

## RETROPECTIVE ANALYSIS OF 25 CASES WITH BORDERLINE OVARIAN TUMORS

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### SUMMARY

**Objective:** To determine the borderline ovarian tumors according to clinical features, treatment methods, recurrence and survival rates.

**Material and methods:** Twenty-five cases were included to this study. Demographic and clinical findings, surgical methods, stage of disease, recurrences and survivals were revealed from hospital records. Data were analyzed with SPSS 13.0.

**Results:** Mean age were  $42.7 \pm 17.9$ . Most of the patients were in premenopausal ( $n=19$ , 76%). Mean tumor size were  $13.44 \pm 9.37$  cm (range 4-30 cm) and 16 of the patients had serous and 9 of them had mucinous histologic type. Mean tumor size of serous and mucinous tumors were  $9.44 \pm 6.78$  cm,  $20.56 \pm 9.4$  cm, respectively and the difference was statistically significant ( $p=0.007$ ). Tumor markers were elevated in 17 of the patients (68%) before the surgery. Twenty-two patients had frozen section (88%), accuracy rate of the frozen section was 90% during surgery. Most of the patients were treated with total abdominal hysterectomy bilateral salpingo-oophorectomy (TAH-BSO) ( $n=12$ ), 6 of the patients were treated with cystectomy and the others were treated with unilateral oophorectomy (USO) ( $n=7$ ). Most of the cases were stage I ( $n=23$ , 92%). Recurrence of the disease was detected in 4 patients (16%) and 2 of them were treated with cystectomy and the others were treated with USO. No recurrence was detected in TAH-BSO group.

**Conclusions:** Borderline tumors have perfect prognosis and most of the cases are premenopausal. The suggested treatment is surgical staging with TAH-BSO. Cystectomy might be chosen in young patients with fertile desire, however, patients should be warned for high recurrence rates.

**Key words:** borderline ovarian tumor, histologic type, tumor markers, recurrence, survival

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### ÖZET

#### BORDERLINE OVER TÜMÖRLÜ 25 OLGUNUN RETROSPEKTİF ANALİZİ

**Amaç:** Borderline over tümörlü vakaların klinik özellikleri ile birlikte uygulanan tedavi yöntemleri, rekürrens ve sağkalım oranlarının ortaya konulmasıdır.

**Gereç ve yöntemler:** Bu çalışmaya 25 borderline over tümörü olgusu dahil edildi. Retrospektif olarak olguların dosya kayıtlarından demografik ve klinik bulguları, yapılan cerrahinin türü, hastalığın evresi, rekürrens durumu ve sağkalım sürelerine ulaşıldı. Bulgular SPSS 13.0 ile analiz edildi.

**Bulgular:** Ortalama yaş  $42,7 \pm 17,9$  idi. Hastaların çoğunluğu premenopozal ( $n=19$ , %76) idi. Ortalama tümör çapı  $13,44 \pm 9,37$  cm (4-30 cm aralığında), histolojik açıdan %64 (16/25) seröz, %36 (9/25) müsinöz olarak belirlendi. Seröz tümörlerde ortalama tümör çapı  $9,44 \pm 6,78$  cm iken, müsinözlerde  $20,56 \pm 9,4$  cm ve iki grup arasında istatistiksel olarak anlamlı fark saptandı ( $p=0,007$ ). Cerrahi öncesinde tümör belirteçleri 17 hastada yüksek saptandı (%68). Yirmiiki hastada frozen kesit uygulandı (%88), frozen doğruluk oranı %90 olarak belirlendi. Olguların 12'si total abdominal histerektomi

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*bilateral salpingoofektomi (TAH-BSO), 6 olgu kistektomi, 7 olgu unilateral salpingoofektomi (USO) ile tedavi edildi. Olguların çoğunluğu evre 1 (n=23, %92) idi. Rekürrens 4 olguda saptandı (16%) ve 2'si sadece kistektomi ile diğer 2'si ise unilateral oofektomi ile tedavi edilen olgulardı. TAH-BSO ile tedavi edilen olgularda rekürrens görülmedi. **Sonuç:** Borderline tümörler sıklıkla premenopozal dönemde görülen, çok iyi prognoza sahip lezyonlardır. Önerilen tedavi TAH-BSO, cerrahi evrelemedir. Kistektomi, fertilitate isteği olan genç olgularda seçilebilir ancak hasta yüksek rekürrens oranları açısından uyarılmalıdır.*

**Anahtar kelimeler:** borderline over tümörü, histolojik tip, rekürrens, sağkalm, tümör belirteçleri

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## INTRODUCTION

Borderline ovary tumor (BOT) was first defined as half-malign ovary tumor<sup>(1)</sup> in 1929 and classified among ovary tumors by FIGO in 1971 and by WHO in 1973<sup>(2,3)</sup>. It constitutes 10-15% of epithelial ovarian cancers and is associated with similar risk factors<sup>(4)</sup>. It is frequently seen in premenopausal women and these tumors have a strong prognosis. It is most frequently seen between the ages 30-50<sup>(5)</sup>.

It has similar clinical manifestations to those in other adnexal masses. It may be asymptomatic or there may be symptoms like abdominal pain and distention. Tumor diameter may be < 1 cm in serous tumors whereas in mucinous tumors it may be determined in a wide range up to > 30 cm<sup>(6,7)</sup>.

Surgery is the main treatment for borderline ovary tumors. In early stage cases, it is reliable and efficient to perform a laparoscopic procedure guided by an experienced laparoscopist but cyst rupture risk should be taken into consideration<sup>(8,9)</sup>. While it is possible to protect uterus and contra lateral ovary in premenopausal cases where fertility is desired<sup>(10)</sup>, TAH-BSO is the most suitable choice in postmenopausal patients. Staging procedures include peritoneal lavage, peritoneal and omentum biopsies and appendectomy (especially in mucinous tumors). While routine pelvic and paraaortic lymph node dissection is controversial; it may not be required if no enlarged lymph node or suspected invasive lesion according to the frozen section is present<sup>(11,12)</sup>.

In this study, it was aimed to determine the clinical features, treatment methods, recurrence and survival rates of the borderline ovary tumor cases that have been surgically treated in our clinic.

## MATERIAL AND METHODS

25 borderline ovary tumor cases that attended to our clinic between the dates 2003-2009 and were treated and followed were enrolled in this study. Approval of ethics committee was taken. Records of the cases were inspected retrospectively. Patients' age, presenting complaints, number of children, menopausal situation, family history, previous ovary cyst operation history, whether infertility treatment was done or not, preoperative ultrasonographic findings and if additional monitoring methods were used or not, tumor diameter and tumor markers were recorded. CA125 level<35 IU/ml and CA19-9 level<37 IU/ml were regarded as normal. Information regarding surgical method used in the treatment of the cases, whether staging and systematic lymphadenectomy was done and tumor stages and histological types from the pathology reports were collected. Follow-up times, presence and time of recurrence information was collected from the records. Information was analyzed with SPSS 13.0. In statistical evaluation, together with descriptive analysis, Mann-Whitney-U and Chi-Square methods were used in comparing the cases with and without recurrence development. p<0.05 value was regarded as statistically significant.

## RESULTS

The mean age was 42,7±17,9. Most of the cases were premenopausal (n=19, 76%). The most frequent presenting complaint was determined as abdominal pain. Infertility history was present in two cases. It was determined that one of these cases had used clomiphene citrate during 6 cycles for ovulation induction and the other had had no treatment. In one of the cases, ovary cancer was present in family history. Before diagnosis, tumor marker level was 68% (n=17) and frequently elevating marker was determined as

CA 125 (n=16, 56%). It was observed that in addition to ultrasonography, one of the pre-operation monitoring methods, computed tomography (CT) or MRI was used in 17 cases. Clinical and demographical findings of the cases are shown in Table I.

**Table I:** Demographic and clinical characteristics of the cases.

Characteristics	n	%
Years(mean±sd)	42,7±17,9	
Menopause	6	24
Benign ovary cyst operation	2	8
Infertility treatment	2	8
Ovary cancer in family history	1	4
CA 12.5 (>35 IU/ml)	14	56
CA 19.9 (>37 IU/ml)	9	36
Histology		
Serous	16	64
Mucinous	9	36
Stage		
I	23	92
Ia	20	80
Ib	2	8
Ic	1	4
III	2	8
IIIb	1	4
IIIc	1	4

In the surgery, laparoscopic approach was used at the ratio of 16% (n=4) and incision by laparotomy at 84% (n=21). Frozen section practice and accuracy ratios were 88% (n=22) and 90% (n=20) respectively. Cystectomy was performed in six cases (24%); unilateral oophorectomy in 7 cases (28%) and total abdominal hysterectomy bilateral salpingoophorectomy (TAH-BSO) in 12 cases (48%). In ten cases lymphadenectomy and staging surgery were performed. Of the cases in which staging was done, in 7; TAH-BSO was performed (70%) and in 3; conservative surgery was performed (30%). In seven cases (70%), appendectomy was added to staging surgery. Distribution of the cases among the applied surgical methods is outlined in Table II.

Mean tumor diameter was 13,44±9,37 cm (between 4-30 cm). Histologically, 64% (n=16) was of serous type and 36% (n=9) was of mucinous type. Mean mucinous type borderline tumor diameter was determined as significantly higher than mean serous type borderline tumor diameter (respectively; 20,56±9,4 cm and 9,44±6,78 cm, p=0.007). Lymph node invasion was determined in none of the lymphadenectomy performed cases. Of the 5 cases borderline tumor

diagnosis of which was unknown in primary surgery; complementary surgery and staging was performed with a second operation in 2 cases.

**Table II:** Distribution of the cases by the method applied.

	n	%
Surgical intervention method		
Laparoscopy	4	16
Laparotomy	21	84
Operation performed		
Cystectomy	6	24
Unilateral oophorectomy	7	28
TAH-BSO		
Lymphadenectomy		
Present	10	40
Not present	15	60

Most of the cases were stage I (n=23, 92%) and 2 patients were stage III (n=2, 8%). 20 patients were stage Ia, 2 patients were stage Ib, 1 patient was stage Ic, 1 patient was stage IIIb and 1 patient wastage IIIc. Microinvasive capsule implant was determined in 1 of the cases and microinvasive peritoneum implant in the other.

Mean follow-up time was 25,6 months (10-82 months). Recurrence was determined in 4 cases (16%). Mean recurrence time was determined as 14,25 months (4-24 months). It was found out that all of the cases with recurrence had serous histology. Mean age and tumor diameter of the cases with recurrence development was found smaller compared to the cases without recurrence (respectively; for age, 25,7±5,5 and 46±17,6, p=0,001 and for tumor diameter, 9±2,1 and 14,2±10,1, p=0,04). No significant difference was determined among the cases with and without recurrence in terms of CA125 and CA 19.9 height, performance of cystectomy, USO and lymphadenectomy (Table III). In 2 of the recurrent cases, cystectomy was performed and USO was done in the other two. While recurrence ratio was 30% (4/13) in the conservative surgery performed cases, no recurrence (0/12) was monitored among the TAH-BSO performed cases. Recurrence ratio was determined as significantly higher in the conservative surgery performed cases (p=0.03). 3 of the recurrent cases were stage Ia and one was stage IIIc. Oophorectomy was performed in 2 recurrent cystectomy cases and 2 cases that developed recurrence in the other ovary. Survival ratio among all the followed patients who was 100%.

**Table III:** Characteristics of the cases with and without recurrence.

	Recurrence present (n=4)(%)	Recurrence not present (n=21)(%)	p
Age (mean±sd)	25.7±5.5	46±17.6	0.001
CA 12.5 >35IU/ml	2(%14)	12(%86)	0.79
CA 19.9>37IU/ml	1(%11)	8(%89)	0.61
Tumor diameter(mean±ss)	9±2.1	14.2±10.1	0.04
Cystectomy	2(%33)	4(%64)	0.18
USO	2(%29)	5(%71)	0.28
TAH-BSO	0(%0)	12(%100)	0.03
Lymphadenectomy	2(%20)	8(%80)	0.65

## DISCUSSION

Compared to invasive ovary tumors, borderline ovary tumors are seen in smaller ages, have stronger prognosis, progress more slowly and recurs later. Therefore treatment approaches are less aggressive but still there are different opinions on some topics<sup>(10,11)</sup>. Though typical ultrasonographic findings are determined as positive crescent sign and unilocular cyst, disseminated papillary projections growing from the internal wall or cysts containing multilocular nodule, these findings aren't found in one third of the cases and they are recognized as preoperative benign cystic lesions<sup>(12)</sup>.

In this study, it was determined that mean age was 42,7 and most of the cases were premenopausal and with serous histology. In the study done by Houck et al, 140 cases were evaluated; mean age was 52,3, mean tumor diameter was 13,7 cm (10,2 cm in serous tumors, 20,1 cm in mucinous tumors), histologically; 57,1% was of serous type, 33,5% was of mucinous type and 9,4% was of other types<sup>(13)</sup>.

In the analysis of 25 cases performed in our clinic retrospectively, tumor marker level was determined at the ratio of 68%. But no relation could be shown between the high tumor markers and recurrence. Mean tumor diameter was 9,44±6,78 cm in serous tumors, 20,56±9,4 cm in mucinous tumors and statistically significant difference was determined among two groups (p=0,007). In previous series, while higher tumor diameter (13,1±7 cm) was monitored in mucinous tumors ultrasonographically, smaller tumor diameter (9,3±6,2 cm) was seen in serous tumors<sup>(14)</sup>.

In the borderline ovary tumor cases in our clinic, it was monitored that frozen section was practiced at the

ratio of 88% (22/25). Borderline tumor diagnosis was established in the frozen sections at the ratio of 90% and benign tumor was determined in 2 patients. In our series, frozen results of the cases with a final diagnosis of borderline were evaluated. Therefore, frozen section sensitivity and specificity values in the borderline ovary tumors can not be calculated. In a research, frozen section records of 48 borderline ovary tumor patients and it was shown that benign incidents could be excluded in frozen sections with a diagnostic accuracy of 94%. But in BOT, diagnostic accuracy of the frozen sections decrease<sup>(15)</sup>. In the study of Houck et al, frozen section was evaluated as invasive cancer at the ratio of 20% and as benign at the ratio of 30% in the patients with BOT. In the permanent sections of the patients with BOT diagnosis in frozen sections, invasive cancer was determined at the ratio of 23-27%<sup>(13)</sup>. In two large researches done in the recent years, concordance ratios of frozen and permanent sections have been reported as 62% and 85%<sup>(16,17)</sup>.

Base of the treatment in borderline ovary tumors is surgery. If fertility is desired, performance of cystectomy or oophorectomy is appropriate; but if the patient is not fertile anymore, then TAH-BSO surgical procedure is suitable. There are different opinions on whether to perform surgical staging or not. A survey study was done among 660 members of Gynecologic Oncology Group. 42 percent of them (274) responded. According to 97% surgical staging is required; to 96% peritoneal lavage; to 92% random peritoneal biopsy; to 97% omentectomy/sampling; to 88% lymphadenectomy (89% para-aortic, 97% pelvic)<sup>(18)</sup>. In our study surgical staging was performed on 10 patients. In a research conducted among 15 patients between the years 1978-87, importance of staging was emphasized and in 46% of the cases, involvement outside the ovary was monitored in the patients for whom surgical staging was performed 3 months after the establishment of BOT diagnosis<sup>(19)</sup>. While deciding on surgical staging, tumor's being bilateral, exophytic involvement presence, >10 cm mass presence, advanced stage disease, high recurrence risk should be taken into consideration<sup>(21,22)</sup>.

In a study, conservative surgery was performed on 62 of 142 BOT patients and fertility sparing surgery was performed; recurrence ratio among patients was found as 6.5% and pregnancy ratios were indicated as 16%<sup>(23)</sup>. In a meta-analysis including 2479 BOT patients, conservative surgery was performed; pregnancy

occurred in 48% and recurrence was monitored in 16% of 923 patients<sup>(24)</sup>. Compared to the literature results, in our series pregnancy ratio is low and we believe the reasons for this are; our relatively shorter mean follow-up time, infertility in addition to borderline ovary tumor, the fact that some of the patients are single or don't have a partner and new pregnancy postponing of the cases who have children.

In the large serial study of Ayhan et al; 100 cases with BOT diagnosis were evaluated, comprehensive surgical staging was performed on 49 patients and fertility sparing surgery was performed on 22. Recurrence ratio was determined as 3% and general survival ratio as above 97.9%. In this study no difference was determined between the cases with and without recurrence in terms of age, parity, microinvasion, micropapiller structure, FIGO stage, surgery type, preoperative serum CA125 levels and lymph node involvement but general survival ratios without tumor decreased significantly in the presence of micropapillary structure or peritoneal implants and in the fertility sparing surgery performed cases under the age 30. In the presence of serous BOT, it was suggested that conservative surgery practice and lymphadenectomy procedure can be performed in serous BOT cases only in academic studies, provided that other ovary is also evaluated<sup>(25)</sup>.

Recurrence ratios after fertility sparing surgery is 2,4-15% following adnexectomy and 15-36% following cystectomy. Cystectomy was performed in 53 patients with BOT stage I, recurrence was monitored in 30%, 20 patients were re-operated and residual BOT was monitored in 3 patients (15%)<sup>(26,27)</sup>.

In this study, recurrence was monitored in 33% of the cystectomy performed patients and 24% of the oophorectomy performed patients. Interestingly, mean ages and tumor diameters of the cases with recurrence were determined as lower than the ones without recurrence. The reason of this situation may be due to the bigger need for fertility sparing procedure performance in young ages or probability of recurrence/residual development in the other ovary. The fact that the cases with recurrence have smaller tumor diameters may be explained with the facts that all the recurrences in our series were seen in serous tumors and the mean serous tumor diameters are determined as smaller than those of the mucinous type.

Though this research is a limited study because of its retrospective nature and few cases; borderline ovary

tumors are rare and a limited number of retrospective studies with few cases can be found in literature. Ideal method to be applied in treatment is not clear yet. Prominent finding of the retrospective analysis of the patients treated at our clinic is that recurrence frequency in fertility sparing aimed cystectomy and USO cases is significantly higher than the ones treated with TAH-BSO. However, it should be known that when suspected from these tumors that may also be seen in young cases where fertility is desired, frozen section should be performed during operation and fertility sparing surgery procedures such as cystectomy and oophorectomy may be performed. But, due to the high ratios following this type surgery procedures, patients should be informed in terms of recurrence and followed.

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