive age is broad, including physiologic or functional cysts, ectopic pregnancy, inflammatory etiologies such as a tuboovarian abscess, endometrioma

or benign and malignant ovarian neoplasms. The most common benign ovarian masses are serous and mucinous cystadenoma, endometrioma and mature cystic teratoma. Many ovarian masses in the premenopausal woman can be managed conservatively. Functional or simple ovarian cysts (thin-walled cysts without internal structures) which are less than 50 mm maximum diameter usually

resolve over 3 cycles without need for intervention (*Practice Committee of the American Society, 2012*).

Endometriosis is an enigmatic disease characterized by development of the endometrial tissue outside of the uterus. The most common location of endometriosis is the ovary, occurring in 17-44% of patients affected by endometriosis. Endometrioma is the formation of ovarian cyst lined by the endometrial glands and stroma (*Nelson, 2013*).

The concept of ovarian reserve views reproductive potential as a function and quality of number of the remaining oocytes. Decreased or diminished ovarian reserve (DOR) describes women of reproductive age having regular menses whose response to ovarian stimulation or fecundity is reduced compared with women of comparable age. Decreased ovarian reserve is distinct from menopause or premature ovarian failure (*Cooper et al., 2012*).

Although ovarian reserve tests have been applied widely, debate continues over the ability of tests currently in use to predict three related outcomes: oocyte quality, oocyte quantity and fecundity. The goal of ovarian reserve testing is to add more prognostic information to the counseling and planning process so as to help couples choose among treatment options (*Rustamov et al., 2012*).

Ovarian reserve tests include both biochemical tests and ultrasound imaging of the ovaries. Biochemical tests of ovarian reserve can be divided further into basal measurements including measurement of follicle-stimulating hormone, estradiol, inhibin B and

antimullerian hormone and provocative tests such as the clomiphene citrate challenge test (CCCT). Ultrasonographic measures of ovarian reserve include antral follicle count (AFC) and ovarian volume. Ovarian doppler velocimetry has not been extensively used to evaluate post-surgical ovarian damage. Being related to microvascular bed: this parameter was higher in the operated than in the non-operated ovary independently on the histological type of the removed cysts (*Cagnacci et al., 2016*).

Antral follicle count (AFC) has been demonstrated to be a reliable marker of ovarian reserve, since it correlates significantly with the age-related follicle count decline, and with ovarian response to in-vitro fertilization (IVF) stimulation cycles (*Shah et al., 2014*).

The most common side effect of ovarian cystectomy is damage to healthy ovarian tissue therefore; application of new techniques with lower adverse effects on ovarian reserve is a current concern (*Asgari et al., 2015*).

Compared with traditional surgery by laparotomy, laparoscopic approach has been shown to be feasible in the vast majority of cases and when associated with a shorter hospital stay, faster recovery, less pain and lower costs (*Ding et al., 2015*).

Laparoscopic cystectomy is the gold standard for managing endometriomas. Laparoscopic cystectomy often leads to inadvertent removal of an amount of the adjacent ovarian cortex and serious bleeding at the ovarian hilus requiring extensive application of bipolar electrocoagulation and hence, adverse changes in ovarian blood supply, as well

as a functional loss in the ovarian reserve (*Mircea et al., 2016*). Mini-laparotomy may be considered for occasional very large cysts of benign appearance. On rare occasions the laparoscopic approach may be specifically contraindicated in an individual patient (*Hayasaka et al., 2010*).

The aim of the present work was to evaluate the impact of laparoscopic ovarian cystectomy on ovarian reserve regarding ovarian volume, antral follicle count (AFC) and ovarian doppler velocimetry.

PATIENTS AND METHODS

The current study was a prospective observational study conducted at 15 Mayo specialized Hospital, 80 female who have been subjected to a laparoscopic stripping of a single ovarian cyst on Maternity Hospital, Faculty of Medicine, Al-Azhar University. The presence of unilateral cyst was diagnosed at the preoperative transvaginal ultrasound (TVUS) scan and confirmed at laparoscopy from June 2018 to December 2019.

In the current study, we excluded women with more than one ovarian cyst either unilateral or bilateral, previous ovarian surgery, suspected ovarian malignancy and pregnancy.

An approval of the study was obtained from Al- Azhar University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

The recruited patients were subjected the following:

- i. Complete history taking and pelvic examination.

- ii. TVUS: Single benign monolateral ovarian cyst was diagnosed by Preoperative transvaginal ultrasound (TVUS) scan which was confirmed at laparoscopy. Diameter of the cyst was recorded at time of the preoperative TVUS.
- iii. Laparoscopy: All laparoscopic ovarian cystectomies was performed under general anaesthesia by the same gynecologic surgeon using with a standardized technique.
- iv. TVUS: Eligible women were asked to repeat a TVUS after two months of laparoscopy. All the TVUS was performed by the same operator at day 3–6 of menstruation.

The following parameters were evaluated:

- i. **Ovarian volume:** volume of both operated and contralateral ovary was evaluated by the prolate ellipsoid (PE) method ($LD \times APD \times TD \times 0.5233$).
- ii. **AFC:** All echofree structures in the operated and contralateral ovary with a mean diameter of 2–10 mm were counted as an antral follicle.
- iii. **Ovarian Doppler:** RI of ovarian artery of operated and contralateral ovary. Ovarian arteries are displayed in the infundibulo- pelvic ligament at the infero-lateral side of the ovaries.

Statistical method:

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for the Social Sciences) software version 25. Descriptive statistics were done for parametric quantitative data by mean and Standard deviation, median and

interquartile range (IQR), while they were done for categorical data by number and percentage. Distribution of the data was done by Kolomogorov Smirnov test. Analyses were done for parametric

quantitative data between the two groups using independent samples T test. Or Mann-whitneg test The level of significance was taken at (P value < 0.05).

RESULTS

This study was conducted on 80 women recruited during the period from 6/2018 to 12/2019. Their ages ranged

from 18-34 years with Mean±SD of 24.28 ± 4.30. Their parity ranged from 0 – 4 with median and IQR of 1 0-1 (**Table 1**).

Table (1): Age, parity, anthropometric measures, cyst diameter and type among of the studied cases

Parameters		No. = 80
Age (years)	Mean±SD	24.28 ± 4.30
	Range	18 – 34
Parity (No)	Median(IQR)	1 (0 – 1)
	Range	0 – 4
Height (cm)	Mean±SD	163.04 ± 9.87
	Range	145 – 188
Weight (kg)	Mean±SD	73.55 ± 16.02
	Range	45 – 111
BMI (kg/m ²)	Mean±SD	27.41 ± 3.92
	Range	19.22 – 35.11
Cyst diameter	Mean±SD	7.40 ± 2.27
	Range	3.9 – 14
Cyst type	Non-endometrial	57 (71.3%)
	Endometrial	23 (28.8%)

There was a statistically significant decrease in OV volume and AFC in operated side than contralateral with p-value < 0.001 and < 0.001 respectively

while no statistically significant difference found between them regarding RI with p-value = 0.204 (**Table 2**).

Table (2): Comparison between operated side and contralateral side regarding OV volume, AFC and RI

Parameters		Side	Operated	Contra lateral	P-value
			No. = 80	No.= 80	
OV volume	Mean±SD		5.26 ± 1.87	7.33 ± 2.75	<0.001
	Range		2.5 – 11	3 – 15	
AFC	Mean±SD		3.16 ± 1.85	6.89 ± 2.77	<0.001
	Range		1 – 8	2 – 12	
RI	Mean±SD		0.80 ± 0.14	0.73 ± 0.15	<0.002
	Range		0.4 – 1.1	0.48 – 1	

There was no a statistically significant correlation found between OV volume and RI and the other studied parameters. The table also shows that there was

statistically significant positive correlation found between AFC with weight and BMI of the studied cases (Table 3).

Table (3): Correlation of OV volume, AFC and RI of the operated side with demographic and anthropometric measures of the studied patients

Operated Parameters	OV volume		AFC		RI	
	r	P-value	r	P-value	r	P-value
Age	-0.017	0.880	-0.101	0.371	0.110	0.331
Height	-0.101	0.375	0.017	0.884	-0.011	0.924
Weight	0.022	0.845	0.261*	0.019	-0.069	0.540
BMI	0.082	0.470	0.401**	0.000	-0.080	0.479
Parity	-0.056	0.622	0.111	0.327	0.047	0.681
Cyst diameter	-0.151	0.181	-0.021	0.855	0.110	0.329

There was no a statistically significant relation found between cyst type and the

other studied parameters in operated and contralateral sides (Table 4).

Table (4): Relation of cyst type with the studied parameters in operated and contralateral sides

Cyst type		Non-endometrial	Endometrial	P-value
Parameters		No. = 80	No.= 80	
Operated				
OV volume	Mean±SD	5.2 ± 1.81	5.4 ± 2.07	0.678
	Range	3 – 11	2.5 – 9.5	
AFC	Mean±SD	3.14 ± 1.81	3.22 ± 2	0.868
	Range	1 – 8	1 – 8	
RI	Mean±SD	0.79 ± 0.15	0.81 ± 0.13	0.367
	Range	0.4 – 1.1	0.6 – 1.1	
Contra lateral				
OV volume	Mean±SD	7.28 ± 2.76	7.46 ± 2.76	0.793
	Range	4 – 15	3 – 13	
AFC	Mean±SD	7.02 ± 2.87	6.57 ± 2.56	0.513
	Range	2 – 12	3 – 11	
RI	Mean±SD	0.73 ± 0.15	0.73 ± 0.16	1
	Range	0.49 – 1	0.48 – 1	

DISCUSSION

Laparoscopic surgery is currently considered the treatment of choice in women with benign ovarian cysts and has gained increasing acceptance among gynecologic surgeons (Hayasaka et al., 2010). Serum concentrations of follicle-stimulating hormone, luteinizing hormone, estradiol, and inhibin, as well as

ovarian volume and ovarian antral follicle counts, may be useful, but are not necessarily considered highly predictive values. Therefore, using those hormonal tests may be not informative enough to assess postsurgical ovarian reserve precisely (Guleria et al., 2018).

Comparison between the previously operated ovary with the contralateral

intact ovary reflected the influence of the surgery more accurately. This technique has been used for treating ovarian endometriotic cysts by five independent researchers, and for treating ovarian non endometriotic cysts by another researcher (*Somigliana et al., 2012*).

The ovarian follicular heritage undergoes a slow decline during the reproductive life. There is a slew of more or less validated markers of ovarian reserve, that in general can be separated in serum (follicle stimulating hormone (FSH), estradiol (E2), inhibin B and anti-Müllerian hormone (AMH)) and ultrasound-determined (ovarian volume, antral follicle count (AFC)). Some exogenous insults, like gonadal surgery, can speed up the process of ovarian follicle loss and lead to early menopause (*Cagnacci et al., 2016*).

Surgery for endometriomas has been associated with a risk of reduced ovarian reserve, documented with a decrease of several ovarian markers like AFC, AMH and volume. Furthermore, it was demonstrated that ovarian color Doppler velocimetry changed after endometriomas removal, with an increase of the resistance index (RI) (*Muzii et al., 2014*).

This study was selected to evaluate the impact of laparoscopic ovarian cystectomy on the ovarian volume, antral follicle count (AFC) and ovarian doppler velocimetry.

The main results of this study were: Their age ranged from 18-34 years with mean \pm SD of 24.28 ± 4.30 and their parity ranged from 0 – 4 with median and IQR of 1 (0-1).

Our results were in agreement with study of *Salem et al. (2017)* as they found that the mean of age of their participants was 24.5 ± 4.5 years. Our results are supported by study of *Asgari et al. (2015)* as they reported that the mean age \pm standard deviation (SD) was 29.72 ± 5.93 of the studied patients.

The present study showed that the mean of BMI of our patients was 27.41 ± 3.92 . Our results were in line with study of *Salem et al. (2017)* as they reported that the mean of BMI of their studied patients was 26.24 ± 5.2 .

In the study in our hands, the mean of cyst diameter was 7.40 ± 2.27 and 71.3% had non -endometrial cysts and 28.8 % of them had endometrial cysts.

Our results were supported by study of *Cagnacci et al. (2016)* as they reported that in 60.6%, a non-endometriotic cyst was removed (16 teratomas, 12 simple cysts, 10 serous cysto-adenomas, 5 mucinous cysto-adenomas). The rest of the cases were endometriomas (28/71, 39.4%).

According to *Ding et al. (2015)* seventy patients underwent laparoscopic ovarian cystectomy, with bilateral endometrioma (n = 21), unilateral endometrioma (n = 29), and unilateral other benign ovarian cyst (n = 20) were included in the study.

However, decreased ovarian reserve which is due to surgical removal of a part of the healthy ovarian tissue together with the endometrioma wall is considered as a major concern after surgery leading to the risk of premature ovarian failure.

The present study showed that there was a statistically significant decrease in

OV volume and AFC in operated side than contralateral, while no statistically significant difference found between them regarding ovarian Doppler RI.

Our results were supported by the study of *Cagnacci et al. (2016)* who reported that both in endometriotic and non-endometriotic cysts the mean volume and AFC of the operated ovary was significantly lower than that of the contralateral non-operated ovary, while RI was significantly higher.

Asgari et al. (2015) revealed that treatment type was negatively correlated with FSH level, so that surgery with the suturing technique had lower FSH concentrations with higher ovarian reserve as compared with patients in bipolar coagulation group.

Furthermore, two other studies conducted by *Zaitoun et al. (2013)* and *Mohamed et al. (2011)* compared ovarian reserve between laparoscopic ovarian cystectomy and open laparotomy with hemostatic suturing and both indicated a significant decrease in ovarian reserve in bipolar group as compared to open suture group.

Other techniques have been also proposed for protecting ovarian reserve in women undergoing ovarian surgery. *Song et al. (2014)* suggested use of hemostatic sealant as a safe technique with fewer side effects on ovarian reserve as compared with bipolar coagulation.

However, *Ding et al. (2015)* reported that there was no detectable difference on ovarian reserve marker levels between 4 groups and from baseline values at 6 and 12 months after laparoscopic ovarian cystectomy of endometrioma, although

these levels significantly declined in the first month postoperatively.

Findings of our results are in contrast with study of *Asgari et al. (2015)* as they reported that age was a significant predictor of AMH. Ovarian reserve is marked as the size and quantity of the remaining ovarian follicular pool at any given time. AMH level has been considered as a reliable and useful marker of ovarian reserve than the levels of inhibin B, estradiol (E2), follicle-stimulating hormone (FSH) and luteinizing hormone (LH) on cycle day.

Furthermore, *Hayasaka et al. (2010)* demonstrated that age at the time of surgery, the diameter of the excised cysts, age at the time of ICSI, basal FSH, body-mass (BMI), duration of stimulation, total amount of gonadotropin, and peak estradiol at the time of ICSI were not significantly different between groups (patients with ovarian endometriotic mono-lateral cyst, patients with ovarian non-endometriotic mono-lateral cysts).

Cagnacci et al. (2016) reported that mean diameter of the removed cysts, significantly smaller for endometriotic than non-endometriotic cysts.

Our results were supported by study of *Cagnacci et al. (2016)* as they had studied the impact on ovarian reserve of the removal of an endometriotic and non-endometriotic cyst, using ultrasound-determined markers like ovarian volume and AFC. The results showed that the removal of any ovarian cyst reduces follicular ovarian reserve in a similar way.

Although in the case of endometriomas, ovarian reserve may be affected by the presence of the disease

itself. 22 Studies evaluating ovarian reserve by Muzii *et al.* (2014), volume or even AMH15 reported, almost consistently, that ovarian reserve is reduced by the surgical removal of an endometriotic cyst.

In another study conducted by Takashima *et al.* (2013), patients undergoing laparoscopic excision of a unilateral ovarian endometrioma showed no significant differences in the serum levels of AMH and FSH were found at 3 months after surgery compared with preoperative levels. Their findings may be due to smaller sample size and use of diluted vasopressin into the cyst wall which reduced both oozing and use of hemostatic methods.

Sugita *et al.* (2013) also evaluated the serum AMH levels at 1 month and 1 year after cystectomy for endometrioma. Although some patients showed higher AMH levels at 1 year after surgery than 1 month after surgery, they suggested ovarian reserve decreased just after surgery, but recovered within 1 year.

The results of the study of Hayasaka *et al.* (2010) suggest that ovarian reserve is decreased more significantly after excision of endometriotic cysts than after surgery for non-endometriotic cysts, possibly not only because of the surgical procedure but also because of the presence of endometriosis in the pelvic cavity.

Data on non-endometriotic ovarian cysts obtained with AFC reported either a reduction or no effect of cyst removal, in spite of a reduced ovarian volume. Biochemical indexes of ovarian reserve such as AMH declined following the removal of non-endometriotic ovarian cysts (Kwon *et al.*, 2014).

CONCLUSION

Ovarian cystectomies are risk factors for decreased ovarian reserve and may impair the future fertility.

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تأثير إستئصال أكياس المبيض بالمنظار على حجم المبيض، عدد الجريبات الطرفية و دوبلر المبيض

محمد صلاح سيد سداوي، عماد معروف عبد اللطيف، مفيد فوزي محمد

قسم أمراض النساء والتوليد، كلية الطب، جامعة الأزهر

E-mail: m.salah_86@yahoo.com

خلفية البحث: يشيع ظهور أكياس المبيض في النساء في فترة سن الإنجاب عموماً وخاصة اللاتي يقمن بعمل فحوصات من أجل الإنجاب. وهناك أسباب وأنواع متعددة لأكياس المبيض ومنها الأكياس الفسيولوجية أو الوظيفية والحمل خارج الرحم و خارج المبيض وقناة فالوب وبطانة الرحم المهاجرة وكذلك الأورام الحميدة والخبيثة للمبيض. وأكثر أنواع أكياس المبيض الحميدة شيوعاً هي أكياس مصلية وميوسينية وأكياس بطانة الرحم المهاجرة وأورام مسخية كيسية ناضجة.

الهدف من البحث: تقييم تأثير إستئصال أكياس المبيض على حجم المبيض، عدد الجريبات الطرفية وكذلك دوبلر المبيض.

المريضات وطرق البحث: تم تنفيذ هذه الدراسة على 80 امرأة قد تعرضن لاستئصال بالمنظار من كيس واحد علي أحد المبيضين والذين تم حزمهم بمستشفى 15 مايو التخصصي وتم التشخيص عن طريق السونار المهبلي وتأكيد التشخيص عن طريق منظار البطن.

نتائج البحث: توجد علاقة إحصائية إيجابية بين إستئصال كيس المبيض بالمنظار وضعف مخزون المبيض بعد الجراحة.

الاستنتاج: إستئصال كيس المبيض بالمنظار يؤدي إلي ضعف مخزون المبيض بعد الجراحة وهناك حاجة إلي طرق جديدة لاستئصال أكياس الرحم للحفاظ علي مخزون المبيض وخاصة في حالات تأخر الإنجاب.

الكلمات الدالة: عدد الجريبات الغارية، الموجات فوق الصوتية عبر المهبل، قياس سرعة دوبلر المبيض، إستئصال كيس المبيض بالمنظار.