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Effects of ovarian cyst types on ovarian reserve after three-dimensional laparoscopic cystectomy

Üç boyutlu laparoskopik kistektomi sonrası yumurtalık kisti tiplerinin yumurtalık rezervi üzerindeki etkileri

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Abstract

Objective: This study aims to compare the effects of three-dimensional (3D) laparoscopic ovarian cystectomy on ovarian reserve according to different types of ovarian cysts.

Materials and Methods: Participants who underwent surgical treatment for ovarian cysts between 2018 and 2020 were included in this study. Anti-müllerian hormone (AMH) and follicle-stimulating hormone (FSH) levels were measured before surgery and six months postoperatively. All procedures were performed under general anesthesia using 3D laparoscopy. Participants were classified into three groups based on histopathological findings: group 1, endometriomas; group 2, mature cystic teratomas (dermoid cysts); and group 3, serous or mucinous cystadenomas.

Results: A total of 51 women were included in the study. No significant differences were observed between the groups in terms of perioperative variables such as operation time, intraoperative blood loss, postoperative hemoglobin decrease, and maximum cyst diameter. There were also no significant differences among the groups in preoperative AMH (p=0.97) and FSH (p=0.22) levels. Postoperative AMH levels were significantly lower than preoperative values in both the endometrioma group (p<0.001) and the dermoid cyst group (p=0.004). The reduction in AMH levels was more pronounced in the endometrioma group compared to the other groups. Postoperative FSH levels tended to increase in all groups compared to preoperative levels; however, this increase was not statistically significant (p=0.092).

Conclusion: 3D laparoscopic cystectomy for the removal of endometriomas and dermoid cysts significantly reduces ovarian reserve. In contrast, laparoscopic cystectomy for serous or mucinous cysts appears to have no significant impact on ovarian reserve.

Keywords: 3D laparoscopy, AMH, dermoid cyst, endometrioma ovarian cyst, ovarian reserve

Öz

Amaç: Çalışmamızın amacı, farklı kist tipleri açısından üç boyutlu (3D) laparoskopik over kistektomisinin over rezervi üzerindeki etkisini karşılaştırmaktır.

Gereç ve Yöntemler: Çalışmamıza 2018-2020 yılları arasında over kistleri nedeniyle cerrahi tedavi görecek katılımcılar dahil edildi. Katılımcıların anti-müller hormon (AMH) ve folikül uyarıcı hormon (FSH) düzeyleri ameliyat öncesi ve ameliyattan 6 ay sonra ölçüldü. Tüm ameliyatlar genel anestezi altında ve 3D laparoskopi ile gerçekleştirildi. Histopatolojik değerlendirmeden sonra katılımcılar üç gruba ayrıldı; grup 1: Endometrioma, grup 2: Olgun kistik teratom (dermoid kist) ve grup 3: Seröz veya müsinöz kistadenom.

PRECIS: Three-dimensional laparoscopic cystectomy significantly reduces ovarian reserve in endometrioma and dermoid cysts but not in serous-mucinous cysts, highlighting cyst-type-specific impacts on ovarian function.

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Bulgular: Çalışmaya toplam 51 kadın dahil edildi. Gruplar arasında ameliyat süresi, intraoperatif kan kaybı, postoperatif hemoglobin azalması ve maksimum kist çapı gibi perioperatif bulgular açısından anlamlı bir fark bulunmadı. Gruplar arasında preoperatif AMH (p=0,97) ve preoperatif FSH (p=0,22) değerleri açısından anlamlı bir fark yoktu. Endometrioma (p<0,001) ve dermoid kist (p=0,004) gruplarında postoperatif AMH değerleri preoperatif AMH değerlerine kıyasla anlamlı derecede düşüktü. Preoperatif ve postoperatif AMH azalması endometriozis grubunda diğer gruplara göre daha belirgindi. Tüm gruplardaki postoperatif FSH seviyeleri preoperatif seviyelere kıyasla artma eğilimindeydi, ancak artış anlamlı bir seviyeye ulaşmadı (p=0,092).

Sonuç: Endometrioma ve dermoid kistleri çıkarmak için yapılan 3D laparoskopik kistektomi over rezervini önemli ölçüde azaltır. Seröz-müsinöz kistler için yapılan laparoskopik kistektomi over rezervi etkilemez.

Anahtar Kelimeler: 3D laparoskopi, AMH, dermoid kist, endometrioma, over kisti, over rezervi

Introduction

Ovarian cysts affect approximately 7% of women during their lifetime and are particularly common during the reproductive years[1]. Given that ovarian cysts often become symptomatic during the reproductive years, fertility preservation is a primary concern in their management. For clinicians, this concern is typically assessed through evaluation of ovarian reserve (OR).

While age remains the leading factor influencing OR, medical interventions like surgery, radiation, and chemotherapy can also have a negative impact on its status[2]. Several biochemical and ultrasonographic markers are used to assess OR. Among these, anti-müllerian hormone (AMH) stands out as a reliable and practical indicator[3]. Moreover, AMH serves as a sensitive marker for assessing iatrogenic damage to ovarian function[4]. In addition, the measurement of basal follicle-stimulating hormone (FSH) levels is a well-established, straightforward, and reliable method for assessing OR[5]. FSH is a glycoprotein polypeptide hormone produced by the gonadotropic cells of the anterior pituitary gland[6].

Although simple functional cysts are typically managed conservatively to preserve OR during reproductive age, surgical intervention is often indicated for cyst types such as endometriomas and mature cystic teratomas, which are unlikely to resolve spontaneously, particularly in the presence of suspicious ultrasonographic findings.

Laparoscopic ovarian cystectomy is the preferred surgical method for ovarian cysts suspected to be benign. Although this procedure is typically regarded as fertility-preserving, recent concerns have arisen about its possible effects on OR. During cyst enucleation, there is a risk of unintentionally removing healthy ovarian tissue or causing mechanical or thermal damage to the ovarian cortex[1]. Literature presents conflicting evidence, and no definitive conclusions have been reached regarding this issue.

Another unresolved question in the literature concerns the comparative advantages of two-dimensional (2D) versus three-dimensional (3D) laparoscopy. 3D laparoscopy offers enhanced depth perception and spatial orientation compared to conventional 2D laparoscopy, potentially enabling greater surgical precision. This improved precision may enhance the surgeon's performance during laparoscopic ovarian procedures and help mitigate the negative impact on OR. Several studies have demonstrated the specific advantages of 3D laparoscopy, particularly during the dissection and laparoscopic suturing phases[7].

This study was designed to evaluate the impact of cystectomy performed using 3D laparoscopy on OR across different cyst types, with the aim of contributing to the clinical management of such cases.

Materials and Methods

Patients who presented to the Department of Obstetrics and Gynecology at Ege University Faculty of Medicine between 2018 and 2020, and underwent surgical treatment for ovarian cysts were evaluated for inclusion in this prospective cohort study based on predefined inclusion and exclusion criteria. All participants were informed about the study both verbally and in writing, and written informed consent was obtained prior to enrollment. The study protocol was approved by the Ethics Committee of Ege University Faculty of Medicine on April 29, 2016 (approval number: 16-4T/56). This research was supported by the Ege University Scientific Research Projects Coordination Unit under project number 17-TIP-056. All procedures in this study were carried out in compliance with the ethical guidelines established by the institutional research committee, the 1964 Declaration of Helsinki, and its subsequent revisions or equivalent ethical standards. The study was registered at ClinicalTrials.gov (NCT05054946).

The inclusion criteria were defined as being between 18 and 40 years of age and having no history of prior ovarian surgery, to standardize the cohort and eliminate potential iatrogenic effects on OR. Exclusion criteria consisted of the presence of endocrinological disorders, suspected malignancy based on preoperative laboratory and ultrasonographic assessments, or histopathological confirmation of malignancy, as these factors could influence OR. The main outcome measure was serum AMH levels, which were evaluated six months after surgery.

All participants underwent a preoperative evaluation of cyst size and morphology using either transvaginal or transabdominal ultrasonography (Voluson E8, GE Healthcare, Chicago, IL, USA) employing a RAB 4-8D 4D transabdominal probe and a multifrequency 5-7.5 MHz transvaginal probe. Cyst size was calculated by averaging the maximum diameter and the diameter perpendicular to it as measured during ultrasonographic examination. Blood samples were collected from all participants during the early follicular phase (days 1-5 of the menstrual cycle) following 8-10 hours of fasting. The

same procedure was repeated for six months postoperatively. To measure serum AMH concentrations, blood samples were first centrifuged at 1600 g for 10 minutes. The separated serum fractions were then preserved at -80 °C until the completion of sample collection from all participants. Subsequently, AMH levels were analyzed in batches using the AMH Gen II ELISA kit provided by Beckman Coulter Inc. (Brea, CA, USA). For FSH measurement, blood samples were collected in separator gel tubes, centrifuged at 1400 g for 10 minutes, and analyzed using the Beckman Coulter DXI 800 immunoassay system (Beckman Coulter Inc., Brea, CA, USA).

Based on histopathological findings, the participants were classified into three distinct groups: Group 1 included cases of endometrioma, group 2 comprised mature cystic teratomas (dermoid cysts), and group 3 encompassed serous or mucinous cystadenomas. During surgery, the cyst wall was carefully dissected and stripped from the adjacent normal ovarian tissue. Hemostasis was achieved by applying bipolar coagulation at bleeding sites. When required, ovarian reconstruction was performed using a 4-0 absorbable suture (polyglycolic acid, Vicryl Rapide™, Ethicon, Germany). To minimize the risk of postoperative adhesion, the surgical field was irrigated extensively with warm saline. All participants were discharged on the first postoperative day following an uneventful recovery period.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). The distribution of variables was examined through the Kolmogorov-Smirnov test. For continuous variables, descriptive statistics are presented as mean ± standard deviation for normally distributed data and as median (range) for non-normally distributed data. Categorical variables are represented as frequencies and percentages [n (%)]. The chi-square test or Fisher's exact test was used for comparing categorical variables, as appropriate. For continuous variables, the Student's t-test was applied when the data followed a normal distribution, while the Mann-Whitney U test was used for non-normally distributed data. A p-value of <0.05 was considered statistically significant.

Results

According to the inclusion criteria, 51 participants were initially enrolled in the study. However, four participants with hypothyroidism, three with malignancies identified through frozen section and final histopathological evaluation, and one who failed to attend the 6-month follow-up were subsequently excluded. No participants declined to participate in the study. Consequently, a total of 43 participants were included in the final analysis.

The mean age of the participants was 28.19±6.14 years in the endometrioma group (n=16), 28.38±6.70 years in the dermoid cyst group, and 26.82±5.72 years in the serous or mucinous cystadenoma group. No significant differences were observed between the groups regarding age, gravidity, or parity (Table 1).

The mean operative times were 68.13±21.86 minutes in the endometrioma group, 74.38±28.10 minutes in the dermoid cyst group, and 77.73±25.53 minutes in the serous/mucinous cyst group. There were no significant differences between the groups (p=0.56) (Table 2). Intraoperative blood loss and postoperative hemoglobin decrease were as follows: 83.75±95.57 mL and 1.55±0.78 g/dL in the endometrioma group; 35.00±35.37 mL and 1.56±1.03 g/dL in the dermoid cyst group; and 71.09±58.00 mL and 1.42±0.77 g/dL in the serous/mucinous cyst group. There were no statistically significant differences among the groups in terms of intraoperative blood loss (p=0.054) or postoperative hemoglobin reduction (p=0.9) (Table 2).

The mean maximum cyst diameters were 54.65±14.91 mm in the endometrioma group, 51.68±16.16 mm in the dermoid cyst group, and 56.09±8.75 mm in the serous/mucinous cyst group. No significant differences were found between the groups regarding cyst diameter (p=0.7) (Table 2).

Preoperative AMH levels were 4.20±3.27 ng/mL in the endometrioma group, 4.40±4.28 ng/mL in the dermoid cyst group, and 4.14±3.06 ng/mL in the serous/mucinous cyst group. The mean preoperative FSH levels were 6.56±2.58 mIU/mL, 6.51±2.46 mIU/mL, and 7.34±0.98 mIU/mL in the endometrioma, dermoid cyst, and serous/mucinous cyst groups, respectively. There were no significant differences among the groups in terms of preoperative AMH (p=0.97) or FSH levels (p=0.22) (Table 3).

Table 1. Patients' characteristics

	Endometrioma (n=16)		Dermoid cyst (n=16)		Serous or mucinous cystadenoma (n=11)		p
	Mean SD	Median (Min-Max)	Mean SD	Median (Min-Max)	Mean SD	Median (Min-Max)	
Age (year)	28.19±6.14	27 (19-39)	28.38±6.70	29 (18-40)	26.82±5.72	25 (20-37)	0.79
Gravida	0.44±1.0	0 (0-4)	0.94±1.28	0 (0-4)	0.45±0.93	0 (0-3)	0.37
Parity	0.38±0.80	0 (0-3)	0.50±0.73	0 (0-2)	0.36±0.67	0 (0-2)	0.73

SD: Standard deviation, Min: Minimum, Max: Maximum

Group-wise analysis revealed a significant postoperative decline in AMH levels compared to preoperative values in both the endometrioma group (p<0.001) and the dermoid cyst group (p=0.004). In contrast, the serous/mucinous cyst group did not exhibit a statistically significant change in AMH levels postoperatively (p=0.297). The reduction in AMH was more pronounced in the endometrioma and dermoid cyst groups compared to the serous/mucinous cyst group (Figure 1). However, no significant difference was found between the endometrioma and dermoid cyst groups in terms of AMH reduction.

Comparison of preoperative and postoperative FSH levels showed a trend toward increased postoperative FSH values across all three groups; however, this increase did not reach statistical significance (p=0.092) (Figure 2).

No significant differences were observed among the three groups regarding postoperative AMH (p=0.14) and FSH (p=0.15) levels.

Table 2. Peri-operative findings

	Endometrioma (n=16)		Dermoid cyst (n=16)		Serous or mucinous cystadenoma (n=11)		p
	Mean SD	Median (Min-Max)	Mean SD	Median (Min-Max)	Mean SD	Median (Min-Max)	
Surgery time (min)	68.13±21.86	61 (45-110)	74.38±28.10	70 (35-130)	77.73±25.53	70 (40-120)	0.56
Blood loss (mL)	83.75±95.57	52.50 (10-400)	35.00±35.37	22.50 (2-110)	71.09±58.00	50 (10-190)	0.054
Hb change	1.55±0.78	1.45 (0.60-3.10)	1.56±1.03	1.30 (0.50-4.20)	1.42±0.77	1.20 (0.50-2.50)	0.9
Max cyst diameter (mm)	54.65±14.91	51 (34-81)	51.68±16.16	52.75 (23.5-74)	56.09±8.75	55 (40-75.5)	0.70

SD: Standard deviation, Min: Minimum, Max: Maximum, Hb: Hemoglobin, min: Minutes

Table 3. Ovarian reserve markers

	Endometrioma (n=16)		Dermoid cyst (n=16)		Serous or mucinous cystadenoma (n=11)		p
	Mean SD	Median (Min-Max)	Mean SD	Median (Min-Max)	Mean SD	Median (Min-Max)	
Preop AMH (ng/mL)	4.20±3.27	2.76 (0.67-10.94)	4.40±4.28	2.52 (0.81-16.12)	4.14±3.06	4.09 (0.67-9.42)	0.97
Postop AMH (ng/mL)	2.14±2.24	1.59 (0.15-7.84)	3.16±2.88	2.27 (0.50-11.8)	3.63±3.24	2.49 (0.92-11.81)	0.14
Preop FSH (mlU/mL)	6.56±2.58	7.14 (0.30-10.09)	6.51±2.46	6.56 (1.68-10.77)	7.34±0.98	7.08 (6.31-9.89)	0.22
Postop FSH (mlU/mL)	7.67±3.51	6.78 (2.94-16.66)	7.12±3.43	7.30 (1.45-16.41)	8.33±1.31	8.13 (5.65-10.4)	0.15

SD: Standard deviation, Min: Minimum, Max: Maximum, AMH: Anti-müllerian hormone, FSH: Follicle-stimulating hormone, Preop: Preoperative, Postop: Postoperative

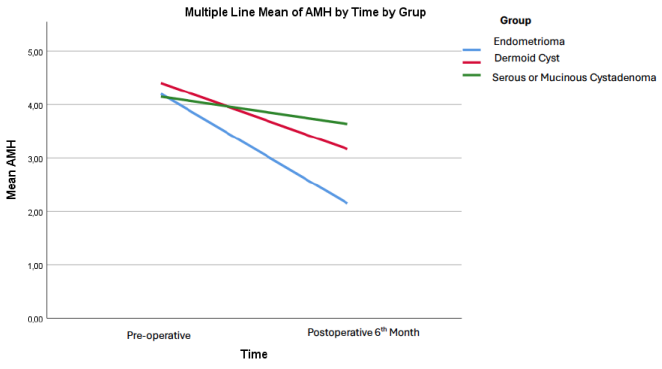

Figure 1. xx

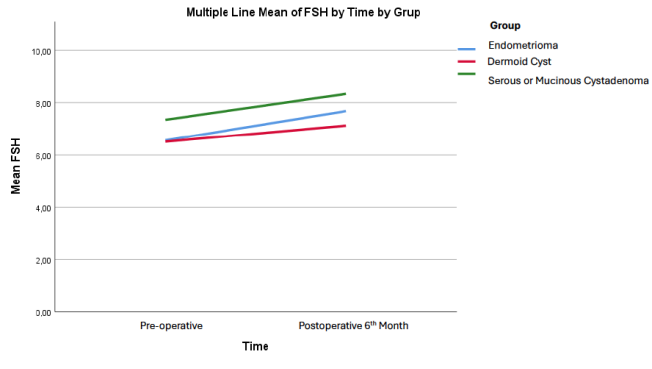

Figure 2. xx

Discussion

In this prospective cohort study, the impact of 3D laparoscopic ovarian cystectomy on OR was evaluated with respect to varying types of ovarian cysts. The analysis demonstrated no statistically significant differences in preoperative AMH (p=0.97) or FSH (p=0.22) levels among the groups, suggesting that the presence of endometriomas, dermoid cysts, or serous/mucinous cysts does not independently influence baseline OR. However, by the end of the study, surgical intervention for endometriomas and dermoid cysts was associated with a significant decline in OR, whereas no such impact was observed in patients with serous or mucinous cysts.

Endometrioma is defined as the presence of ectopic endometrial tissue within the ovary. Surgical treatment is often indicated to alleviate pelvic pain, prevent complications such as cyst rupture or ovarian torsion, exclude malignancy, and address infertility. Among its potential complications are ovarian torsion and spontaneous rupture. In subfertile patients, surgical removal of endometriomas has been associated with improved pregnancy rates[8]. While surgical treatment of endometriomas has been shown to increase spontaneous pregnancy rates, it does not appear to significantly influence the outcomes of in vitro fertilization[8]. Whether endometriomas impair ovarian function remains a subject of ongoing debate. In a study evaluating 1,199 cycles in 244 women with unilateral endometrioma, ovulation was found to occur at similar rates in both the affected and unaffected ovaries[9]. In contrast, a meta-analysis encompassing eight studies demonstrated that endometrioma excision led to an average reduction of 38% in serum AMH levels, suggesting a potentially detrimental effect on OR[10]. OR loss is higher in recurrent surgeries compared to one definitive surgery[11]. Therefore, repetitive ovarian endometrioma surgeries should be avoided as much as possible. The recurrence rate of endometriomas is up to 25%[12]. Postoperative hormonal suppression options should be considered to avoid repetitive surgeries.

Ovarian germ cell tumors arise from ovarian primordial germ cells and constitute 20-25% of ovarian neoplasms. Malignancies are detected in only 5% of these neoplasms[13]. These tumors usually affect females between the ages of 10 to 30. Benign cystic mature teratomas, also known as dermoid cysts, are the most frequently encountered ovarian germ cell tumors. Almost all are benign[14]. Surgery is recommended for confirmation of diagnosis, exclusion of malignancy, preservation of OR, prevention of complications such as torsion and rupture, and relieving symptoms, if any. The abdomen should be washed with plenty of water to avoid chemical peritonitis at the end of the surgery.

Serous and mucinous cystadenomas are the most common benign ovarian neoplasms. These cysts may be thin-walled, unilocular, or multilocular, and typically range in size from 5 to 20 cm. Mucinous cysts are less common than serous cysts and are more frequently multilocular. Histologically, the inner lining of serous cysts resembles tubal epithelium, whereas mucinous cysts are usually lined with endocervical or gastrointestinal-type epithelium. Most serous and mucinous cystadenomas are asymptomatic and are often detected incidentally during ultrasound examinations.

According to current literature, surgical excision of endometriomas is generally associated with a more substantial decline in OR compared to other cyst types. The impact of dermoid cyst removal on OR remains controversial. One study investigating the early postoperative effects of laparoscopic unilateral ovarian cystectomy reported comparable reductions in AMH levels in both the endometrioma and dermoid cyst groups, with significantly smaller decreases observed in the simple cyst group[15]. Although our study focuses on longer-term outcomes, these findings align with our observations.

Cyst size also plays a role in OR outcomes. Henes et al.[16] demonstrated a significant AMH decrease post-surgery only in women with cysts ≥5 cm. Conversely, Lind et al.[1] reported that factors such as cyst size, patient age, timing of surgery, and intraoperative blood loss did not significantly influence OR. In their study, which included 75 women undergoing ovarian surgery, AMH levels were measured preoperatively and at six months postoperatively. A significant reduction in AMH levels was observed in patients with endometriomas when compared to those with dermoid cysts. While a postoperative decrease in AMH was also noted in the functional cyst group, it did not reach statistical significance. Interestingly, the study revealed that patients with elevated baseline AMH levels (AMH >4 ng/mL) experienced a more substantial decrease in AMH six months after surgery compared to those with normal or low baseline AMH levels[1]. Our findings are consistent with previous research, demonstrating a greater decline in OR in the endometrioma group compared to the dermoid cyst group. However, this difference did not reach statistical significance.

In another prospective observational study involving 71 women undergoing their first unilateral ovarian cystectomy via laparoscopy, investigators assessed antral follicle count, ovarian volume, resistance index, and OR at six months postoperatively. The aim was to evaluate the impact of different cyst types on OR by comparing the operated ovary with the contralateral one. The study concluded that surgical intervention led to a reduction in OR, regardless of cyst type[17]. This study is inconsistent with many studies in the literature and our study.

A retrospective evaluation of 97 patients revealed that postoperative AMH levels declined more markedly in individuals with endometrioma than in those with other types of benign ovarian cysts. Furthermore, an inverse correlation was identified between cyst size and preoperative AMH concentrations[18].

The reduction in OR following endometrioma excision is primarily attributed to the unintentional removal of healthy

ovarian tissue, which may occur due to the invaginating nature of the cyst into the ovarian cortex[19]. While the reduction in OR following endometrioma excision can be explained by the mechanisms described above; the decline associated with dermoid cyst removal is thought to result from the cyst's firm adhesion to the ovarian tissue and the hemostatic techniques employed during surgery[1]. Conversely, the reduction in OR during dermoid cyst removal is often attributed to cyst adherence and the hemostatic methods employed.

3D laparoscopy has been reported to provide significant benefits in complex surgical procedures, including improved image quality, reduced operative time, and decreased intraoperative blood loss. Despite these advancements, particularly enhanced depth perception and greater surgical precision, our study demonstrated that the use of 3D laparoscopy in ovarian surgery did not prevent the decline in OR associated with different cyst types[20,21]. While we observed significant postoperative AMH reductions in the endometrioma and dermoid cyst groups, FSH levels did not show a similar pattern, possibly due to differing kinetics during the menstrual cycle compared to AMH. The findings of our study are further substantiated by the recent systematic reviews and meta-analyses conducted by Moreno-Sepulveda et al.[22] and Samartzis et al.[23], both of which emphasize the limited efficacy of current surgical techniques in preserving OR during endometrioma surgery. Their conclusions resonate with our observations, reinforcing the notion that despite advancements in surgical approaches, the preservation of ovarian function remains a significant clinical challenge.

Study Limitations

Our study's strengths include its prospective design, robust sample size across various cyst types, and standardized surgical protocols by experienced minimally invasive surgeons at a tertiary university hospital. Future studies could explore additional factors influencing OR outcomes post-ovarian cystectomy, including long-term hormonal assessments and fertility outcomes.

Conclusion

This study demonstrates that 3D laparoscopic cystectomy for endometriomas and dermoid cysts is associated with a significant reduction in OR, whereas cystectomy for serous and mucinous cysts does not appear to have a significant impact. Preoperative assessment of OR and appropriate patient counseling regarding potential fertility implications are particularly important for reproductive-aged women undergoing ovarian cyst surgery.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Ege University Faculty of Medicine on April 29, 2016 (approval number: 16-4T/56).

Informed Consent: Written informed consent was obtained prior to enrollment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.Ö.Y., T.Ç., Concept: S.A.A., A.M.E., M.C.T., İ.M.İ., Design: S.A.A., A.M.E., M.C.T., İ.M.İ., Data Collection or Processing: Ç.Ş., Analysis or Interpretation: Ç.Ş., A.A., Literature Search: S.A.A., T.Ç., Writing: S.A.A., M.C.T., İ.M.İ.

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