



Is there Any Difference between the Patients with Primary Endometriomas and those with Recurrent Endometriomas?

Reküren Endometriyoma Nedeniyle Opere Olan Hastalar ile İlk Kez Opere Olan Hastalar Arasında Herhangi Bir Fark Var mıdır?

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Abstract / Öz

Introduction: Repeated surgery for recurrent endometriomas is harmful to the ovarian reserve. The aim of the study was to identify predictive factors determining recurrence of endometriomas based on demographic and clinical characteristics.

Methods: A total of 151 patients who underwent surgery for endometriomas between May 2014 and May 2016 were included in this retrospective cohort study. The patients were grouped according to the presence of recurrent surgery for endometriomas and compared based on demographic and clinical characteristics.

Results: A total of 8 patients had repeated surgery for recurrent endometriomas. The patients with recurrent endometriomas had larger cysts and higher cancer antigen-125 levels. There is no statistically significant difference between patients who underwent surgical treatment primarily or secondarily.

Conclusion: There was no significant difference found in patients who underwent primary or secondary surgery for endometriomas according to demographic and clinical characteristics. It was found that it is not possible to predict the patients in whom endometriomas will recur. Therefore, excision of the cyst in the first surgery should be carefully performed to minimize the ovarian damage and delay recurrence.

Keywords: Endometrioma, recurrence, laparoscopy, ovarian damage

Amaç: Reküren endometriyoma nedeniyle tekrarlayan cerrahi, over rezervine zarar vermektedir. Çalışmamızın amacı, endometriyoması olan hastaların demografik ve klinik özelliklerine bakarak rekürsini öngören bir belirteç olup olmadığını tanımlamaktır.

Yöntemler: Mayıs 2014 ve Mayıs 2016 tarihleri arasında endometriyoma nedeniyle kliniğimizde opere edilmiş 151 hasta bu retrospektif kohort çalışmaya dahil edildi. Hastalar önceden endometriyoma nedeniyle opere olup olmamalarına göre gruplandırıldı ve demografik ve klinik özelliklerine bakılarak karşılaştırma yapıldı.

Bulgular: Populasyonda 8 hasta ikinci kez endometriyoma endikasyonu ile opere edilmekteydi. Reküren endometriyoması olan hastalar, ilk kez opere olan hastalara göre daha büyük boyutlu kistlere sahipti ve kanser antijeni-125 (CA125) değerleri daha yüksekti. Demografik ve klinik özellikler bakımından iki grup arasında istatistiksel anlamlı bir fark bulunmadı.

Sonuç: Primer ve sekonder endometriyoma cerrahisi geçiren hastalar arasında demografik ve klinik özellikler bakımından istatistiksel anlamlı bir farklılık izlenmedi. Hangi hastada endometriyomanın nüksedeceğini öngörmek mümkün gözükmemektedir. Dolayısıyla endometriyoma nedeniyle opere olan hastalarda overyan hasarını önlemek ve rekürsini azaltmak için ilk cerrahi dikkatlice yapılmalıdır.

Anahtar Kelimeler: Endometriyoma, rekürs, laparoskopi, over hasarı

Introduction

Endometriosis is the presence of endometrial glands and stroma outside the uterine cavity affecting mostly women of reproductive age and is encountered in 10%-15% of women during their reproductive age. This disease is usually manifested by dysmenorrhea (62.2%), infertility (14%), and chronic pelvic pain (13.3%) (1).

Endometriosis can be divided into three types: superficial endometriosis, deep endometriosis, and ovarian endometriosis called endometrioma. Endometrioma is the formation of the cyst containing chocolate-colored content and is encountered in 17%-44% of patients with endometriosis. It is hypothesized that endometriomas arise as coelomic metaplasia of the ovarian epithelium or invaginations of the inverted ovarian cortex after implantation of the endometriotic foci on the ovarian surface (2).

There is no consensus about definitive treatment of endometriomas to relieve pain, optimize fertility, and delay recurrence. At present, the optimal treatment is the surgical excision of the ovarian endometriomas. Fenestration or aspiration of endometriomas is considered an alternative to minimize damage to the ovarian reserve (3). Although laparoscopic excision of the entire cyst wall is believed to be more effective than excision by laparotomy, ovarian injury is inevitable in laparoscopic surgery (4). Characteristics of the cyst, surgical method, and experience of the surgeon affect the ovarian damage, particularly in repeated operations for recurrent endometriomas (5).

Endometriomas tend to recur after the operation, and repeated surgery for recurrent endometriomas is harmful to the ovarian reserve. Guo (6) reported that the recurrence rate was 21.5% and 40%-50% at 2 and 5 years, respectively, after primary surgery. Repeated surgery for these recurrent cysts is harmful to the ovarian reserve, especially because of dense adhesions. There is a debate

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about the postoperative medical suppression of ovulation with oral contraceptives, danazol, or gonadotropin-releasing hormone agonists to prevent recurrence (7).

We aimed to identify whether there is a predictive factor for determining the correlation between the recurrence of endometriomas and demographic and clinical characteristics.

Methods

A total of 151 patients who underwent surgery for endometriomas between May 2014 and May 2016 were included in this retrospective cohort study. Inclusion criteria were as follows: (1) the presence of endometrioma with a diameter of at least 2 cm, (2) reproductive age (18-45 years) with regular menstrual cycles, and (3) absence of any endocrine disease. Exclusion criteria were as follows: (1) high levels of follicle-stimulating hormone compatible with postmenopausal period and (2) any suspicion of malignant ovarian disease. Clinical and demographic characteristics, including age, gravidity parity, the complaint of the patient on admission, cyst size, serum cancer antigen-125 (CA 125) level, surgical characteristics, such as the presence of adhesion, and laterality of the endometrioma were obtained from the patients' medical records. Details such as surgical method (laparoscopy or laparotomy, cystectomy, oophorectomy, or hysterectomy), postoperative medications, and recurrence time were obtained from the medical reports of the patients. The operative findings at the first operation in recurrent cases could not be compared with the findings at the second operation. Because the first operation in most patients had been done in other clinics, the information about the findings during the operation was not available.

The recurrence was described as the occurrence of endometriomas sized at least 2 cm. The recurrence time was defined as the time from the primary surgery in years. Oral contraceptives had been generally preferred as postoperative medication to suppress ovulation. All the cystectomies were performed under general anesthesia by the experienced surgeons. The laparoscopic surgery was preferred and performed as follows. After establishment of pneumoperitoneum using the Verres needle through a 10 mm subumbilical vertical incision, a 10 mm laparoscope was inserted. Then, two to three additional 5 mm trocars were suprapubically placed to introduce ancillary instruments. At entrance to the abdomen pelvis, abdomen, and the surface of the cyst and ovaries were assessed for any suspicious sign of malignancy. The cleavage plane was identified at first, and the cyst wall was stripped off the ovary by traction and countertraction by two atraumatic grasping forceps. Bipolar electrocoagulation was occasionally applied for hemostasis on the ovarian parenchyma with caution not to damage ovarian reserve. The cyst wall was removed from the abdomen by means of an endobag. If the oophorectomy was performed, the utero-ovarian ligament and the infundibulopelvic ligament were ligated, and the ovary was removed. The laparotomy was performed in the appropriate anatomic planes. The postoperative pathological examinations confirmed that the cysts were endometriomas.

Our study was designed as a retrospective cohort study and conducted according to the guidelines of the Helsinki Declaration. There was no ethical approval required because we collected data of the patients from the records in the archive, and we did not

document any personal information. Furthermore, in our hospital, informed consent is taken from every patient concerning the medical information which may be used in scientific publications. The possibility of receiving subsequent phone calls to ascertain follow up is also stated in this informed consent, which has been signed by all participating women.

Statistical Analysis

Data are given as mean±standard deviation for normally distributed continuous variables and as frequencies for categorical variables. Relevant parameters were separately examined using chi-square test or independent samples t-test, depending on the parameter type and its relationship with the delivery method. The SPSS (Statistical Package for Social Sciences) for Windows version 22.0 software (IBM Corp.; Armonk, NY, USA) was used for the analysis, and a two-sided $p < 0.05$ was considered significant.

Results

The mean age in our study population was 34.5 ± 7.1 . The cyst size ranged between 2 and 20 cm with mean values of 6.9 ± 3.0 cm. The mean serum CA 125 level was 148.9 ± 420.6 . Clinical and demographic characteristics are shown in Table 1. A total of 8 patients underwent repeated surgery for recurrent endometriomas. The time to recurrence was 2.6 ± 0.7 years. Only 25% of these patients with recurrent endometriomas had used medication for ovulation suppression after primary surgery.

When patients were compared with regard to primary or secondary surgery for endometriomas, there was no any statistically significant difference between the groups, except the surgical method (Table 2). Patients with recurrent endometriomas had larger cysts and higher CA 125 levels. Pelvic pain was the most common complaint on admission in both groups. Although there is no statistically significant difference, the patients in the recurrent group had received more postoperative treatment. Bilaterality and adhesion formation were observed more frequently in the recurrent group. The surgical method included laparoscopic cystectomy, cystectomy with laparotomy, oophorectomy, and hysterectomy. In the recurrent group, oophorectomy was not performed.

Discussion

Endometriomas affect 17%-44% of patients with endometriosis. Because both the cyst itself and surgical intervention create problems in the ovarian reserve, there is no consensus about the preferred approach for these patients (8). According to recent guidelines, surgical excision of the entire cyst wall is the gold standard treatment for endometriomas. Surgical intervention improves patients' symptoms, but could also be harmful to the ovarian reserve. Because of these reasons, the first operation should be carefully performed. As mentioned before, endometriomas have a very high recurrence rate and short recurrence time after the first operation, particularly in the treated ovary (9). Based on the reproductive capacity, repeated surgery via either laparoscopy or laparotomy can cause damage to the ovaries.

Several methods have been tried to minimize the time interval of recurrence. Chang et al. (10) used the combination of transvaginal-ultrasound-guided aspiration and sclerotherapy in recurrent endometriomas and found it as an effective and safe alternative to treat

Table 1. Characteristics of the patients

Characteristics	number(%) or mean±standard deviation
Age	34.5±7.1
Gravida	1.4±1.3
Parity	1.1±1.0
Cyst size (cm)	6.9±3.0
Serum CA125 level (U/mL)	148.9±120.6
Comorbidity	
Absent	131 (86.8)
Present	20 (13.2)
Complaint	
Only control	8 (5.3)
Pelvic pain	97 (64.2)
Menstrual irregularities	7 (4.6)
Dysmenorrhea/dysparonia	17 (11.3)
Infertility	22 (14.6)
Previous history	
Absent	143 (94.7)
Present	8 (5.3)
Postoperative treatment	
Absent	122 (80.8)
Present	29 (19.2)
Operation	
Laparoscopic cystectomy	106 (70.2)
Cystectomy by laparotomy	30 (19.9)
Oophorectomy	9 (6)
Hysterectomy	6 (4)
Laterality	
Right	49 (32.5)
Left	69 (45.7)
Bilateral	33 (21.9)
Adhesion	
Absent	49 (32.5)
Present	102 (67.5)

recurrent cysts. Because ovulation plays a fundamental role in the pathogenesis of the cyst, regular oral contraceptives, continuous or cyclic, have been used until the patient desires pregnancy (11, 12). Noretindrone acetate is another choice in recurrent endometriomas until the resolution of symptoms (13). Lee et al. (14) tried postoperative cyclic oral contraceptives after the gonadotropin-releasing hormone agonist treatment and found that the recurrence of endometriomas effectively reduced in women who did not desire pregnancy in the near future.

In our study, we compared the clinical and demographic characteristics of the patients who underwent primary and secondary surgery for endometriomas. We found that there was no statistically significant difference regarding these characteristics. We did

Table 2. Comparison of the characteristics of the patients between the two groups

	Patients with primary operation	Patients with recurrent endometriomas	p
Age	34.6±6.9	33.0±10.1	NS
Gravida	1.4±1.3	1.8±2.3	NS
Parity			
Nulliparity	54 (37.8)	3 (37.5)	NS
Multiparity	89 (62.2)	5 (62.5)	
Cyst size (cm)	6.9±2.9	7.3±4.1	NS
Serum CA125 level (U/mL)	137.8±107.4	348.4±212.9	NS
Comorbidity			
Absent	124 (86.7)	7 (87.5)	NS
Present	19 (13.3)	1 (12.5)	
Complaint			
Only control	7 (4.9)	1 (12.5)	NS
Pelvic pain	92 (64.3)	5 (62.5)	
Menstrual irregularities	6 (4.2)	1 (12.5)	
Dysmenorrhea/Dysparonia	17 (11.9)	0	
Infertility	21 (14.7)	1 (12.5)	
Postoperative treatment			
Absent	116 (81.1)	6 (75)	NS
Present	27 (18.9)	2 (25)	
Operation			
Laparoscopic cystectomy	102 (71.3)	4 (50)	.015
Cystectomy by laparotomy	28 (19.6)	2 (25)	
Oophorectomy	9 (6.3)	0	
Hysterectomy	4 (2.8)	2 (25)	
Laterality			
Right	49 (34.3)	0	NS
Left	64 (44.8)	5 (62.5)	
Bilateral	30 (21)	3 (37.5)	
Adhesion			
Absent	47 (32.9)	2 (25)	NS
Present	96 (67.1)	6 (75)	

not analyze the ovarian reserve because data about the hormone profile in our medical reports were missing. However, data from the literature indicate that each operation reduces the ovarian reserve and reproductive capacity (15). Thus, every woman should be informed about the high recurrence rate and the available treatment modalities (16).

There is also conflicting data about the effect of postoperative medications to minimize the recurrence risk. Long-term postoperative oral contraceptive use is a good choice for this purpose. According to our results, patients in the recurrent group underwent more postoperative treatment, although there was no statistically significant difference. The reason for this result could be that more adhesion or more advanced stage could be observed during the

first operation, and these patients could be managed with postoperative treatment.

In case of recurrence, medical treatment is the first step, particularly in small cysts. If medication is ineffective, if the cyst is rapidly growing, if infertility or suspicion of malignancy is present, or if patient is suffering from pain, surgery may be offered for the recurrent endometriomas to such patients. In our study, the main indication for surgery in both primary and secondary cases was pelvic pain.

Many studies have been performed to determine the risk factors for the recurrence of endometriomas after operation. Cyst size, operative time, intraoperative blood loss, and several serum markers change the recurrence rate of endometriomas (17, 18). Some studies showed that there were several risk factors for endometrioma recurrence such as the cyst size >8 cm, young age (<25 years), preoperative cyst rupture, or preoperative dysmenorrhea. Authors explained that recurrent cysts occur in the lesions in which a cystectomy was performed, whereby endometrial cells touched the peritoneal surface. The impact of postoperative hormone therapy on ovarian endometriosis remains unclear. Maul et al. (19) found that patients did not significantly benefit from additional postoperative hormone therapy (gonadotropin-releasing hormone agonist, oral contraceptive, medroxyprogesterone acetate, or danazol) in terms of reducing the risk of disease and pain recurrence. A retrospective study performed by Koga et al. (20) indicated that prior use of medical treatment for endometriosis is a significant risk factor for recurrence in later life. Higher diameter of the mass, previous pelvic surgery, operation type, presence of adhesion, and higher CA 125 levels were found as risk factors for endometrioma recurrence, whereas demographic and obstetric past history had no difference for endometrioma recurrence in another study (21). The reason for this could be that larger endometriomas are more prone to rupture before or during surgery resulting in more adhesion formation and peritoneal spread of endometrial cells. But we did not find any correlation between the clinical and demographic characteristics and the recurrence of endometriomas after surgery. This could be explained with the small number of recurrent endometriomas in our population. Fedele et al. (22) did not find any difference between the patients with endometriomas and patients with recurrent endometriomas according to these characteristics, similar to our results.

According to recent guidelines, there is a strong recommendation for clinicians about the use of oxidized regenerated cellulose during endometriosis surgery to prevent adhesion formation (23, 24).

Conclusion

It is not possible to accurately predict the patients in whom endometriomas will recur. As a result, maximum excision of the cyst should be performed in the first operation and should be carefully done to minimize damage to the ovaries and delay recurrence of the cyst.

Ethics Committee Approval: Since our study was designed as retrospective cohort study, no ethics committee approval was applied.

Informed Consent: Informed consent was obtained from every patient who participated in this study.

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