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## Research Article

# Direct Proportional Relationship between Histopathologic and Sonographic Analysis of Laparoscopic Removal Ovarian Endometriotic Cyst: Evaluating the Effects on Ovarian Reserve

## Abstract

**Background:** The aim of this study was to evaluate ovarian damage following laparoscopic endometrioma cystectomy using ultrasound and pathologic samples.

**Materials and Methods:** This is a prospective cohort study in General Women Hospital affiliated to Tehran University of Medical Sciences. 40 patients with endometrioma, total of 44 cysts including bilateral cysts, underwent laparoscopic cystectomy with stripping technique. Amount of excised parenchyma, number of lost oocytes and cyst wall fibrosis thickness were histologically studied. Before and 3 months after surgery antral follicle count was evaluated by ultrasound.

**Results:** Mean antral follicle count (AFC) before the operation was  $4 \pm 1.29$  and after operation was  $1.64 \pm 1.03$ . The reduction in AFC after cystectomy was statistically significant ( $P < 0.000$ ), and with each 1 centimeter increase in cyst diameter a reduction of AFC averaging 0.421 was observed. On pathological examination, it was shown that every millimeter of inadvertently excised ovarian tissue and cyst wall fibrosis thickness leads to reduction of 1.06 and 1.2 in AFC respectively.

**Conclusion:** Laparoscopic cystectomy for endometrioma is associated with reduction in ovarian reserve and this reduces proportionally with cyst diameter, amount of normal ovarian parenchyma excised and cyst wall fibrosis.

## Introduction

Ovarian reserve is the functional potential of ovaries and is defined by number and quality of oocytes within them [1]. Total number of oocytes is determined by genetic factors; from 1–2 million oocytes at birth to 300,000 at puberty, 25000 at age 40 and less than 1000 at menopause. Diminishing ovarian reserve happens steadily with age [2]. Ovarian reserve tests reflect qualitative and quantitative aspects of ovarian reserve [3], and are divided into 2types: static and dynamic tests [4]. Static laboratory tests include FSH, estradiol, LH, serum Anti-Müllerian hormone (AMH), B-inhibin level and LH/FSH ratio. Static sonographic tests include ovarian volume, antral follicle count (AFC) and ovarian stromal blood flow (Abha 4). Dynamic tests are clomiphene citrate challenge test, GnRH agonist stimulation test and xogenous FSH ovarian reserve test (EFORT) [4].

Laparoscopic cystectomy is the gold standard approach for ovarian endometriomas [5], and other benign symptomatic cysts that are resistant to therapies [6]. The most commonly used technique in ovarian cystectomy is stripping [7,8]. When excising the endometrioma wall with the stripping technique, recurrent bleeding are controlled by sutures or bipolar coagulation; thus it is possible that the adjacent normal ovarian tissue get damaged due to focal pressure or hypoxia or the inadvertent resection [9–11]. The objective of this trial was to evaluate ovarian damage following laparoscopic endometrioma cystectomy using ultrasound and pathology samples.

## Materials and Methods

This is a prospective cohort study conducted between May, 2011 and December, 2012 in women hospital affiliated to Tehran University of Medical Sciences. 40 patients with

endometrioma, total of 44 cysts including bilateral cysts, were included and studied by ultrasound and pathology.

Inclusion criteria were as follows: 1) Age between 15-35, 2) having regular menses (21-35 days), 3) Benign cysts, 4) No history of endocrine disease, 5) No history of surgery on ovaries, 6) No medical conditions that can affect gonadal function, 7) Consent for being included in the study.

After obtaining informed consent from the patients, demographic data was collected using a questionnaire. Transvaginal ultrasound with an 8 Mega Hz probe (sonoline-G40, SIEMENS) was performed by one particular radiologist during the follicular phase (before day 10 of the menstrual cycle). Size and morphology of cysts and number of antral follicles (all follicles 2-10mm) in both ovaries were reported. Patients' demographic data and information related to cysts are illustrated in Table 1.

Laparoscopic cystectomy using stripping technique was carried out by 3 gynecology professors, all laparoscopic surgeries were performed in our hospital under general anesthesia. Direct three-port laparoscopy has been used with an umbilical 10 mm port and two additional 5mm port for the scope and operating respectively (Olympus). Laparoscopic procedure has been done from both suprainguinal regions under direct laparoscopic observation. Adhesiolysis and mobilization of the ovaries were performed completely, however if required an incision was made at the antimesenteric site of the cysts. Dissection of cysts have been done by traction and countertraction with two atraumatic 5 mm grasping forceps. Bleeding was blocked by bipolar cauterization of the minimally required area for the shortest possible duration to avoid thermal damage to the ovarian cortex. None of the operated ovaries were sutured. The excised ovarian specimen was sent for pathological analysis. Histological specimens of excised endometriomas were reviewed by one pathologist (s.s.), who carried out serial sections and randomly chose, for each section, 2-3 70. Different sites to measure the thickness of glandular epithelium and stroma, of subjacent fibrosis, depending on the cyst, and of the ovarian parenchyma removed with the cyst, according to reference [12]. The same pathologist recorded kind of cysts, amount of parenchyma, ovarian oocyte loss and fibrosis in cyst's wall.

3 months postoperative patients underwent ultrasound by the same blinded radiologist and the numbers of antral follicles were reported.

Respectively statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 18.0. mean and standard deviation for quantitative parameters were calculated. Qualitative variables were expressed in frequency and percentage. The relationship between quantitative parameters and reduced number of antral follicles were calculated by general linear model (univariate – multivariate).

Numbers of follicles per ovary before and after surgery were compared using nonparametric signed-rank Wilcoxon test.

## Results

In total, 44 ovarian endometriomas in 40 women were managed by cystectomy. No complications during and after surgery occurred, and the patients were discharged within 24 hours after the operation. Clinical features of ovarian endometriotic cysts treated with laparoscopy was reported in Table 2.

Antral follicle count was found to be significantly reduced after excision ( $P < 0.001$ ). The relationship between size of the excised cyst and reduction of antral follicle count was statistically significant ( $P < 0.001$ ). Our results suggest that an increase in cyst diameter of 1 cm leads to reduction of AFC averaging 0.421.

We found a tendency towards a positive correlation between cyst diameter and fibrosis layer thickness (each 1 cm leads to 0.205mm fibrosis) and also to an increase in a removed supplementary thickness of the ovarian parenchyma averaging 0.352mm.

An increase of 1mm in removed thickness of parenchyma leads to 1.06 loss of AFC which was statistically significant. Every mm increase in the cyst wall fibrosis thickness was associated with 1.2 reduction of AFC. Relationship of the number of lost oocytes and reduced AFC was statistically significant (each lost oocyte 0.033 reduced AFC).

Increase of 1 mm in fibrosis layer thickness was associated with an increase of removed parenchyma thickness averaging 1.016 mm. The relationship between the number of lost oocyte and removed thickness of parenchyma was statistically Significant ( $P = 0.036$ ). An increase of 1mm in removed thickness of parenchyma leads to increase 6.02 the number of lost oocytes.

**Table 1:** Characteristics of patients enrolled in the study.

Age (yrs) Mean $\pm$ SD	26.23 $\pm$ 4.82	
Body Mass Index (BMI)(kg/m <sup>2</sup> ) Mean $\pm$ SD	22.54 $\pm$ 2.12	
Diameter of cyst (cm) Mean $\pm$ SD	5.57 $\pm$ 1.75	
Ovarian side/No. (%)	left	32
	right	4
	Bilateral	4
Gravidity/No. (%)	virgin	13(32.5%)
	nulligravida	18(45%)
	$\geq$ G1	9(22.5%)
Blood group/No. (%)	O	27(67.5%)
	A	10(25%)
	B	3(7.5%)

**Table 2:** Clinical features of ovarian endometriotic cysts treated with laparoscopy.

Endometriosis Stage/No. (%)	II	3(7.5)
	III	31(77.5)
	IV	6(15)
Operating time(min)	75 $\pm$ 22.3	
Resection time(min)	10.3 $\pm$ 6.12	

The relationship between cyst size, cyst wall fibrosis thickness and lost a number of follicles during cystectomy was not significant.

There were no statistical significant relationships between the thickness of ovarian parenchyma removed and bilateral endometrioma and staging of endometriosis.

## Discussion

According to our best knowledge, this the first study that has reported the number of antral follicles after laparoscopy concurrent with histopathologic changes. On the basis of our findings, endometrioma cystectomy leads to reduction in antral follicle count averaging 59% and this reduction is more significant in cysts with larger diameter [13].

in a study included 32 patients who underwent laparoscopic cystectomy for endometrioma showed 53% reduction in antral follicle count in comparison with the contra lateral intact ovary compared AFC following electrocoagulation and suture after laparoscopic stripping of ovarian endometrioma in 22 patients and reported a statistically significant reduction in ovarian reserve in all patients undergoing stripping [14]. These are all in agreement with a Metaanalysis on 21 studies in 2011 which showed reduced ovarian reserve after cystectomy of endometrioma [15]. The number of follicles after the operation in other studies has been shown in Table 3.

Histopathologic studies have shown removal of normal ovarian parenchyma following cystectomy [16,17]. In our study, the amount of normal ovarian tissue resected during laparoscopy had a significant direct relationship with cyst wall fibrosis thickness and number of lost oocytes. The more normal parenchyma was resected the more reduction in antral follicle count occurred.

Muzzi et al. (2002), reported that in only 6% of cases with well-defined cysts including dermoid cysts, serous cysts and mucinous cystadenoma Ovarian tissue was inadvertently excised during cystectomy and this rate for endometrioma cysts was 54%–69% [12,18]. Maneschi's study in 1993 is in agreement with this [19]. Dogan et al. (2011) [20], reported that in 127 cysts including 61 endometrioma and 66 non-endometriosis cysts underwent cystectomy and in 92% and

82% of samples normal ovarian tissue adjacent to cyst was detected respectively, the amount of removed tissue was more in endometriomas (1.64±1.35 versus 1.11±1.22, p=0.022) [21]. In our study, 91% of cyst excisions were associated with ovarian parenchyma removal.

In a study by Kuroda et al. (2012) on pathology samples, the amount of normal ovarian parenchyma excised inadvertently in cyst endometriomas was significantly higher than non endometriomas [22].

Roman et al. (2010), conducted a study including 38 endometrioma cystectomies and found a significant correlation between the amounts of normal ovarian parenchyma removed during endometrioma cystectomy and cyst diameter and reported that an increase in cyst diameter of 1cm leads to removal of 200micrometer supplementary ovarian parenchyma [23]. In our study, every centimeter increase in cyst diameter leads to an increase in removed supplementary thickness of the ovarian parenchyma averaging 0.352mm. An increase of 1mm in removed thickness of parenchyma leads to 1.06 loss of AFC. Several authors have reported that inadvertent removal of ovarian tissue is even more frequent where surgeons considered that the stripping procedure was easy to perform [12].

This means that the hypothetical cleavage plan, which surgeons might intraoperatively identify around the cyst, is in fact not located between the endometrioma fibrous wall and ovarian parenchyma, but rather within the ovarian tissue itself, and is due to the strong fusion between the ovarian parenchyma and fibrosis [16]. However, the question is remained: Does with finding the fibrous tissue and sharp removing the cyst from ovarian parenchyma through fibrous region can be reduce the damage to ovarian reserved.

## Conclusion

The results of the present study support that laparoscopic cystectomy for endometrioma is associated with a significant reduction in ovarian reserve and this has a direct correlation with cyst size and amount of normal ovarian

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**Table 3:** Studies comparing The number of follicles in follicles after the operated and in the Contralateral not operated ovary during IVF techniques.

Authors	Operated Ovary	Control Ovary	P
Rogni et al. [24]	1.8±1.8	4.5±2.0	<0.001
duru et al. [25]	3.1±1.8	4.4±1.0	<0.05
Somigliana et al. [13]	2±1.5	4.2±2.5	<0.001
HO et al. [11]	1.9±1.5	3.3±1.5	<0.001
Loh et al HO et al. [10]	4.6	3.6	n.s
Alborzi et al. [26]	3.2±1.1	3.2±1.7	n.s
Almog et al. [27]	4.5±3.8	7.4±5.2	0.05
Benaglia et al. [28]	3.4±2.4	5.7±3.0	<0.001
Shimizo et al. [21] (Laser ablation)	4.2±2.7	7.3±3.6	n.s

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