Risk factors of recurrence and pregnancy in patients with borderline ovarian tumors: a retrospective study with 16-year follow-up

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Abstract

Objective: This study analyzed the risk factors affecting recurrence in patients with borderline ovarian tumors （BOTs） after radical surgery and influencing recurrence and pregnancy in patients after fertility sparing surgery (FSS).

Methods: This is a retrospective cohort study. Data was collected from clinical data of patients in the Beijing Chaoyang Hospital affiliated to Capital Medical University from January 2005 to November 2021. The clinicopathological and surgical variables were analyzed by univariate analyses and survival curves.

Results: A total of 169 BOT patients were included in the study. The median age was 45 years. Median follow-up time was 81months. Among these patients, 21 patients relapsed. There were 60 patients with FSS, of the 16 patients attempting to conceive, 13 patients have successfully conceived spontaneously. In univariate analyses, FIGO stage, invasive implantation, and chemotherapy were risk factors for recurrence of BOTs. FIGO stage was the only one risk factor after multivariate analysis. Tumor size and tumor site were risk factors for recurrence of BOTs receiving FSS. We didn't find any risk factor for pregnancy of BOTs receiving FSS.

Conclusion: After univariate analysis and multivariate analysis, we found some risk factors for recurrence after radical surgery or FSS, but they didn't affect the overall survival rate and pregnancy rate. Laparoscopy procedure is recommended and chemotherapy is not recommended for patients receiving FSS. We suggest that patients who preserve fertility should get pregnant as soon as possible and follow up closely.

Introduction

Borderline ovarian tumors (BOTs), first described by Taylor in 1929, account for 10% -20% of epithelial ovarian tumors. BOTs are characterized by atypical epithelial proliferation without stromal invasion. Its histopathology and biological behavior are between benign and malignant tumors [1]. It was estimated that about 2.5 to 5.5 per 100,000 women were diagnosed as BOTs every year. BOTs of all stages combined have favorable 5-year and 10-year survival rates of 95% and 90%, respectively [2]. The recommended treatment for BOTs, as for ovarian cancer, consist of peritoneal washing, hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and multiple peritoneal biopsies. Appendectomy is also recommended for women with mucinous BOTs. Compared with malignant tumors, BOTs are more frequently diagnosed in young women of childbearing age, and approximately one-third of them are diagnosed before 40 years of age [3]. For the past ten years, with the implementation of the two-child policy in China and delay in childbearing age, fertility sparing surgery (FSS) is widely accepted for treatment of BOTs. So far, the main issue of BOTs is that there is still no consensus on the risk factors for recurrence and pregnancy. Therefore, the purpose of this study was to analyze the influencing factors for recurrence of BOTs and evaluate the efficacy of FSS in terms of fertility outcomes.

Materials And Methods

A retrospective cohort study was carried out. Data was collected from clinical data of patients who met the following criteria in the Beijing Chaoyang Hospital affiliated to Capital Medical University from January 2005 to November 2021.

Inclusion criteria:1) Patients with initial treatment and operation in Beijing Chaoyang Hospital; 2) Postoperative pathology was diagnosed as BOTs; 3) Clinical data is complete; 4) patients with complete follow-up data. Exclusion criteria: 1) Patients complicated with gynecological malignant tumors; 2) Patients have a history of other malignant tumor; 3) Patients complicated with severe heart, lung, liver, kidney dysfunction; 4) Clinical data is incomplete; 5) patients without complete follow-up data.

The clinical pathological data concerned age, obesity, preoperative fertility, menopause, chief complaint, tumor size, tumor location, pathology, micropapillary pattern, invasive implantation, surgical approach, surgery with or without fertility preserving, lymphadenectomy, omentectomy, FIGO stage (2014 FIGO classification system), preoperative CA125.

Surgery without fertility preserving consist of peritoneal washing, hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and multiple peritoneal biopsies. Appendectomy was performed for patients with mucinous BOTs. Fertility sparing surgery was defined as the preservation of the uterus and at least part of one ovary. It includes the following surgical methods: unilateral cystectomy (UC), unilateral salpingo-oophorectomy (USO), bilateral cystectomy (BC), unilateral salpingo-oophorectomy combined with contralateral ovarian cystectomy (USO+CC). Patient follow-up consisted of physical and gynecological examinations, CA-125, and ultrasound scan every 3 months during the first 2 years and every 6 months afterwards. Disease-free survival (DFS) defined as the duration from primary surgery to the first recurrence or the last visit. Overall survival (OS) defined as the duration from primary surgery to death or the last visit.

Data were statistically analyzed using SPSS 25.0 statistical software. The comparison between groups was performed by t-test. The adoption rate of counting data was expressed by chi-square test and Fisher exact probability method. The variables with statistically significant differences in univariate analysis were included in the COX regression model for multivariate analysis. DFS and OS were assessed using the Kaplan-Meier method, whereas statistically significant difference was examined by log rank test. The difference is statistically significant at P□0.05.

Results

A total of 169 BOT patients from January of 2005 to November of 2021 in Beijing Chaoyang hospital were included in the study. The median age was 45 years (range, 14-88 years), and 49 patients (29%) had not history of fertility. Median follow-up time was 81months (1-203months). The characteristics of patients are shown in Table 1. Majority of patients (54.4%) found the disease by physical examination, then abdominal pain. 55% patients' tumors diameter of BOTs were larger than 10 cm and 81.7% were

unilateral. The most common pathology type was serous (48.5%), then mucinous (43.8%). 57.4% patients underwent laparoscopic surgery. There were 127 patients diagnosed at early stage.

A total of 21 patients relapsed, with a recurrence rate of 12.4%. The shortest interval of recurrence was 2 months and the longest was 148 months. The median recurrence interval was 62 months. Through univariate analysis, we found that FIGO stage, invasive implantation and chemotherapy affected BOT recurrence, and the differences were statistically significant (P <0.05). The recurrence rate of FIGO stage I was 8.7% and FIGO stage II and III was 24.4%. The recurrence rate of the patients with invasive implantation was 40% and patients without invasive implantation was 10.8%. The recurrence rate of patients receiving chemotherapy was 25% and not receiving chemotherapy was 9%. The survival curves of patients in these groups are provided in Fig. 1. Univariate analysis of factors affecting recurrence are shown in Table 2. Through multivariate analysis, we found that FIGO stage was only one independent risk factor affecting BOT recurrence rate (P=0.039).

In this study, 60 patients underwent fertility sparing surgery. The median age was 28 years (range, 14-46 years). There were 40 patients undergoing USO, 10 patients undergoing UC, 4 patients receiving BC and 6 patients receiving USO+CC. The recurrence rates of these patients were 10%, 0%, 25% and 33.3% respectively, indicating that the groups showed no statistically significant difference. The recurrence rate of laparoscopic group was 15% and of laparotomy was 10%, but the differences were not statistically significant (P=0.570). The recurrence rate of patients with tumor size smaller than 10cm was 20.7%, and tumor size larger than 10cm was 3.2%, the difference has statistically significant (P=0.035). The recurrence rate of patients with unilateral tumor was 8% and with bilateral tumors was 30% (P=0.048). Univariate analysis of factors affecting recurrence in BOT patients with FSS are shown in Table 3.

Because of some reasons, only 16 patients still had fertility desire after operation. Among them, 13 patients have successfully conceived spontaneously and all of them had term live births. The pregnancy rate was 81.3%. There were no serious complications in obstetric and neonatal outcomes among women with live births. No tumor recurrence happened during pregnancy. The pregnancy rates in these patients receiving USO, UC, BC or USO+CC were 88.9%, 66.7%, 50% and 100% (P=0.899) respectively. The pregnancy rates in FIGO stage I and advanced FIGO stage were 81.1% and 80% (P=0.148). The pregnancy rate of patients underwent chemotherapy was 75%, which lower than patients without chemotherapy (83.3%), however, the difference was not statistically significant. The pregnancy rate in laparoscopic group was 100% and in laparotomy group was 75% (P=0.825). The pregnancy rates in patient with lymphadenectomy or without lymphadenectomy were 80% and 81.8%, respectively. Through univariate and multivariate analysis, no factor was found to be significantly correlated with pregnancy rate. (Table 4)

After the median follow-up times of 81months, six patients in radical surgery group died of their disease, and no patient in FSS died (P=0.035). Two patients in FIGO stage I and four patients in advanced FIGO stage died of their disease (P=0.086). One patient with invasive implantation and five patients without invasive implantation died of their disease (P=0.852). Five patients receiving chemotherapy and one

patient didn't receiving chemotherapy died of their disease (*P*=0.887). The Kaplan-Meier analysis of OS in these groups are illustrated in Fig.2.

Discussion

Swanton et al. conducted a system review included 923 BOTs patients from 19 studies, the recurrence rate in the system review was 16% [4]. In other literature, the recurrence rate of BOTs was 19% [5]. Alvarez et al. reported that the recurrence rate of BOTs was 12%-58% [6]. In this study, a total of 21 patients relapsed and the recurrence rate of BOTs patients was 12.4%, which was consistent with the literature reports.

Through retrospective analysis and literatures review, we found some recurrence factors, although our results do not confirm data from those previous studies. We found that FIGO stage, invasive implantation and chemotherapy were risk factors for recurrence of BOTs (*P*0.05). Many studies have demonstrated that higher FIGO stages are always accompanied by worse prognosis. While only 5% of patients initially diagnosed in FIGO stage I are confronted with relapse of the disease, patients with extended disease are faced with recurrence in up to 25% of cases [7-8]. Seong SJ et al. [9] reported that the 5-year survival for FIGO stage I BOT patients was approximately 95% to 97%, while stage II-III BOTs patients was only 65% to 87%. In the analysis of this study, the recurrence rate of FIGO stage I was 8.7% and FIGO stage II-III was 24.4% (*P*=0.035). The DFS between FIGO stage I group and FIGO stage II–III group had significant difference (*P*=0.021). However, the 5-year survival for FIGO stage I BOT patients was 95.2%, while stage II-III BOTs patients was 93.8% (*P*=0.086). Invasive implantation was one risk factor for the recurrence of BOTs in this study. Alvarez et al. showed the recurrence rate is higher in patients with invasive implantation [6]. Shih et al. also demonstrated that the presence of invasive implantation was the independent risk factors for the recurrence of BOTs [10]. Research have shown that the most important predictors of recurrence were the FIGO stage and the presence of invasive implantation [11]. In this study, the recurrence rate of patients with invasive implantation was 40% and without invasive implantation was 10.7% (*P*=0.006). Through Kapan-Meier analysis, the DFS and OS were no significant difference between the two groups. In our study, chemotherapy as a treatment instead became a risk factor for recurrence. It is possible that the only patients with BOTs for whom chemotherapy is considered are those with advanced FIGO stage disease and invasive implants, because studies have found that this group of patients have a high recurrence rate. However, there is no proven benefit from chemotherapy, even in advanced disease stages or when there is presence of invasive implants. Longacre et al. Published a study of 276 patients with BOT. of 113 patients with advanced serous BOTs, 42 received chemotherapy. 71% of the patients in the chemotherapy group were still alive after a median follow-up of 126.5 months. In contrast, 87% of the patients without chemotherapy survived after 93 months of median follow-up [12]. In our study, there were 36 patients received chemotherapy after surgery. The recurrence rate was 25%, which was significantly higher than patients without chemotherapy (9.1%), however, the DFS and OS had no significant difference between these group.

Previous studies showed that histology type was one of the controversial risk factors. Fang et al. [13] showed that the patients with serous borderline ovarian tumors had a higher recurrence rate (58% vs 12%, *P*=0.003), and a shorter recurrence interval (*P*=0.007) than patients with mucinous tumors. Uzan et al. reported that 140 mucinous BOTs and 114 serous BOTs, 43 patients had developed at least one recurrence, 26 among patients with SBOT and 17 among patients with MBOT (P=0.01) in the median follow-up of 45 (range 3-136) months [14]. Loizzi et al. observed no difference in the survival rate between different histological types [15]. Our data showed the recurrence rate was 10% in serous BOTs and was 16.2% in mucinous BOTs. There was no difference in the recurrence rate between different histological types. Many articles have reported that micropapillary pattern are always accompanied by higher recurrence rate. Shih et al. showed that of the 196 patients with borderline tumor of serous histology, those with a micropapillary pattern had a 3-year PFS of 75.9% compared with 94.3% for patients without micropapillary pattern (P□0.001) [10]. In silva's study, micropapillary pattern was the only feature that was associated with a higher recurrence rate (26% vs. 4%, P =0.008) [16]. On the controversy, Uzan et al. demonstrated that the recurrence rate was 71% in patients without micropapillary pattern and 51% in patients with micropapillary (*P*=0.1) [14]. In this study, we found that the recurrence rate was 14.9% in patients without micropapillary pattern and 10.8% in patients with micropapillary pattern. There was no difference in the recurrence rate between patients with or without micropapillary pattern. Song et al. showed that a retrospective analysis was performed on 687 patients who underwent laparoscopy (n=312), or laparotomy (n=375) due to BOTs. After the median 41.8 months follow-up times, 21 patients in laparoscopy group, and 24 patients in laparotomy group had recurrence, and 4 patients in the laparoscopy group and 6 patients in the laparotomy group died of the disease. The rates of recurrence-free survival and overall survival did not differ between groups [17]. In this study, we found that the recurrence rate was 14.4% in laparotomy group and 9.8% in laparoscopic group, the difference was no significant.

BOTs are typically present in reproductive age women, diagnosed at the early stage, and have a favorable prognosis. Median age at diagnosis is 45 years with 34% of patients being under 40 [18-20]. BOTs present more frequently as a disease limited to the ovaries compared with invasive carcinoma, as was reported in a systematic review of 6362 cases that 78.9% of the patients with BOTs are diagnosed at FIGO stage I [21]. Therefore, a fertility sparing surgery is the preferred choice for young patients who desire to preserve fertility. In this study, the recurrence rate of FSS was 11.7%. Others studies have the similar conclusion. Seong et al. reported that recurrence rate of BOTs patients with fertility sparing is 10% to 20% [9]. Qi et al also reported that the recurrence rate of BOT patients with FSS was 10.2% [22].

Through univariate analysis, we found that tumor size and tumor site were the risk factors for recurrence of patients receiving FSS. However, they do not affect the pregnancy rate. In our study, the recurrence rate of tumor size smaller than 10cm was 20.7% and of tumor size larger than 10cm was 3.2% (*P*=0.035), however, the pregnant rate of tumor size smaller than 10cm was 80% and larger than 10cm was 83.3% (*P*=0.282). Qi et al. reported that the recurrence rate was 10.3% in tumor size smaller than 10cm group and 10.1% in tumor size larger than 10cm group, the pregnant rate was 54.5% and 57.9%, respectively. The difference was not statistically significant [22]. Fang et al. showed that the recurrence rate was 40.7%

in tumor size smaller than 10cm group and 29.6% in tumor size larger than 10cm group (P=0.569) [13]. In all of these studies, tumor size smaller than 10cm seem to be more likely to recur. We speculate that it may be because small tumors are more likely to be cystectomy rather than salpingo-oophorectomy, or it may be that small tumors are less likely to be removed completely. We also found that bilateral tumor was a risk factor for recurrence. In this study, the recurrence rate of bilateral BOTs was 30% and unilateral was 8%, the difference has statistically significant (*P*=0.048), however, it didn't affect the pregnancy rate. Some researchers reported that the 5-year RFS was 74% and 48% in patients with unilateral and bilateral tumors, respectively [23]. Fang et al. also showed that patients with bilateral tumors had a higher recurrence rate after FSS (27.9% vs 63.6%, P=0.038). The pregnancy rate was no significant difference between the two groups [13]. Qi et al reported that there were 7.4% recurrence rate in unilateral group and 24.2% in bilateral group (*P*=0.009). The pregnancy rate was 59.6% in unilateral group and 43.7% in bilateral group, the difference was no significant(*P*=0.271) [22]. Chen et al. reported that patients with bilateral tumors had a higher recurrence rate (4.7% vs 18.7%, P=0.07) and a shorter recurrence interval (33.2months vs 23months, P=0.00) after conservative treatment [24].

In our population, FSS includes the following surgical approach: unilateral cystectomy (UC), unilateral salpingo-oophorectomy (USO), bilateral cystectomy (BC), unilateral salpingo-oophorectomy combined with contralateral ovarian cystectomy (USO+CC). Through analysis, surgical approach did not influence recurrence or fertility. 10 patients recurred after UC with a recurrence rate of 10%, which was higher than that of 0% after USO. Compared with USO+CC, the recurrence rate of BC was lower (25% vs 33.3%). Qi et al. reported that regarding the comparison of USO with UC, 5 cases recurred after UC with a recurrence rate of 8.9%, which was higher than that of 6.5% after USO (P=0.812). 10 cases pregnant after UC with a pregnancy rate of 66.7%, which was higher than that of 56.2% after USO (P=0.498), but there were no significant differences between the two groups. Compared with USO+CC, the recurrence rate of BC was lower (18.7% vs 29.4%), the pregnancy rate of BC was also lower (40% vs50%), there were no significant differences between the two groups [22]. There were 106 patients with unilateral BOTs in a study, 47 patients underwent unilateral adnexectomy and 59 underwent unilateral cystectomy. The study showed that more patients relapsed in shorter time in unilateral cystectomy group, though this difference was not statistically significant (6.8% vs 2.1%, P=0.38), and there was also no difference between these two group in pregnancy outcome [24].

Uzan et al. reported that surgery approach (laparoscopic or laparotomy) was not associate with recurrence for patients underwent FSS [14,23]. Chen et al. analyzed that, compared to laparotomy, laparoscopy had no disadvantage in terms of recurrence rate and pregnancy rate [24]. In this study, surgery procedure was also not associate with recurrence rate and pregnancy rate for patients underwent FSS. Qi et al. showed that the recurrence rate of laparotomy in FSS patients is higher than in laparoscopic surgery (14.3% vs 4.3%, *P*=0.029). The pregnancy rate between laparotomy and laparoscopic has no significant difference (60.6% vs 50%, P=0.397) [22]. Therefore, laparoscopy seems to be the most attractive surgical approach to BOT due to well-proven benefits such as faster recovery, lower perioperative complication rates and reduce pelvic adhesion that could possibly impair fertility.

In our study, there were 13 patients received chemotherapy after FSS. The recurrence rate was 15.4% and the pregnancy rate was 75%, compared to without chemotherapy patients, the difference was not statistically significant. Fang et al. Studied 12 patients underwent chemotherapy and concluded that there was no significant difference in recurrence rate and pregnancy rate [13]. All the evidence demonstrated that the patients did not receive any benefit from chemotherapy, especially for patients underwent FSS. Chemotherapeutic agents which reach the ovaries lead to damage to the primordial follicles. The detrimental effect of cytotoxic agents on the ovary is thought to be caused by damage to peri-oocyte granulosa cells in the ovaries. Damage to ovarian tissue as a result of the use of cytotoxic agents is irreversible. Histological samples of ovarian tissue after chemotherapy have shown range of damage, from a reduction in follicle count to complete failure [25]. Therefore, chemotherapy was not recommended for patients even with advanced BOT, especially of patients who have fertility desire.

There are some limitations in this study. It is a retrospective study and the nature of the study might be a source of bias. The number of included patients was limited, and the relatively small number of patients attempt to conceive might limit the statistical power of our findings.

Conclusion

BOT are tumors with a favorable prognosis. After univariate and multivariate analysis, we found some risk factors for recurrence after radical surgery, but they don't affect the overall survival rate. FSS is a feasible approach for young patients. Although tumor size and tumor site are risk factors for recurrence, they do not affect long-term survival and pregnancy rate. Laparoscopy procedure is recommended and chemotherapy is not recommended for patients receiving FSS. We suggest that patients who preserve fertility should get pregnant as soon as possible and follow up closely.

Declarations

Ethics approval and consent to participate

Not applicable. Because this study was a retrospective study, the ethics approval and consent to participate were waived by the Medical Ethics Committee of Beijing Chaoyang Hospital. All procedures performed in this study involving human participants were in accordance with the ethical standards of the1964 Helsinki declaration and its later amendments.

Consent for publication

Not applicable. No details on individual patients have been reported in this study.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All the authors declare that they have no conflict of interests.

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Authors' contribution

Qi Lu and Chongdong Liu conceived of the study and participated in its design and implementation. Qi Lu and Yupeng Deng participated in the drafting of the manuscript; Yupeng Deng and Zhiqiang Zhang collected and analyzed the data; Chongdong Liu revised the manuscript critically.

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Tables

Table 1. Clinicopathological and biological data of BOT patients

characteristic	Number	Percentage (%)
Median age (min, max)	45 (14-88)	
History of fertility		
No	49	29
Yes	120	71
Sexual history		
No	25	14.8
Yes	144	85.2
Menopause		
No	105	62.1
Yes	64	37.9
Chief complaint		
Abdominal pain	48	28.4
Touching mass	9	5.3
Physical examination	92	54.4
Others	20	11.8
Tumor size (cm)		
10	76	45
≥10	93	55
Tumor site		
Unilateral	138	81.7
Bilateral	31	18.3
CA125		
≤35	65	38.5
35	57	33.7
None	47	27.8
Frozen section diagnosis		
Benign	49	29
Borderline	104	61.5

None	16	9.5
Ovarian tumor rupture		
Spontaneous rupture	24	14.2
Intraoperative rupture	6	3.6
None	139	82.2
Pathology		
Serous	82	48.5
Mucinous	74	43.8
others	13	7.7
Micropapillary pattern		
No	76	45
Yes	93	55
Invasive implantation		
No	159	94.1
Yes	10	5.9
Surgical approach		
Laparotomy	97	57.4
Laparoscopy	72	42.6
Lymphadenectomy		
No	71	42
Yes	98	58
Omentectomy		
No	52	30.8
Yes	117	69.2
Fertility-sparing surgery		
No	109	64.5
Yes	60	35.5
FIGO stage		
I	127	75.1

≥II	42	24.9
Chemotherapy		
No	133	78.7
Yes	36	21.3
Involvement ovary		
Reserved	13	7.7
Excision	156	92.3
Complete Staging surgery		
No	61	36.1
Yes	108	63.9

Table 2 Univariate analysis of factors affecting recurrence in patients with BOT

characteristic	No recurrence (%)	Recurrence (%)	*P* value
Median age (min, max)			
History of fertility			
No	43 (87.8)	6 (12.2)	0.964
Yes	105 (87.5)	15 (12.5)	
Menopause			0.982
No	92 (87.6)	13 (12.4)	
Yes	56 (87.5)	8 (12.5)	
Tumor size (cm)			0.794
10	66 (86.8)	10 (13.2)	
≥10	82 (88.2)	11 (11.8)	
Tumor site			0.196
Unilateral	123 (89.1)	15 (10.9)	
Bilateral	25 (80.6)	6 (19.4)	
CA125			0.691
≤35	54 (88.5)	7 (10.8)	
35	84 (86.7)	5 (8.9)	
None			
Frozen section diagnosis			0.559
Benign	44 (89.8)	5 (10.4)	
Borderline	89 (85.6)	15 (14.4)	
None	15 (93.8)	1 (6.2)	
Ovarian tumor rupture			0.438
No	123 (88.5)	16 (11.5)	
Yes	25 (83.3)	5 (16.7)	
Pathology			0.225
Serous	73 (89.0)	9 (11.0)	
Mucinous	62 (83.8)	12 (16.2)	
others	13 (100)	0 (0)	

Micropapillary pattern			0.466
No	65 (85.5)	11 (14.5)	
Yes	83 (89.2)	10 (10.8)	
Invasive implantation			0.006
No	142 (89.3)	17 (10.7)	
Yes	6 (60.0)	4 (40.0)	
Surgical approach			0.359
Laparotomy	83 (85.6)	14 (14.4)	
Laparoscopy	65 (90.3)	7 (9.7)	
Lymphadenectomy			0.133
No	59 (83.1)	12 (16.9)	
Yes	89 (90.8)	9 (9.2)	
Omentectomy			0.460
No	47 (90.4)	5 (9.6)	
Yes	101 (86.3)	16 (13.7)	
Fertility-sparing surgery			0.824
No	95 (87.2)	14 (12.8)	
Yes	53 (88.3)	7 (11.7)	
FIGO stage			0.035
I	116 (91.3)	11 (8.7)	
≥II	32 (76.2)	10 (23.8)	
Chemotherapy			0.011
No	121 (90.9)	12 (9.1)	
Yes	27 (75.0)	9 (25.0)	
Involvement ovary			0.590
Reserved	12 (92.3)	1 (7.7)	
Excision	136 (87.2)	18 (12.8)	
Complete Staging surgery			0.838
No	53 (86.0)	8 (13.1)	

Yes	95 (88.0)	13 (12.0)

Table 3. Univariate analysis of factors affecting recurrence in BOT patients with FSS

characteristic	No recurrence (%)	Recurrence (%)	P
Number	53 (88.3)	7 (11.7)	
Median age (min, max)	28 (14-46)	29 (24-36)	0.929
History of fertility			0.704
No	34 (87.2)	5 (12.8)	
Yes	19 (90.5)	2 (9.5)	
Tumor size (cm)			0.035
10	23 (79.3)	6 (20.7)	
≥10	30 (96.8)	1 (3.2)	
Tumor site			0.048
Unilateral	46 (92.0)	4 (8.0)	
Bilateral	7 (70.0)	3 (30.0)	
CA125			0.336
≤35	15 (83.3)	3 (16.7)	
35	23 (95.8)	1 (4.2)	
None	15 (83.3)	3 (16.7)	
Frozen section diagnosis			0.564
Benign	17 (85)	3 (15)	
Borderline	29 (87.9)	4 (12.1)	
None	7 (100)	0 (0)	
Ovarian tumor rupture			0.512
Spontaneous rupture	9 (90)	1 (10)	
Intraoperative rupture	4 (100)	0 (0)	
None	46		
Pathology			0.737
Serous	23 (88.5)	3 (11.5)	
Mucinous	26 (86.7)	4 (13.3)	
others	4 (100)	0 (0)	
Micropapillary pattern			0.795

No	25 (89.3)	3 (10.7)	
Yes	27 (87.1)	4 (12.9)	
Invasive implantation			0.711
No	51 (87.9)	7 (12.1)	
Yes	1 (100)	0 (0)	
Surgical approach			0.570
Laparotomy	36 (90)	4 (10)	
Laparoscopy	17 (85)	3 (15)	
Lymphadenectomy			0.055
No	25 (80.6)	6 (19.4)	
Yes	28 (96.6)	1 (3.4)	
Omentectomy			0.903
No	24 (88.9)	3 (11.1)	
Yes	29 (87.9)	4 (12.1)	
Fertility-sparing surgery			
USO	36 (90)	4 (10)	0.297
UC	10 (100)	0 (0)	
BC	3 (75)	1 (25)	0.778
USO+CC	4 (66.7)	2 (33.3)	
FIGO stage			0.082
I	44 (91.7)	4 (8.3)	
≧ II	9 (75)	3 (25)	
Chemotherapy			0.657
No	42 (89.4)	5 (10.6)	
Yes	11 (84.6)	2 (15.4)	
Involvement ovary			0.547
Reserved	13 (92.9)	1 (7.1)	
Excision	40 (87)	6 (13)	
Complete Staging surgery			0.228

No	25 (83.3)	5 (16.7)
Yes	28 (93.3)	2 (6.7)

Table 4. Univariate analysis of pregnancy factors in BOT patients with FSS

characteristic	Non-pregnancy	N patients achieving/ attempting pregnancy (%)	P
Number	47	13/16 (81.3)	
Median age (min, max)	29	28□20-36□	0.309
History of fertility			
No	28	11/13 (84.6)	0.094
Yes	19	2/3 (66.7)	
Tumor size (cm)			
□10	21	8/10 (80.0)	0.282
≥10	26	5/6 (83.3)	
CA125			
≤35	16	2/4 (50.0)	0.420
□35	18	6/7 (85.7)	
None	13	5/5 (100.0)	
Pathology			
Serous	19	7/10 (70%)	0.640
Mucinous	25	5/5 (100.0)	
others	3	1/1 (100.0)	
Micropapillary pattern			
No	21	7/9 (77.8)	0.601
Yes	25	6/7 (85.7)	
Invasive implantation			
No	45	13/15 (86.7)	0.592
Yes	1	0/1 (0)	
Surgical approach			
Laparotomy	31	9/12 (75.0)	0.825
Laparoscopy	16	4/4 (100.0)	
Lymphadenectomy			
No	22	9/11 (81.8)	0.152

Yes	25	4/5 (80.0)	
Omentectomy			
No	20	7/10 (70.0)	0.469
Yes	27	6/6 (100.0)	
Fertility-sparing surgery			
USO	32	8/9 (88.9)	0.899
UC	8	2/3 (66.7)	
BC	3	1/2 (50.0)	
USO+CC	4	2/2 (100.0)	
FIGO stage			
I	39	9/11 (81.8)	0.148
II	8	4/5 (80.0)	
Chemotherapy			
No	37	10/12 (83.3)	0.889
Yes	10	3/4 (75.0)	
Complete Staging surgery			
No	22	8/10 (80.0)	0.347
Yes	25	5/6 (83.3)	

Figures

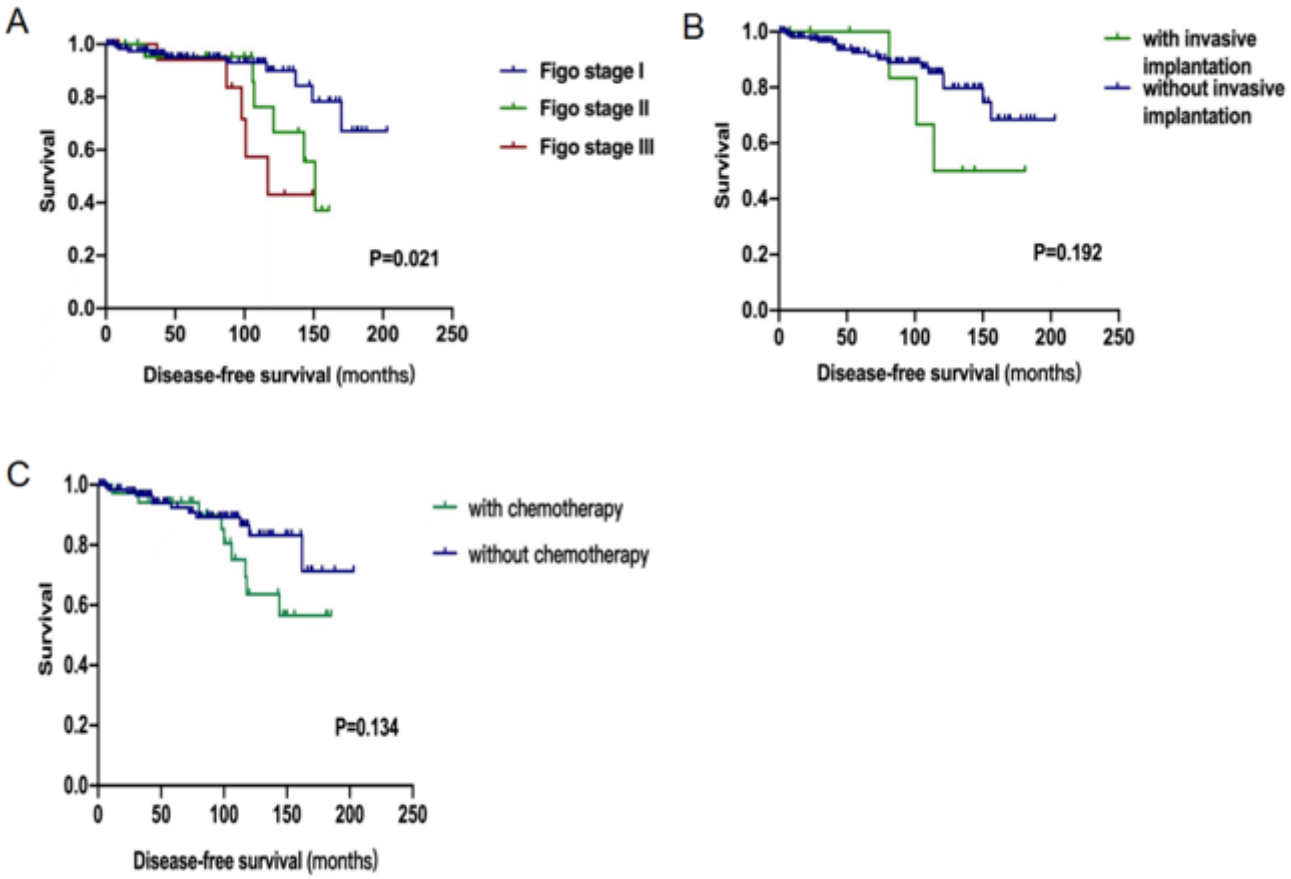

Figure 1

Disease-free survival curves (DFS) for different clinicopathologic factors. **A** comparison of DFS curves between FIGO stage I and advanced stage BOTs. **B** comparison of DFS curves between patients with invasive implantation and patients without invasive implantation. **C** comparison of DFS curves between patients with chemotherapy and without chemotherapy.

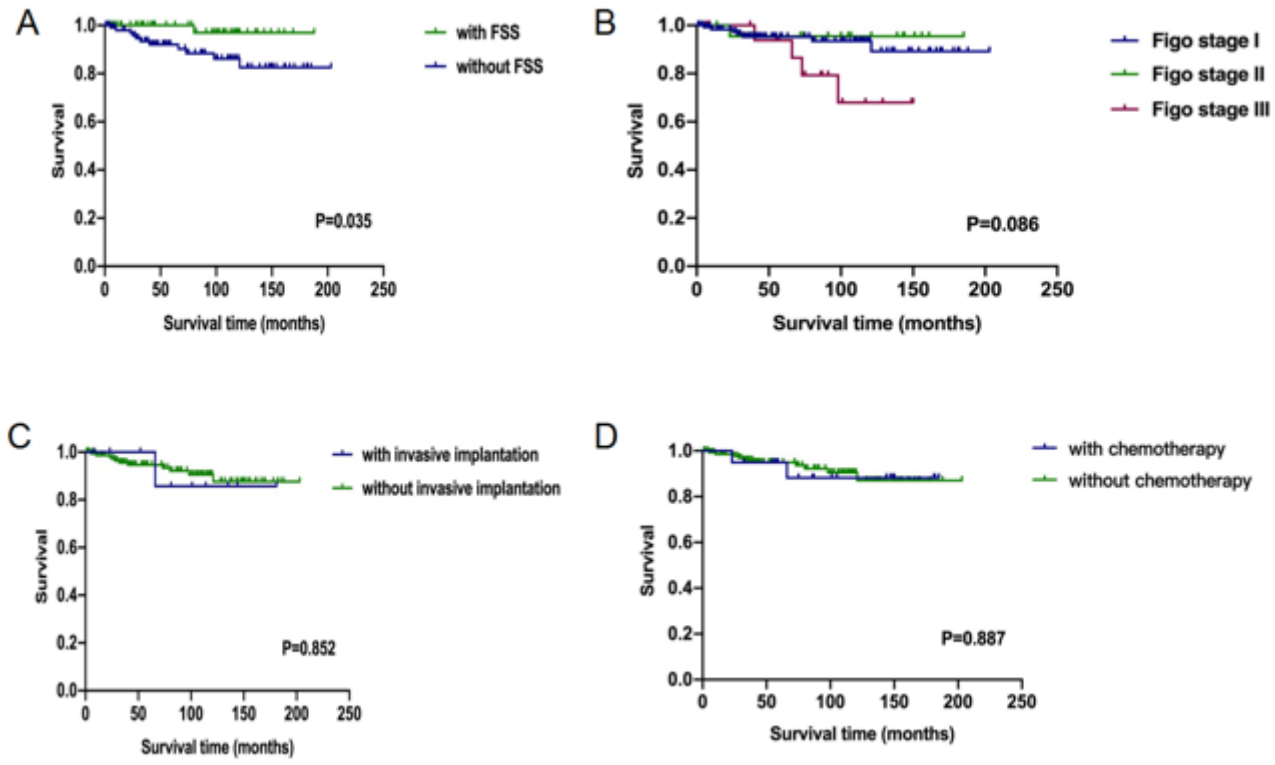

Figure 2

Overall survival curves (OS) for different clinicopathologic factors. **A** comparison of OS curves between patietns with FSS and patients without FSS. **B** comparison of OS curves between FIGO stage I and advanced stage BOTs. **C** comparison of OS curves between patients with invasive implantation and patients without invasive implantation. **D** comparison of OS curves between patients with chemotherapy and without chemotherapy.