



Evaluation of risk factors for the recurrence of ovarian endometriomas



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ABSTRACT

Objectives: To evaluate the risk factors for the recurrence of ovarian endometrioma after laparoscopic cystectomy.

Study design: Reproductive aged patients who underwent laparoscopic ovarian endometriotic cystectomy and with histopathologically confirmed diagnosis of ovarian endometrioma were evaluated retrospectively. Histopathologic specimens were reevaluated and histopathologic characteristics of ovarian endometriotic cysts (thickness of cyst wall, thickness of fibrosis [ToF], thickness of ovarian tissue, the number of follicles per cyst, the depth of penetration [DoP] of endometrial tissue into the cyst wall) were determined. Along the determined histopathologic findings, demographic characteristics (age at surgery, number of pregnancies), clinical symptoms (dysmenorrhea, infertility), intraoperative findings (revised American Society for Reproductive Medicine [rASRM] stage), imaging features (bilaterality, cyst diameter), and biochemical parameters (Ca125, Ca19.9, Ca15.3) were evaluated as possible risk factors for the recurrence of endometrioma. The variables with $p < 0.2$ in univariate analysis were introduced into regression analysis to determine the risk factors for recurrence.

Results: There were statistically significant differences in age group (≤ 35 years and > 35 years), the ToF and DoP between patients with recurrence and those with no recurrence. In Cox regression analysis, age ≤ 35 years and DoP were significant risk factors for presence of recurrence. DoP, ToF, preoperative cyst diameters in ultrasonographic examination were inversely correlated with recurrence interval. In multivariate regression analysis, the DoP was found the only significant risk factor for the recurrence interval. 1.2 mm of DoP was found as the optimum cut off value for presence of recurrence according to Youden index criteria in ROC curve analyze. The sensitivity (62.9%), specificity (75%) were obtained at the cut off value of 1.2 mm for DoP.

Conclusion: Histopathological features of ovarian endometriotic cyst may have important roles on predicting the recurrence of the endometrioma. Predicting the recurrence risk of particular patient is very important in future management of the disease. Knowing the recurrence risk of an endometrioma will help in deciding the optimal treatment modalities for each individual patient. High risk patients should be offered appropriate treatments according to the clinical status without delay and low risk patients should be protected from overtreatment.

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Introduction

Endometriosis is a common gynecologic disease affecting all pelvic organs and one of the most effected pelvic organ is ovary.

Ovarian endometriotic cysts are presented in 17–44% of patients who suffer from endometriosis [1]. Laparoscopic cystectomy is considered as a gold standard for the surgical management of ovarian endometriotic cysts. This excisional technique is shown to be more successful compared to drainage, ablation and fenestration techniques in terms of recurrence [2–4].

The recurrence rate of ovarian endometrioma is reported between 19% and 50% and is a major problem [5,6]. Recurrent endometriomas cause to persistence of infertility, reappearance of pelvic pain and adnexal mass requiring repetitive surgery with the

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detrimental effects on ovarian reserve and the quality of life of women. Possible risk factors affecting the recurrence rates of endometriomas were evaluated in the literature however reported results are conflicting because of methodological differences [5–7]. Interestingly, the relationship between histopathological characteristics of the excised tissue and recurrence rate has not been evaluated adequately.

If the pathogenesis of endometriosis is considered, the assessment of the histopathologic features of removed tissue in recurrent cases may enlighten the pathophysiological mechanisms of recurrence and may identify high risk patients. Therefore, in present study, it was aimed to evaluate the clinical and histopathological possible risk factors for recurrence of endometrioma after laparoscopic cystectomy.

Materials and methods

Study population

In this retrospective study, data were obtained from a review of hospital database. Inclusion criteria were reproductive aged patients who underwent laparoscopic ovarian endometriotic cystectomy, patients with histopathologically confirmed diagnosis of ovarian endometrioma, patients with regular postoperative follow up period.

Exclusion criteria were patients who underwent bilateral oophorectomy at the time of endometrioma surgery, ovarian endometrioma treated with drainage, ablation, fenestration techniques or incompletely stripped, postmenopausal status, patients who were lost to postoperative follow-up period, patients with postoperative medical therapy for endometriosis. Demographic characteristics (age at surgery, number of pregnancies), clinical symptoms (dysmenorrhea, infertility), intraoperative findings (revised American Society for Reproductive Medicine [rASRM] stage), imaging features (bilaterality, cyst diameter), biochemical parameters (Ca125, Ca19.9, Ca15.3) were recorded. Histopathologic specimens were reevaluated and findings were determined. The histopathologic examination was performed by a single pathologist blinded to the clinical features of the patients. On multiple sections, the thickness of cyst wall, thickness of fibrosis (ToF), thickness of ovarian tissue, the number of follicles per cyst, the depth of penetration (DoP) of endometrial tissue into the cyst wall were histologically evaluated. Recurrence rate and recurrence interval of the disease was also identified from the follow-up records. Patients were presented for follow up every three months for the first year after surgery, every six months in the second year, and then yearly. The ultrasonographic presence of an ovarian endometriotic cyst with round shaped cystic mass with a minimum diameter of 2 cm, with thick walls, regular margins, homogeneous low echogenic fluid content with scattered internal echoes, and without papillary proliferations was accepted as recurrence of the endometriotic cyst [8]. To avoid the misdiagnosis of possible transient corpus luteum cyst or an intraovarian hematoma as an endometriotic cyst, ultrasonographic examinations were repeated in two consecutively menstrual cycles and recurrence was accepted when the cyst persisted after 30 days [9].

Recurrence interval was defined as the number of months between the operation and the first ultrasonographically detected signs of recurrence in women with adequate follow-up. Surgeries were performed by the three experienced surgeons with the same instruments and technique (Laparoscopic stripping technique).

Laparoscopic procedure

Laparoscopic cystectomy was performed under video control through a subumbilical incision and two lower abdominal

incisions using 5 mm scissors and grasping forceps. A veress needle was inserted to abdominal cavity to maintain pneumoperitoneum. In all cases CO₂ was used to obtain pneumoperitoneum with 16–20 mm Hg intraabdominal pressure. After exploration and confirmation of endometrioma cyst, the endometriotic cysts were freed from adjacent tissues by blunt and sharp dissections. After aspiration of the cyst content the cyst capsule was stripped from the normal ovarian tissue by using two atraumatic grasping forceps pulled in opposite directions; due to some adhesions to the surrounding ovarian tissue in several places, a sharp dissection by scissors was needed in most of the cases. The detached capsule was placed in a bag and removed from the abdominal cavity through subumbilical incision. The remaining ovarian tissue was left without suturing after obtaining hemostasis. Deep infiltrating endometriosis was completely excised via mechanical instruments and electro surgery. Peritoneal superficial endometriotic lesions were excised or coagulated with bipolar current.

Histopathologic examination

The resected specimens of the endometrioma cyst walls were fixed in 10% neutral-buffered formaldehyde overnight, and tissue samples obtained at 0.5 cm intervals were embedded in paraffin wax. Three consecutive sections of 4- μ m thickness were cut from each paraffin-embedded block. Routine hematoxylin and eosin staining was performed on the all sections for histopathologic examination. For the diagnosis of endometriosis was applied the criteria suggested by the American College of Obstetricians and Gynecologists; in particular, two or more of the following features had to be present to diagnosis endometriosis: endometrial epithelium, endometrial glands, endometrial stroma, or hemosiderin laden macrophages [10]. The thickness of endometrioma cyst wall, thickness of ovarian parenchyma, ToF and DoP were measured at 3 different portions in each patient. The mean values of the 3 different portions were calculated [11]. The thickness of the cyst wall was evaluated considering all the glandular epithelium and stroma and the fibrotic layer and the ovarian parenchyma. DoP of the endometriotic tissue into the cyst wall was measured and it was selected to be the deepest location. All follicles, including primordial, primary and secondary follicles, were individually counted under low-power field magnification ($\times 40$) in 3 areas where the most watched along the cystic wall.

Statistical analysis

Statistical analysis was performed using SPSS 11.5 software. Mann–Whitney *U* test and Pearson's chi-square tests were performed in univariate analysis of possible risk factors for presence of ovarian endometriotic cysts recurrence. Cox regression analysis was carried out to evaluate the independent risk factors for recurrence. The variables with $p < 0.2$ in univariate analysis were introduced into Cox regression analysis. Spearman's correlation analysis was used for the assessment of correlation between continuous variables and recurrence interval. The variables with $p < 0.2$ in Spearman's correlation analysis were introduced into multivariate regression analysis which was performed by logistic regression analysis to assess the independent risk factors for recurrence interval. The ROC curve analysis is performed for continuous variable which is found significant risk factors for presence of recurrence in Cox regression analysis. Optimum cut off value was assessed with Youden index criteria. A value of $p = 0.05$ was accepted as the degree of significance.

The study protocol was approved by the Local Research and Ethics Committee of our hospital.

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