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Management of borderline ovarian tumors: A retrospective study in Northern Greece

Kyriaki Mitta, Ioannis Tsakiridis, Akriola Fachiridou, Fotios Zachomitros, Themistoklis Dagklis, Apostolos Mamopoulos, Apostolos Athanasiadis, Ioannis Kalogiannidis

[1] Third Department of Obstetrics and Gynaecology, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece

Corresponding Author

Ioannis Tsakiridis, 49 Konstantinoupoleos street, 54642, Thessaloniki, Tel.: +30 2313 312120, Fax: +30 2310 992950, e-mail: igtsakir@auth.gr

Abstract

Introduction: Borderline ovarian tumors (BOTs) are tumors of low malignant potential commonly presented in women of reproductive age. Their incidence has been increasing over the years and issues regarding fertility preservation are very crucial.

Material and Methods: This was a retrospective cohort study including all cases of BOTs diagnosed and surgically treated, during a 12-year period (2010 - 2022) at the Third Department of Obstetrics and Gynecology, School of Medicine, Aristotle University of Thessaloniki, Greece. Student's t-test and Mann-Whitney tests were used to compare age, parity, serum Ca-125 and maximum dimensions of the tumors between the patients treated radically and those treated conservatively. The Fisher's exact test was used to compare categorical variables between the groups with radical versus conservative surgery.

Results: In total, 34 cases were managed during the study period with a median follow-up of 114.5 months. The mean age was 50 years, the median parity was 2, the median of Ca-125 was 20.6 U/ml and the median of the maximum dimensions of the tumors was 10 cm. Laparotomy was performed in 82.4% of the cases. In 29.4% of cases, the BOT was bilateral. There was no case with residual disease, the majority were serous tumors at stage I. The mean age (53.9 vs 32.2, p-value<0.001), the median parity (2 vs 1, p-value=0.009) and the median serum Ca-125 (21.1 vs 13, p-value=0.046) were significantly higher in women who underwent radical surgery than those with conservative surgery. The recurrence rate was 2.9%.

Conclusion: A favorable long-term prognosis was observed in women diagnosed with BOTs, without any tumor-related deaths. Conservative surgery for fertility preservation may appear as beneficial.

Key words: Borderline ovarian tumors, management, treatment, follow-up, histopathology, recurrence

Introduction

Borderline ovarian tumors (BOTs), sometimes noted as tumors of low malignant potential, encompass a diverse range of growths characterized by atypical epithelial cell proliferation without invading the surrounding stromal tissue.[1] Their behavior differs significantly from low-grade ovarian carcinomas, and they are considered a distinct clinical entity; they account for 14 to 15% of all primary ovarian neoplasms.[2] Borderline neoplasm is currently the most widely used designation and has been adopted by the World Health Organization (WHO).[3]

The estimated incidence of BOTs ranges from 1.8 to 5.5 per 100,000 women per year and current data suggest an increasing incidence.[2,4] BOTs are staged using the same criteria as other ovarian neoplasms; most patients present with stage I disease (70%), while stages II to IV disease are infrequent.[5] BOTs are more common in younger women compared to invasive ovarian cancer. More specifically, around 33% (1/3 of patients) diagnosed with BOTs are under the age of 40.[2,6] Regarding histopathology, the majority of cases are serous (65-70% of all BOTs) or mucinous and rarely, endometrioid, clear-cell or Brenner tumors are found.[7]

Some BOTs are diagnosed incidentally.[8] Regarding primary treatment for BOTs, complete staging with total hysterectomy and bilateral salpingo-oophorectomy (BSO) is required for patients with stage II or higher and those who do not wish fertility preservation.[6] In cases of stage I, salpingo-oophorectomy of the affected ovary, along with pelvic washings, omental biopsy and biopsies from peritoneal lesions is preferred; management may be different in women wishing to preserve fertility i.e. excision of the tumor.[9-12] Unlike invasive ovarian cancer, adjuvant chemotherapy is not typically recommended for BOTs, as they are not highly aggressive.[13] The prognosis for patients with BOTs is generally quite favorable; most women with BOTs have a good long-term outcome, with a 5-year survival rate around 99% (Stage I).[14] Recurrence is possible but typically associated with a more favorable prognosis than recurrent invasive ovarian cancer.[15]

This study aimed to report the incidence of BOTs in a tertiary hospital in Northern Greece, analyze the management protocols, surgical approaches and outcomes of the women with BOTs.

Material and Methods

This was a retrospective cohort study including all cases of borderline ovarian tumors diagnosed and surgically treated, during a 12-year period (2010 - 2022) at the Third Department of Obstetrics and Gynecology, School of Medicine, Aristotle University of Thessaloniki, Greece. The diagnostic modalities used were pelvic ultrasound, CT and magnetic resonance imaging/MRI. The age, parity, serum Ca-125, the maximum dimensions of the adnexal masses, the histological type, stage and the type of surgery (radical versus conservative) were reported in detail.

The women consented for the anonymity of their data and the possible use for future research purpose, while no incentives were provided. Following policy for observational studies that do not involve any intervention or modification on the routine care of the patients, no institutional board review was required for this study.[16]

Qualitative variables were presented as frequencies (n) and proportions (%). Normality of the quantitative variables was examined with Shapiro-wilk test. Student's t-test and Mann-Whitney test were used to compare age, parity, serum Ca-125 and maximum dimensions of the tumors between the patients who were treated radically and those treated conservatively. The Fisher's exact test was used to compare the different variables (laparoscopy vs laparotomy and bilateral vs unilateral location of the tumor) between the groups with radical versus conservative surgery. The p-value was calculated as two-tailed and results

were considered statistically significant if p<0.05. The statistical analysis was carried out using the SPSS 28.0 statistical software package.

Results

In total, 34 cases of borderline ovarian tumors were reported during the study period. The mean age was 50 years old (SD=15.2), the median parity was 2 (IQR=1), the median of the serum marker Ca-125 was 20.6 U/ml (IQR=22) and the median of the maximum dimensions of the tumors was 10 cm (IQR=15) (Table 1). A pelvic ultrasound was performed in all cases (34/34, 100%), a CT was performed in 76.5% (26/34, 76.5%) and MRI was performed in 41.2% (14/34, 41.2%); whereas in 17.6% both MRI and CT were performed (6/34, 17.6%). As for management, laparotomy was performed in 28 out of 34 cases (28/34, 82.4%) and the for the rest 6 cases, laparoscopy was performed (6/34, 17.6%). In 29.4% (10/34) of case, the BOT was bilateral, whereas in 70.6% (24/34, 70.6%) the location was unilateral.

Lymph node dissection was performed in 4 out of 34 cases (11.7%), omentectomy and appendectomy were performed in 27/34 (79.4%) and 7/34 (20.6%), respectively. Ascites was not found in any case, whereas, in 3 cases the cytological findings from the peritoneal washings were positive (3/34, 8.8%) and in the rest 31 cases (31/34, 91.2%) were negative. Moreover, 13 cases were treated with a conservative surgery (13/34, 38.2%) and the rest 21 cases were treated with a radical surgery (61.8%). There was no case with residual disease and the median follow-up was 114.5 months (IQR=110). At the end of the follow-up, all patients were alive without any evidence of disease.

Regarding the histopathological results, the majority were serous tumors (18/34, 52.9%), 10 cases were mucinous (10/34, 29.5%), 6 cases were papillary serous (6/34, 17.6%). As far as the stage is concerned, most of the cases (94%) were at stage I, [(Ia: 21/34, 61.8%), (Ib: 6/34, 17,7%), (Ic1: 1/34, 2.9%), (Ic2: 1/34, 2.9%), (Ic3: 3/34, 8.9%)]; whereas there was one case of stage IIIa and one of stage IIIc [(IIIa: 1/34, 2.9%), (IIIc: 1/34, 2.9%)] (Table 2).

Patients who underwent radical surgical procedures were subjected to a comparative analysis with those who opted for conservative surgical approaches, based on various characteristics. The mean age of patients who underwent radical surgery was significantly higher than those who underwent conservative surgery (53.9 vs 32.2, p-value<0.001). Furthermore, concerning the median parity within the two groups, a notable disparity in median parity was identified between the patients who underwent radical and conservative surgery (2 vs 1, p-value=0.009). However, the median maximum tumor diameter was not significantly different between those who underwent radical and conservative surgeries (10 vs 9 cm, p-value=0.670). Conversely, the median value of the tumor marker, Ca-125, was significantly higher in the group of women treated with radical versus those with conservative surgery

Table 1. Descriptive characteristics of the sample.

	MEAN/MEDIAN	SD/IQR	MINIMUM-MAXIMUM
Age (years)	50	15.2	25-77
Parity (n)	2	1	1-3
Ca-125 (U/ml)	20.6	22	8-150
Maximum diameter of the ovarian tumor (cm)	10.0	15.1	3-43
Follow-up (months)	114.5	110	1-158

Table 2. Stages and histopathological results of the borderline tumors

STAGES	N (%)	HISTOPATHOLOGY	N (%)
Ia	21 (61.8%)	Serous	18 (52.9%)
Ib	6 (17.7%)	Mucinous	10 (29.5%)
Ic1	1 (2.9%)	Papillary-serous	6 (17.6%)
Ic2	1 (2.9%)		
Ic3	3 (8.9%)		
II	0		
IIIa	1 (2.9%)		
IIIb	0		
IIIc	1 (2.9%)		
IV	0		

(21.1 vs 13, p-value=0.046). The bilateral location of the tumor was not associated with increased risk for radical surgery (90 vs 10%, OR: 9.0, 95% CI: 0.982-82.5, p-value=0.051) (Tables 3, 4).

In total, the recurrence rate was 2.9% (1/34); a 32 years old woman, with a unilateral borderline ovarian tumor of maximum diameter of 4 cm and a serum Ca-125=15 U/ml, treated with unilateral salpingo-oophorectomy via laparoscopy. The histopathological results showed serous BOT, with negative peritoneal washings and the stage was Ic3.

Discussion

This was a cohort of 34 patients with BOTs treated either with a radical or a conservative type of surgery. Regarding the histopathology, the majority of the cases concerned a serous histology (52.9%). Additionally, the vast majority of the tumors were at stage I (94.2%),

Table 3. Comparison of the continuous variables between radical surgery and conservative.

	CONSERVATIVE SURGERY	RADICAL SURGERY	P-VALUE
Age (mean, years)	32.2	53.9	<0.001
Parity (median)	1	2	0.009
Maximum tumor diameter (median, cm)	9	10	0.670
Ca-125 (median, U/ml)	13	21.1	0.046

Table 4. Comparison of the nominal variables between radical and conservative surgery.

LOCATION OF THE TUMOR	RADICAL SURGERY N (%)	CONSERVATIVE SURGERY N (%)	P-VALUE	OR	95% CI
Unilateral	12 (50%)	12 (50%)	0.051	9.0	0.982-82.5
Bilateral	9 (90%)	1 (10%)			

OR: odds ratio, 95% CI: 95% Confidence Interval

which is in agreement with the literature.[17] Furthermore, the recurrence rate was 2.9% (1/34), which was quite low compared to the literature; recurrence rate is reported to range from 5 to 20%.[17]

Regarding the main findings of this study, the mean age, median parity and serum marker Ca-125 were significantly different between those who underwent a radical versus those who underwent a conservative surgery. All the aforementioned can be reasonably explained; Ca-125 is included in the International Ovarian Tumor Analysis (IOTA) score, which directs along with the clinical evaluation, the type of surgery (radical vs conservative).[18] The management approach for BOTs adheres to the guidelines by the National Comprehensive Cancer Network (NCCN) and takes into careful consideration various factors, including the nature of the disease, the patient's age and the fertility preservation preferences.[19]

As already mentioned, there are two primary surgical options available for the management of BOTs, while woman's age, parity, desiring for fertility preservation are obviously the most significant factors that should be taken into consideration before proceeding to a radical surgery for a BOT; explaining the reason why there was a significant difference in age and parity between the two groups (conservative vs radical surgery).

In 17.6%, staging was performed via laparoscopy; for early stages of BOT, if surgery without risk of tumor rupture is possible, laparoscopy with protected extraction is recommended over laparotomy.[20] In our study though, laparotomy was the preferred surgical approach. The age was the only factor that was significantly different between those who were managed with laparoscopy compared to laparotomy (p-value=0.024). Neither the mean dimension of the tumor nor the serum Ca-125 were significantly different between the two groups (p-values:0.670 and p-value:0.147, respectively).

According to our findings, patients with bilateral BOT had a nine-fold chance of radical surgery compared to those with unilateral BOT. For the treatment of a bilateral serous early-stage BOT with a strategy to preserve fertility and/or endocrine function, bilateral cystectomy is recommended where possible.[20] In our cohort, the mean age of women with bilateral BOTs was higher, although not statistically significant, than those with unilateral BOT. All cases with bilateral BOTs, apart from one, either did not want to preserve fertility or had already completed their family planning; consequently, they were managed with radical surgery. However, there was one case of a 20 years old woman, with bilateral BOTs treated with unilateral salpingo-oophorectomy and contralateral cystectomy, as recommended in the literature.[20]

To our knowledge, there are limited research studies regarding the management, the clinical findings and the histopathological results of BOTs in the Greek population. One of the major strengths of this study is that clinical features such as age, serum Ca-125 and dimensions of the tumors were described, along with the management, histopathological results, type of surgery and the follow-up of the patients. However, one of the major limitations of the study is the small sample size (n=34), along with the small number of cases with recurrence (n=1), which may limit the generalizability of our findings.

In conclusion, recurrence was observed in one out of the 34 cases with BOTs in our study, no deaths related to the tumors were recorded and there was a favorable long-term prognosis. Opting for conservative surgery seems a worthwhile approach to preserving fertility, given the favorable prognosis. There is no consensus on various aspects such as the significance of surgical staging. To strengthen the findings of our current study, large-scale prospective multicenter longitudinal studies are encouraged.

References

1. Seidman JD RP, Kurman RJ. Surface epithelial tumors of the ovary. Blaustein's pathology of the female genital tract. 2002;5th:791.

2. Skirnisdottir I, Garmo H, Wilander E, Holmberg L. Borderline ovarian tumors in Sweden 1960-2005: trends in incidence and age at diagnosis compared to ovarian cancer. Int J Cancer. 2008;123:1897-901.
3. Karseladze AI. [WHO histological classification of ovarian tumors. Geneva, 1999 (R.E.Scully, L.H.Sobin]. Arkh Patol. 2005;Suppl:1-64.
4. Hannibal CG, Huusom LD, Kjaerbye-Thygesen A, Tabor A, Kjaer SK. Trends in incidence of borderline ovarian tumors in Denmark 1978-2006. Acta Obstet Gynecol Scand. 2011;90:305-12.
5. Tinelli R, Tinelli A, Tinelli FG, Cicinelli E, Malvasi A. Conservative surgery for borderline ovarian tumors: a review. Gynecol Oncol. 2006;100:185-91.
6. Harter P, Gershenson D, Lhomme C, et al. Gynecologic Cancer InterGroup (GCIG) consensus review for ovarian tumors of low malignant potential (borderline ovarian tumors). Int J Gynecol Cancer. 2014;24:S5-8.
7. Hart WR. Borderline epithelial tumors of the ovary. Mod Pathol. 2005;18 Suppl 2:S33-50.
8. Goff BA, Mandel LS, Melancon CH, Muntz HG. Frequency of symptoms of ovarian cancer in women presenting to primary care clinics. JAMA. 2004; 291:2705-12.
9. Ayhan A, Celik H, Taskiran C, Bozdag G, Aksu T. Oncologic and reproductive outcome after fertility-saving surgery in ovarian cancer. Eur J Gynaecol Oncol. 2003;24:223-32.
10. Morice P, Camatte S, El Hassan J, Pautier P, Duvillard P, Castaigne D. Clinical outcomes and fertility after conservative treatment of ovarian borderline tumors. Fertil Steril. 2001;75:92-6.
11. Suh-Burgmann E. Long-term outcomes following conservative surgery for borderline tumor of the ovary: a large population-based study. Gynecol Oncol. 2006;103:841-7.
12. Boran N, Cil AP, Tulunay G, et al. Fertility and recurrence results of conservative surgery for borderline ovarian tumors. Gynecol Oncol. 2005;97:845-51.
13. Trope C, Kaern J, Vergote IB, Kristensen G, Abeler V. Are borderline tumors of the ovary overtreated both surgically and systemically? A review of four prospective randomized trials including 253 patients with borderline tumors. Gynecol Oncol. 1993;51:236-43.
14. Trimble CL, Kosary C, Trimble EL. Long-term survival and patterns of care in women with ovarian tumors of low malignant potential. Gynecol Oncol. 2002;86:34-7.
15. Crispens MA, Bodurka D, Deavers M, Lu K, Silva EG, Gershenson DM. Response and survival in patients with progressive or recurrent serous ovarian tumors of low malignant potential. Obstet Gynecol. 2002;99:3-10.
16. Wade DT. Ethics, audit, and research: all shades of grey. BMJ. 2005;330:468-71.
17. Sozen H, Vatansever D, Topuz S, et al. Clinicopathological analysis of borderline ovarian tumours and risk factors related to recurrence: experience of single institution. J Obstet Gynaecol. 2019;39:253-8.
18. Mina M, Kosmas I, Tsakiridis I, et al. Prediction Models of Adnexal Masses: State-of-the-Art Review. Obstet Gynecol Surv. 2021;76:211-22.
19. Vasudevan G, Jaiprakash P, Guruvare S, Samanta N. Ovarian borderline mucinous tumor with squamous overgrowth: An unusual finding with review of literature. Indian J Pathol Microbiol. 2018;61:261-3.
20. Bourdel N, Huchon C, Abdel Wahab C, et al. Borderline ovarian tumors: Guidelines from the French national college of obstetricians and gynecologists (CNGOF). Eur J Obstet Gynecol Reprod Biol. 2021;256:492-501.

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