

Aim of the study: The purpose of the study was to evaluate patients with borderline ovarian tumors.

Material and methods: Clinical features, treatment and survival status of 100 patients with borderline ovarian tumors were retrospectively evaluated between 1998 and 2007.

Results: Patients' mean age was 37.75 years (range: 15–72); 22 of them were postmenopausal. Histopathological diagnoses were serous, mucinous, endometrioid and clear cell in 54%, 41%, 2% and 3% of the patients, respectively; 70 patients had stage IA disease, 8 were at stage IB, 16 at stage IC, 2 at stage IIIA, 3 at stage IIIB and 1 at stage IIIC. Restaging laparotomies were performed on 19 patients; fertility-sparing surgery was performed on 52 patients; 2 patients received chemotherapy because of advanced-stage disease. All patients are currently alive. The 5-year disease-free survival rate for 71 cases was 100%.

Conclusions: Borderline ovarian tumors have excellent prognoses, and fertility-conserving surgery can be performed in young patients with early-stage disease.

Key words: borderline ovarian tumors, survival, fertility-sparing surgery.

Borderline ovarian tumors: a study of 100 cases from a Tertiary Care Hospital

Ahmet Uysal^{1,2}, Semih Mun¹, Fatma Uysal³, Murat Öztekin¹, Cem Büyüktosun¹, Salim Şehirali¹, Ömer Başoğlu¹, Cüneyt E. Taner¹

¹Ministry of Health, Aegean Maternity and Teaching Hospital, Department of Obstetrics and Gynecology, Izmir, Turkey

²Çanakkale Onsekiz Mart University Faculty of Medicine, Department of Obstetrics and Gynecology, Çanakkale, Turkey

³Ministry of Health, Aegean Maternity and Teaching Hospital, Department of Radiology, Izmir, Turkey

Introduction

Epithelial ovarian tumors of low malignant potential constitute a subgroup of ovarian malignancies called borderline ovarian tumors. Borderline tumors occur in younger women, present at an earlier stage and have a favorable prognosis. The incidence rate of borderline ovarian tumors is lower than that of invasive cancers with borderline ovarian tumors ranging from 12 to 33% among epithelial tumor series [1–3]. Mean age at diagnosis is 47, with the highest frequency in women 30–50 years of age [3]. The most common histological type is serous; the others are mucinous, endometrioid and, rarely, clear cell. When tumors are localized to one or both ovaries, prognosis is excellent [4, 5]. However, the most appropriate management of patients with extra-ovarian disease is unclear, as some tumors progress despite aggressive cytoreductive surgery and chemotherapy [6].

The purpose of this retrospective study was to evaluate the clinical features, treatment and survival status of patients with borderline ovarian tumors.

Material and methods

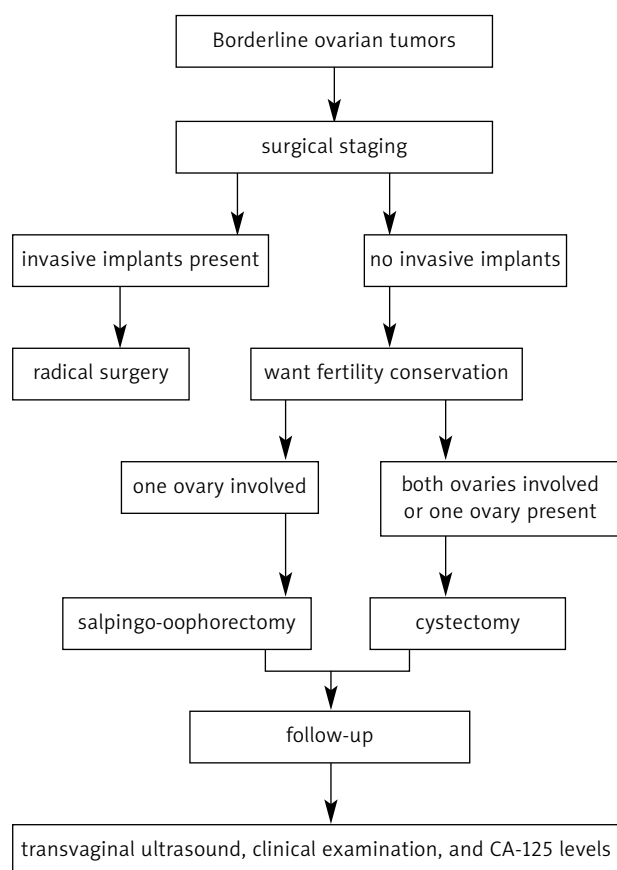
One hundred eight patients with borderline ovarian tumors who were treated at the Aegean Maternity and Teaching Hospital between January 1998 and December 2007 were retrospectively reviewed. Follow-up information was not available for eight patients, who were therefore excluded. Clinical features, treatment and survival data were all noted. All patients were treated surgically; their tumors were classified by our hospital's pathologists in accordance with WHO criteria for histological typing [7]. During the study period, we utilized intraoperative assessments (frozen sections) in 60/100 cases. Follow-up was performed by reviewing patients' hospital records, or by contracting patients and reviewing them personally.

Staging followed the FIGO system, which, for borderline ovarian tumors, is similar to that used for ovarian epithelial carcinomas (Fig. 1). Suggested FIGO guidelines include taking specimens from the omentum; intestinal serosa and mesentery; pelvic peritoneum including the cul-de-sac, bladder peritoneum, and pelvic wall; and abdominal peritoneum including paracolic gutters, diaphragmatic surface, and retroperitoneal nodes [8].

Statistical analysis was performed using a commercial computer system (SPSS 10.0 for Windows, SPSS Inc., Chicago, IL).

Results

Mean age of all patients in the sample was 37.75 years (range: 15–72 years); 18 patients were younger than 30 years, and 22 patients were postmenopausal. Mean ages were 35.13 years for patients with serous tumors and



Schematic representation of management and surveillance algorithm for borderline ovarian neoplasms. Information from [8] was incorporated in this algorithm.

Fig. 1. Summary of International Federation of Obstetric Gynecology (FIGO) Staging

42.25 years for those with mucinous tumors. Mean parity was 1.6 (range: 0–5). Preoperative ultrasound found mean ovarian mass diameter to be 10.8 cm (range: 5–21 cm), with 9.05 cm for serous tumors and 15.61 cm for mucinous tumors. Twenty-two cases were bilateral (22%; 22/100), of which 17 (77%; 17/22) were serous and 5 (23%; 5/22) were mucinous. High CA 125 level (> 35 IU/ml) was detected in 46 cases, including 31 of the 54 serous tumors (57%), 11 of the 41 mucinous tumors (27%), 2 of the 3 clear cell tumors (67%), and 2 of the 2 endometrioid tumors (100%). Histological diagnosis and stage distribution are shown in Table 1.

Table 1. Histological subtypes of borderline ovarian tumors and stages of the cases according to the FIGO system

Histopathological subtypes of BOTs	Stage (n and %)						Total (n and %)
	IA	IB	IC	IIIA	IIIB	IIIC	
serous BOT	36	6	10	–	1	1	54
mucinous BOT	32	1	5	2	1	–	41
endometrioid BOT	2	–	–	–	–	–	2
clear-cell BOT	–	1	1	–	1	–	3
total (n and %)	70	8	16	2	3	1	100

BOT – borderline ovarian tumor

Nineteen patients underwent restaging laparotomies after diagnosis. Three patients had pseudomyxoma peritonei. As we could not show gastrointestinal origin in these cases using upper or lower gastrointestinal endoscopies, we accepted them as having primary ovarian origin. Patients' operations are shown in Table 2.

Fertility-sparing surgery (conservation of the uterus and at least one ovary, in patients younger than 40 years) was performed for 52 patients. Patients with advanced disease underwent hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy sampling, omentectomy and cytoreductive surgery. No residual tumor was larger than 1 cm after surgery. The 22 patients with advanced disease received cisplatin-based chemotherapy. The mean number of extracted lymph nodes was 14.5 in 22 cases who underwent pelvic and para-aortic lymphadenectomy sampling. One patient had lymph metastasis in 3 of her 16 extracted lymph nodes.

Mean follow-up was 62 ± 2 months (range: 4–120 months). All patients in this study are currently alive; the 5-year tumor-free survival rate is 100% for 71 patients; 9 had recurrence (9%); 20 are still within 5 years of their diagnoses. Four patients who had stage IA disease had pregnancies; they delivered with no relevant problems.

Patients' characteristics (an also patients who had serous and mucinous tumor comparing table, diagnostic measurements as well as surgery summary) are shown in Table 3.

Discussion

Borderline ovarian tumors occur in women of all ages, with an average age in the mid-40s. They account for 9.2–16.3% of ovarian malignancies. Serous and mucinous types make up the vast majority; other histological types are endometrioid and clear cell [1–3].

Recent cytogenetic advances have given unique insights into the pathogenesis and behavior of serous borderline ovarian tumors. In several studies, investigators found that only a small subset of serous cyst adenomas progress to serous borderline ovarian tumors, and that activating mutations of *BRAF* and *KRAS* genes are early events in tumorigenesis of borderline ovarian tumors [9]. Anfinan *et al.* reported the mean age of 138 patients with borderline ovarian tumors as 46 years; Sanci *et al.* reported it to be 47.1 years in 96 cases [1–3]. In our study, mean age was 37.8 years – 35.1 years for those with serous tumors, and 42.2 years for patients

with mucinous tumors. Patients with borderline tumors tend to be younger than those who develop invasive carcinomas [8,11].

Kliman *et al.* reported 51.3% of 76 tumors to be mucinous and 38.2% serous [10]. In another study, 60% of tumors were mucinous and 37% were serous [11]. In our study, 54% of tumors were serous and 41% were mucinous. Other studies also reported more serous tumors than mucinous tumors in their series [10–12].

Buttin *et al.* identified micro-invasion by the primary ovarian tumor as a risk factor for recurrence and death [13]. Seidmen *et al.* suggested that borderline tumors be classified as benign and malignant [14]. Survival for patients whose serous borderline tumors were confined to the ovaries was 100%, whereas those with invasive peritoneal implants and with micropapillary serous carcinomas had a 30–40% mortality rate; these tumors were thus classified as carcinomas.

The rate of stage I disease among borderline ovarian tumor diagnoses is reportedly 67.5–91.6% [3–9, 15]; it was 94% in our group.

Some authors advise treating with fertility-sparing surgery and adequate surgical staging procedures, especially in young stage I patients, as no such patients have died of tumors [4–6, 11]. Marice *et al.* reported that conservative management of ovarian tumors with low potential for malignancy significantly increases risk of recurrence, but does not affect overall survival [16]. Morris *et al.* also noted that recurrence was more frequent in patients treated with ovarian cystectomy than in those treated with oophorectomy [15].

Identifying clinical disease stage is crucial in determining prognosis. The overall 5-year survival rate for patients with stage I disease is reported to be approximately 95% [9–11, 16], but survival rates decrease to 40–75% in stage II and 56–65% in stage III [1–3, 16]. Upstaged disease has been reported at restaging surgery for borderline ovarian tumors after initial conservative surgery [4–6].

Tamokoshi *et al.* reported that the patients with borderline serous/mucinous tumors at stages II and III had 5- and 9-year survival rates of 91.7% and 73.3%, and 38.9% and 13.0%, respectively [9]. They found patients with advanced mucinous tumors to have poor prognoses—emphasizing the need to develop more effective treatments for mucinous tumors. Similar survival rates were reported by other authors [1–3].

Postoperative treatment of borderline ovarian tumors is controversial. Patients treated with adjuvant therapy reportedly show no difference in survival rate compared with those treated with surgery alone [5–16]. We administered chemotherapy to 22 patients with advanced disease. In one study, most patients received adjuvant chemotherapy and none had recurrent tumor in stage I patients [9]. Others reported recurrence rates of 2–7% in patients with stage I borderline ovarian tumors [1–3]. In our study the recurrence rate for all stages was 9%. Tamokoshi *et al.* reported that they had a clinically complete response in 5 of 16 patients with residual tumors of < 2 cm [9]. Their reported overall response rate was 50% in cases with residual tumors of < 2 cm, but they found no effect with cisplatin-based chemotherapy in patients with gross residual tumors, especially with mucinous tumors.

Table 2. Operations performed for borderline ovarian tumors

Operation	n
TAH + BSO	48
USO	26
USO + contralateral cystectomy	1
unilateral cystectomy	25
PPLA	22
appendectomy	40

TAH + BSO – total abdominal hysterectomy and bilateral salpingo-oophorectomy; USO – unilateral salpingo-oophorectomy; PPLA – pelvic para-aortic lymphadenectomy

Table 3. Patients' characteristics, treatment, diagnosis and surgery summary

	Age	
	mean	range
	37.75	15–72
	Menopausal status	
	premenopausal	postmenopausal
	78	22
	Borderline ovarian tumors	
	serous	mucinous
Age	35.13	42.25
USG*	9.05 cm	15.61 cm
Bilaterally	17/54	5/41
High CA-125 levels (>35 IU/ml)	31/54	11/41
Chemotherapy for advanced disease	10/54	8/41
	Fertility sparing surgery	
	yes	no
	52/100	48/100
Residual disease**	-	100
Lymph node dissection for advanced disease	22/100	78/100
Lymph node positivity	1/22	21/22
Extracted lymph node number	mean 14.5	range 8–19

*USG – ultrasonography (mean diameter given)

**residual disease: (> 1 cm tumor volume after surgery) with pathological confirmation

Current treatment reports are of residual tumors < 1 cm [1–17]. In our study we had no case with residual tumor > 1 cm (with pathological correlation) and had clinically complete responses after chemotherapy in 6 patients with advanced disease.

In conclusion, Patients with borderline ovarian tumors have excellent prognosis. Fertility-conserving surgery can be performed in young patients with early-stage disease.

The authors declare no conflict of interest.
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Address for correspondence

Ass. Prof. Dr. **Ahmet Uysal**
Çanakkale Onsekiz Mart University Faculty of Medicine
Department of Obstetrics and Gynecology
Çanakkale, Turkey
tel: + 90 533 263 55 40
e-mail: drahmetuysal@hotmail.com

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