Recurrence and 5-year survival rate in patients with borderline ovarian tumors and related factors in Kurdistan

Seyedeh Reyhaneh Yousefi Sharami (1), Fariba Farhadifar (2), Roya Tabatabaei (1)

(1) Department of Obstetrics and Gynecology, Kurdistan University of Medical Sciences, Sanandaj, Iran; (2) Social Determinants of Health Research Center, Department of Gynecology, Faculty of Medicine, Kurdistan University of Medical Science, Sanandaj, Iran.

Abstract

The aim of this study was to investigate the recurrence rate and five-year survival in patients with borderline ovarian tumors and related factors. This retrospective cohort study was performed on 20 women diagnosed with a borderline ovarian tumor in Kurdistan province, Iran, between 2007 and 2019. Patients' records were reviewed and a researcher-made questionnaire was completed for each patient, which included demographic and clinical variables related to patient survival. The most common type of ovarian borderline tumor was the serous borderline ovarian tumor (75%). In fifty percent of the cases, cystectomy was used as th treatment. Recurrence was observed in three patients (15%), two of which were treated with cystectomy, and the other case was treated by TAH + BSO method ($p = 0.64$). There was no significant difference in terms of the type of surgery, history of infertility, history of taking contraceptive pills, age, age at diagnosis, and BMI between the two groups with and without recurrence ($p > 0.05$). The overall survival rate was 100% and none of the patients died at the end of follow-up. There was no relationship between any of the clinical and demographic variables with disease recurrence, and since all patients were alive after the end of the follow-up period. In summary, it was not possible to assess the relationship between patients' survival rate and studied variables.

Key Words: Recurrence; survival; borderline ovarian tumors, ovary; serous borderline ovarian tumor.

Eur J Transl Myol 33 (1) 10779, 2023 doi: 10.4081/ejtm.2023.10779

Ovarian cancers are among the most important cancers in women. The lifetime risk of developing ovarian cancer in women is about 1.5% and its mortality rate is about 0.5%.[1,2] Although ovarian cancer accounts for a small percentage of cancers in women, it is the fifth leading cause of death from malignancy in women.[2,3] Borderline ovarian tumors (BOT) are a group of ovarian tumors that are associated with a low potential for malignancy and remain confined to the pelvis for a long period of time.[1,4] These tumors make up about 20% of ovarian epithelial tumors.[5] In fact, BOT represent a heterogeneous group of non-invasive tumors with unknown malignant potential. These tumors are clearly associated with a relatively good prognosis. Molecular changes in BOT indicate an association between this disease and type I ovarian tumors (low-grade ovarian carcinoma).[6,7] One of the special histological features of interstitial ovarian tumors is that the malignant cells do not invade the ovarian stromal tissue. However, there are other malignant changes such as malignant cell proliferation, nuclear atypia, and mitotic changes.[7] The age of onset of these tumors is lower than invasive ovarian tumors and they are mostly seen in the age group of 30-50 years.[8] The pathological stage of the disease and the sub-classification of extra-ovarian disease into invasive and non-invasive implants, along with the presence of postoperative macroscopic disease, are the main predictors of recurrence and survival in these patients.[5,9] However, it should be emphasized that the most important factor in the negative prognosis of recurrence is the use of conservative surgery without affecting the patient's survival because most recurrent diseases are borderline types that are easily treated and have an excellent prognosis.[10,11] As mentioned, ovarian cancer is one of the most important types of cancer in women and can have a high mortality rate. Also, BOT are one of the most important types of ovarian cancer, and these types of tumors can be associated with recurrence in some people. Therefore, recognizing the

Table 1. *Frequency distribution of history of infertility, number of deliveries, and history of contraceptive use.*

Variable	Variable levels	Frequency (percentage)
History of infertility	No	18(90)
	Yes	2(10)
Number of deliveries	0	4(20)
	1	4(20)
	≥2	12(60)
History of contraceptive use	No	16(80)
	Yes	4(20)
Type of tumor	Serous borderline tumor	15(75)
	Mucinous tumor	4(20)
	Endometrioid borderline tumor	1(5)

factors related to recurrence in patients is necessary and important in order to prevent its occurrence.
Thus, the aim of this study was to investigate the recurrence and 5-year survival rate in patients with BOT in Kurdistan province.

Materials and Methods

This retrospective cohort study was performed on all women with borderline ovarian tumor at Besat Hospital in Sanandaj, Kurdistan Province, West of Iran, from 2007 to 2019. Eligible patients who had a medical record in Besat Hospital in Sanandaj were selected. Samples were selected using the census method. The number of samples, considering the type of study, was considered to be 100 people, and after considering the inclusion and exclusion criteria, the number of people in the study was reduced to 20 people. Therefore, in this study, the files of 20 patients with BOT were investigated. Inclusion criteria were definitive diagnosis of borderline ovarian tumor and completeness of the clinical record. Exclusion criteria included any type of cancer other than borderline ovarian cancer, patients who had been diagnosed with borderline ovarian cancer before the study period (previous visit), and patients who came to Kurdistan from other provinces for treatment. In order to collect information, based on the studied variables, a researcher-made checklist was completed, which recorded the demographic and clinical variables of patients in two study groups. After approval of the plan by the Research Council of the Besat Hospital and Sanandaj Hospital and the Ethics committee of Sanandaj University, a total of 20 patients who met the inclusion criteria were included in the study. Records and pathology reports of all patients with BOT were investigated and a researcher-made questionnaire was completed for each patient, which included the variables of age, age at the time of diagnosis, history of infertility, number of deliveries, history of contraceptive use, duration of pregnancy (weeks), body mass index (BMI), type of pathology,

Table 2. *Frequency of surgical methods used based on the pathological types of borderline ovarian tumors..*

	Type of surgery		
Types of tumors	SO	Cystectomy	TAH+BSO
Serous borderline tumor (n=15)	4 (6/26)	7 (8/46)	4 (6/26)
Mucinous tumor (n=4)	1(25)	3(75)	0(0)
Endometrioid borderline tumor (n=1)	1(25)	0(0)	0(0)
Total (n=20)	6(30)	10(50)	4(20)

Table 3. *Characteristics of recurrences of borderline ovarian tumors in women.*

Characteristics of patients	**Cases of recurrence**		
	First case	**Second case**	**Third case**
Age at the time of diagnosis (years)	32	54	34
Age at recurrence (years)	42	61	36
The time between diagnosis and treatment until recurrence (months)	136	25	36
Site of recurrence	Pelvis	Pelvic mass	Pelvis
Type of surgery used	Cystectomy	TAH+BSO	Cystectomy

type of surgery, recurrence treatment, disease stage, mean time of recurrence, site of recurrence, 5-year survival, recurrence, and outcomes (death). Data were first summarized using descriptive indicators such as mean, standard deviation, and frequency. Data were statistically analyzed by Stata software version 14. Relationships between variables were analyzed using Fisher's exact test, independent t-test, and Mann-Whitney U test, depending on the type of variable. Also, Fisher's exact test was used to investigate the differences in the frequency of qualitative variables in the group of patients with and without recurrence. Kaplan-Meyer method was used to calculate the survival ratio at any point in time when mortality was observed.

Results

Twenty patients with a mean age of 44.9 years and a standard deviation of 15.6 were studied. The mean follow-up duration was 60.6 months (minimum 22 and maximum 158 months). 90% of women surveyed had no history of infertility, and 20% of them had no history of delivery. The most common type of borderline ovarian tumor was serous borderline tumor, which was observed in 15 patients (75%). (Table 1).

Treatments for each pathogenic type of borderline ovarian tumor are listed in Table 2. In 50% of cases cystectomy, in 30% SO, and in 20% TAH + BSO treatments were used.

In three cases (15%) recurrence was observed. The recurrence site was in the pelvis. The mean recurrence time in the present study was about 65.6 months. Details of recurrences can be seen in Table 3.

According to Table 4, 2 cases of tumor recurrence were related to patients treated with cystectomy and the other case underwent TAH + BSO operation. Although no recurrence was seen in patients treated with the SO method, no statistically significant difference was observed between different treatment methods in terms of the frequency of recurrence cases (p = 0.64)..

Two of the women had a history of infertility, one of

Table 4. *Relationship between surgical procedure and recurrence of borderline ovarian tumors.*

	Recurrence		*P value
Type of surgical procedure	No N(%)	Yes N(%)	
SO	(6(100)	0	0.64*
Cystectomy	8(80)	2(25)	
TAH+BSO	3(75)	1(25)	
* Fisher's exact test			

Table 5. *Relationship between demographic parameters and recurrence of borderline ovarian tumors.*

		Recurrence		*p value*
Paramteres		No Number (%)	Yes Number (%)	
History of infertility	No	16(9/88)	2(1/11)	0/26
	Yes	1(50)	(1(50)	
History of contraceptives	No	13(3/81)	3(7/18)	0/58
	Yes	4(100)	0	
Age		43.82 ±16.23	43.67 ±16.25	0.99
Age at diagnosis		38.82 ±15.73	40.44 ±16.52	0.90
BMI		29.07 ±3.48	27.67 ±0.58	0.85

whom (50%) had tumor recurrence, and among the other 18 who had no history of infertility, one (1.11%) had recurrence (p = 0.26). Four of the women in the study had a history of taking contraceptives, but none of them had a recurrence of the tumor, and out of 16 other people who did not have a history of using contraceptives, three (18.7%) had a recurrence (p = 0.58). In addition, the difference between the two groups with and without recurrence in terms of mean age, age at diagnosis, and BMI was not statistically significant (p > 0.05) (Table 5).

The Kaplan-Meier curves are based on survival probability scores (Figure 1). The overall survival rate was 100% and none of the patients died at the end of follow-up.

Discussion

Ovarian cancer is the second most common malignancy in women worldwide and induces many complications for women every year.[5] Therefore, the study of survival and recurrence of this disease can be effective in understanding the treatment strategies and their effectiveness. Our findings with an average follow-up time of 60.6 months show that the 5-year survival rate of patients during the follow-up period was 100% and none of the patients died at the end of follow-up. A similar study in Iran aimed to assess the recurrence rate and 5-year survival in patients with borderline ovarian tumor and reported that the survival rate of these patients was not measurable because none of the patients died during this study. However, according to statistical analysis, there was no significant relationship between postoperative drug therapy (chemotherapy) and recurrence rate. They reported that the mean recurrence time of BOT was 14 months.[12] The survival rate of interstitial ovarian tumors is higher than ovarian cancer. The findings of a study by Momenimovahed et al. showed that the 5-year survival rate for patients with ovarian cancer was approximately 45%.[13] Our studies showed that in 15% (3 cases) of patients undergoing surgery, the tumor recurred. Two cases of tumor recurrence were related to patients treated with cystectomy and the other patient underwent TAH + BSO operation. The mean recurrence time in the present study was about 65.6 months. Similar studies have estimated the rate of borderline tumor recurrence to be 10 to 32%. In a study by Morris et al, patients with BOT were followed for about 6 years. They reported that recurrent tumors were observed in 32% of patients.[14] The findings of a study by Sanci et al. have shown that BOT recur in about 10% of patients.[15] Sobiczewski et al. reported that in many patients no recurrence of the disease was observed for several years, and recurrence of borderline ovarian tumor occurred in 10% of patients. Also, invasive recurrences were rare and occurred in only 3% of patients; however, these recurrences are often associated with high mortality despite treatment.[16] In our study, 75% of patients had interstitial serous tumors, 20% had mucinous tumors, and 5% had endometriosis. Our findings showed that the most common type of borderline ovarian tumor was serous interstitial tumor. In similar studies, the frequency of serous interstitial tumors was the highest in comparison to other types of tumors.[14] In some studies, the number of serous borderline tumors was less than half of the population, but in general, the frequency of these tumors was higher than other types of borderline tumors.[17,18] In their study, Auer et al. reported that most frequent BOT

are serous or mucinous, while other tumors such as mixed, endometrioid, or clear cell types are rare.[18] In the present study, there was no significant difference between the two groups with and without recurrence in terms of the type of surgery, history of infertility, history of taking contraceptives, age, age at diagnosis, and BMI. This indicates that the studied demographic and clinical variables were not significantly related to tumor recurrence. Various findings have shown that ovarian cancer is associated with high mortality, and in most cases, it is diagnosed after the metastasis of cancer beyond the ovaries and often throughout the abdomen, which should be considered because early detection can lead to effective treatment and lower recurrence.[19-21] One of the limitations of this study was the small number of samples studied. During the 12 years of study, we tried to increase the sample as much as possible to a reasonable and measurable level.

In conclusion, fifteen percent of women with BOT had a recurrence after 60 months of follow-up. The overall survival rate after 5 years of follow-up was 100% and none of the patients died after follow-up. Conduction of further studies especially studies with larger sample sizes, and possibly the use of multicenter data and data modeling using Cox regression to clarify the relationship between different demographic and clinical variables related to recurrence and survival of patients are recommended.

List of acronyms

BMI – body mass index
BOT - Borderline ovarian tumors
BSO – Bilateral Salpingo-oophorectomy
SO - Salpingo-oophorectomy
TAH – Total Abdominal Hysterectomy

Contributions of Authors

All authors have read and approved the final edited typescript.

Acknowledgments None

FundingNone

Conflict of Interest

The authors declare no conflicts of interest.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Corresponding Author

Roya Tabatabaei, Social Determinants of Health Research Center, Department of Gynecology, Faculty of Medicine, Kurdistan University of Medical Science, Iran.
Tel: +98-5433522636, Fax: +98-5433518352.
ORCID ID: 0000-0001-8947-4066
E-mail: Rm_tabatabaie@yahoo.com

E-mails and ORCID iD of co-authors
Seyedeh Reyhaneh Yousefi Sharami: Yousefi805@yahoo.com
ORCIDiD: 0000-0002-4050-4137
Fariba Farhadifar: None
ORCID iD:0000-0001-5823-8482

References

1. Lalwani N, Prasad SR, Vikram R, Shanbhogue AK, Huettner PC, Fasih N. Histologic, molecular, and cytogenetic features of ovarian cancers: implications for diagnosis and treatment. Radiographics. 2011;31:625-46. doi: 10.1148/rg.313105066.
2. Kanat-Pektas M, Ozat M, Gungor T, Dikici T, Yilmaz B, Mollamahmutoglu L. Fertility outcome after conservative surgery for borderline ovarian tumors: a single center experience. Arch Gynecol Obstet. 2011;284:1253-8. doi: 10.1007/s00404-010-1804-7.
3. Rauh-Hain JA, Krivak TC, Del Carmen MG, Olawaiye AB. Ovarian cancer screening and early detection in the general population. Rev Obstet Gynecol. 2011;4:15-21.
4. Reid BM, Permuth JB, Sellers TA. Epidemiology of ovarian cancer: a review. Cancer Biol Med. 2017;14:9-32. doi: 10.20892/j.issn.2095-3941.2016.0084.
5. Lawton FG, Pavlik EJ. Perspectives on Ovarian Cancer 1809 to 2022 and Beyond. Diagnostics (Basel). 2022;12. doi: 10.3390/diagnostics12040791.
6. Fischerova D, Zikan M, Dundr P, Cibula D. Diagnosis, treatment, and follow-up of borderline ovarian tumors. Oncologist. 2012;17:1515-33. doi: 10.1634/theoncologist.2012-0139.
7. Harter P, Sehouli J, Vergote I, Ferron G, Reuss A, Meier W, et al. Randomized Trial of Cytoreductive Surgery for Relapsed Ovarian Cancer. N Engl J Med. 2021;385:2123-31. doi: 10.1056/NEJMoa2103294.
8. Seong SJ, Kim DH, Kim MK, Song T. Controversies in borderline ovarian tumors. J Gynecol Oncol. 2015;26:343-9. doi: 10.3802/jgo.2015.26.4.343.
9. Abascal-Saiz A, Sotillo-Mallo L, de Santiago J, Zapardiel I. Management of borderline ovarian tumours: a comprehensive review of the literature. Ecancermedicalscience. 2014;8:403. doi: 10.3332/ecancer.2014.403.
10. Patrono MG, Minig L, Diaz-Padilla I, Romero N, Rodriguez Moreno JF, Garcia-Donas J. Borderline tumours of the ovary, current controversies regarding their diagnosis and treatment. Ecancermedicalscience. 2013;7:379. doi: 10.3332/ecancer.2013.379.
11. Loizzi V, Selvaggi L, Leone L, Latorre D, Scardigno D, Magazzino F, Cormio G. Borderline

epithelial tumors of the ovary: Experience of 55 patients. Oncol Lett. 2015 Feb;9(2):912-914. doi: 10.3892/ol.2014.2758. Epub 2014 Dec 2.
12. Karimi Zarchi M, Mehdizadeh Kashi A, Allahqoli L, Sadat Tabatabai R, Shamsi F, Hashemian Asl N. The Recurrence and 5-Year Survival Rates in Patients with Borderline Ovarian Tumors in Yazd from 2006 to 2016. Journal of Obstetrics, Gynecology and Cancer Research (JOGCR). 2019;4:57-61.
13. Momenimovahed Z, Tiznobaik A, Taheri S, Salehiniya H. Ovarian cancer in the world: epidemiology and risk factors. Int J Womens Health. 2019;11:287-99. doi: 10.2147/ijwh.s197604.
14. Morris RT, Gershenson DM, Silva EG, Follen M, Morris M, Wharton JT. Outcome and reproductive function after conservative surgery for borderline ovarian tumors. Obstet Gynecol. 2000;95:541-7. doi: 10.1016/s0029-7844(99)00619-5.
15. Sanci M, Gultekin E, Cingillioglu B, Gultekin OE, Ozvural S, Emirdar V, et al. Second primary cancers following borderline ovarian tumors. Arch Gynecol Obstet. 2011;283:1391-6. doi: 10.1007/s00404-010-1585-z.
16. Sobiczewski P, Kupryjanczyk J, Michalski W, Śpiewankiewicz B. The Evaluation of Risk Factors Associated With Relapse and Recurrence of Borderline Ovarian Tumors With Long-Term Follow-up. Int J Gynecol Cancer. 2016;26:1053-61. doi: 10.1097/igc.0000000000000722.
17. Yasmeen S, Hannan A, Sheikh F, Syed AA, Siddiqui N. Borderline tumors of the ovary: A clinicopathological study. Pak J Med Sci. 2017;33:369-73. doi: 10.12669/pjms.332.11847.
18. Auer K, Bachmayr-Heyda A, Aust S, Sukhbaatar N, Reiner AT, Grimm C, Horvat R, Zeillinger R, Pils D. Peritoneal tumor spread in serous ovarian cancer-epithelial mesenchymal status and outcome. Oncotarget. 2015 Jul 10;6(19):17261-75. doi: 10.18632/oncotarget.3746.
19. Cadoo K, Simpkins F, Mathews C, Liu YL, Provencher D, McCormick C, ElNaggar AC, Altman AD, Gilbert L, Black D, Kabil N, Bennett J, Munley J, Aghajanian C. Olaparib treatment for platinum-sensitive relapsed ovarian cancer by BRCA mutation and homologous recombination deficiency status: Phase II LIGHT study primary analysis. Gynecol Oncol. 2022 Sep;166(3):425-431. doi: 10.1016/j.ygyno.2022.06.017. Epub 2022 Jul 5.
20. Lapke N, Chen CH, Chang TC, Chao A, Lu YJ, Lai CH, Tan KT, Chen HC, Lu HY, Chen SJ. Genetic alterations and their therapeutic implications in epithelial ovarian cancer. BMC Cancer. 2021 May 4;21(1):499. doi: 10.1186/s12885-021-08233-5.
21. Lu H, Cunnea P, Nixon K, Rinne N, Aboagye EO, Fotopoulou C. Discovery of a biomarker candidate for surgical stratification in high-grade serous ovarian cancer. Br J Cancer. 2021;124:1286-93. doi: 10.1038/s41416-020-01252-2.

Disclaimer

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Submission: August 5, 2022
Revision received: August 28 2022
Accepted for publication: August 29, 2022