Ovarian serous borderline tumors with recurrent or extraovarian lesions: a Japanese, retrospective, multi-institutional, population-based study

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Research Article

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Abstract

Background

Ovarian serous borderline tumors (SBT) are typically unilateral and are primarily treated using hysterectomy and bilateral salpingooophorectomy (SO). However, most young patients prefer fertility-sparing surgeries (FSS) with tumorectomy or unilateral SO. Micropapillary morphology and invasive implants have been designated as histopathological risk indicators for recurrence or metastasis, but their clinical impact remains controversial because of limitations like diagnostic inconsistency and incomplete surgical staging.

Methods

A nationwide multi-institutional population-based retrospective surveillance was conducted with a thorough central pathology review to reveal the clinical features of SBT. Of 313 SBT patients enrolled in the Japanese Society of Clinical Oncology's Surveillance of Gynecologic Rare Tumors, 289 patient records were reviewed for clinical outcomes. The glass slides of patients at stage II–IV or with recurrence or death were reevaluated by three gynecological pathologists.

Result

The 10-year overall and progression free survival (PFS) rates were 98.6% and 92.3%. A recurrence of 77.0% was observed in the contralateral ovary within a few years. Patients aged ≤ 35 years underwent FSS more frequently and relapsed more (p<.001). A clinic-pathological analysis revealed diagnosis during pregnancy, FSS, and treatment at non-university institutes as well as advanced stage and large diameter were independent risk factors of recurrence. Among patients having pathologically-confirmed SBTs, PFS was not influenced by the presence of micropapillary pattern or invasive implants.

Conclusion

The recurrence rate was lower in this cohort than previous reports, but the clinical impacts of incomplete resection and misclassification of the tumor were still significant on the treatment of SBT.

Introduction

Epithelial borderline malignant tumors of the ovary are a group of tumors in which epithelial cells proliferate with mild-to-moderate cellular atypia without apparent stromal invasion. Tumors of this type exhibit wide-ranging clinical features, ranging from benign to malignant. The prognostic outcome of some patients who undergo excision of localized tumors may be good, while that of others may be poor with extraovarian extension and/or repeated recurrence. Serous and mucinous borderline malignancies are frequently encountered among the various epithelial borderline malignancies, whereas clear and other histological subtypes are clinically rare. Mucinous borderline tumors (BTs) rarely hinder treatment decisions in clinical settings because they are mainly confined to the unilateral ovary and have a low

incidence of capsular disruption, which can be cured with unilateral salpingo-oophorectomy (SO). In contrast, serous borderline malignant tumors (SBTs) are not considered easy to treat because of their epidemic frequency and diversity in histopathology and clinical behaviors.

The pathological classification of SBTs and low-grade serous carcinomas (LGSCs) has contributed to the difficulty in treating SBTs. The 2010 Ovarian Cancer Treatment Guidelines [1] complied with the National Comprehensive Cancer Network (NCCN) guidelines and recommended the classification of SBT considering the risk factors. The listed risk factors for SBTs are advanced stage, presence of microinvasion, invasive peritoneal implants, lymph node metastasis, micropapillary pattern, and malignant transformation, all of which correlate with each other [2]. In particular, the mortality rate of SBT in cases involving invasive implants is as high as 34% [2]; therefore, those with invasive implants are currently diagnosed with LGSC, rather than SBTs, after revision of the World Health Organization (WHO) classification. SBTs with a micropapillary pattern have a high N/C ratio in tumor cells and cribriform structures, frequently accompanied by peritoneal implants. These findings make it difficult to distinguish them from LGSCs, although the actual clinical background is reported to be closer to SBT than LGSC [3]. Kurman et al. performed a prognostic analysis of nearly 500 cases of SBT in a multicenter study that showed that survival differed depending on whether the peritoneal implant was invasive (66% vs. 95%, $p < .0001$) [4]. However, it was not found to differ in another observational study by Kane et al. (75% vs. 74%, $p = .6$), which helped conclude that central pathology is mandatory for assessing pathological prognostic factors in a multicenter study [5].

Furthermore, as SBTs occur mainly in young people, with > 30% of cases involving bilateral lesions, fertility preservation is essential in many patients. SBTs occurring outside the ovary have a relatively poor prognosis and require careful handling [2]. Although it has been confirmed that stage I patients have a good prognosis without extended excision or adjuvant chemotherapy [1], it is unclear whether stage II–IV patients can be safely treated in a fertility-sparing manner. Long-term surveillance of stage II–IV patients with noninvasive implants revealed recurrence of SBTs as LGSC in > 30% of cases, with a mortality rate of 25% (n = 80) [6]. In addition, 58% of stage II–III patients who underwent fertility-sparing surgery (FSS) had a recurrence, even though only 34% were pregnant (n = 41) [7]. Thus, because incomplete surgical excision is a universally common occurrence, the actual prognostic outcomes of SBTs, such as recurrence rate and survival, are difficult to determine not only in stage II–IV cases but also in putative stage I cases.

To date, there have been a couple of Japanese case series reports of SBT. However, because of their small sample size (23 and 47 patients, respectively) and the recruitment period in which LGSC was considered as the diagnosis in those finally diagnosed with SBT [8, 9], it is difficult to utilize these reports for the assessment and treatment of current Japanese patients. Due to the change in the definition of the diagnosis and the lack of preference for radical surgery, there are few studies even in the world that have reproducibly demonstrated the exact features of SBT. The aim of this study was to conduct a nationwide, multi-institutional, population-based, retrospective study with a thorough central pathology review to reveal the clinical features of SBT.

Patients and Methods

Patients

A total of 25 member hospitals of the Gynecologic Cancer Study Group of Japan Clinical Oncology Group (JCOG-GCSG) participated in this retrospective study. The study design was approved by the institutional review board of each hospital and conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived owing to the retrospective nature of the study. We formed a database of patients with ovarian SBTs who had received initial treatment between 1999 and 2008 at one of the JCOG-GCSG member hospitals. The following patients were excluded: (1) insufficient data on the clinical course, (2) untreated, and (3) not diagnosed with SBT after central document review.

Methods

Patient data

This surveillance study was approved by the Cabinet Board of JCOG-GCSG. To protect patient privacy, patient identification was anonymized within each facility and registered using only the name of the facility and a consecutive number. The following clinical information on patients was collected: age, marital status, parity at the start of treatment, clinical findings, surgical procedures, pathological findings, therapeutic process, prognosis, and reproductive outcomes. The clinical stages were restaged according to FIGO 2008 staging system. The patients were further classified according to the guidelines of the 7th edition of the Union for International Cancer Control TNM Classification of Malignant Tumors. The tumor histology of patients for the following two categories was reviewed by the central pathological review (CPR) according to the criteria for the classification of ovarian tumors documented by the WHO 2014.

Category 1: Stage II–IV

Category 2: Stage I resulting in recurrence or death

Due to the limited sample size of CPR for document reviewed cases, 10 Category 1 and 8 Category 2 cases that had not been included in the document review were further recruited. CPR was conducted using slide glass analysis by three pathologists specializing in gynecological cancers.

Statistical analysis

All endpoints were calculated from the date of the start of initial treatment to death, recurrence, progression, or censored at the last follow-up. Overall survival (OS) and progression-free survival (PFS) curves were drawn using the Kaplan–Meier method and compared using the log-rank test. Categorical incident comparisons were performed using Fisher's exact test. Statistical analyses were performed using Prism (version 7.0; GraphPad Software Inc., La Jolla, CA, USA) and IBM SPSS Statistics ver28. (IBM, Armonk, NY, USA) p-values of < 0.05 were considered significant.

Results

Prognostic outcome of patients initially treated for SBTs in JCOG-GCSG accredited institutes

In total, 313 patients from 25 cancer institutes were included in this study. Of these, 24 were excluded based on the guidelines of the central document review because of other diagnoses (n=13) or insufficient clinical information (n=11). A total of 289 patients were eventually included for further analysis of the initial diagnosis of ovarian SBT (Supplementary Figure 1A). In this cohort, the 10-year OS and PFS rates were 98.6% (Figure 1) and 92.3%, respectively. Among the included 289 cases, the most common tumor gross size was 5–10 cm (41%), and papillae on the internal surface were the most common tumors (55%, Table 2). Sixty-two cases had SBT lesions on both ovaries (15.2%), whereas SBT lesions were unilaterally present in 183 cases at stage IA (63.3%) (Table 2). Patient characteristics were clinically and pathologically variable (Supplementary Figure 1B).

The number of patients with no recurrence, recurrence in the contralateral ovary, recurrence in other sites of the body, and death due to disease was assessed for each stage (Supplementary Table 1). Two hundred and forty-two patients were at stage I without any recurrence (83.7%), 12 had recurrence of SBT (IA, n=6; IC, n=2; and III, n=4), and two died of the disease (0.7%). Complete tumor excision was achieved in 276 patients (95.5%), and the PFS and OS rates were significantly higher in those who underwent complete excision (p<.001, Figure 2A). Incomplete excision was more frequent in patients with papillae on the external surface or solid masses on the cyst (7.1%) than in those that exhibited other tumor appearances (1.5%, p<.05). Six of the 183 stage IA cases had recurrence in the contralateral ovary within a few years after the primary surgery (3.3%, 1127± 586 days). Three patients had recurrence other than in the contralateral ovary: one at stage IC with multiple intra-abdominal lesions and two at stage III with lymph node metastases in the mediastinum and axilla, respectively.

The numbers of patients and treatments according to age are presented in Table 1. The mean age of the patients was 47.3 ± 16.0 years; women aged 26–45 years formed a larger proportion of cases, and 79 patients were aged ≤ 35 years. Sixty-four of the 79 patients were nullipara (81.0%), which was higher than that observed in patients aged > 35 years (24.3%, p<.001). Furthermore, 10.1% of patients aged ≤ 35 years were pregnant at the time of surgery compared with 1.0% of patients aged > 35 years (p<.001). Half of the patients aged ≤ 35 years were diagnosed with stage IA disease (Supplementary Figure 1B).

For the surgical procedures, cystectomy and unilateral SO were conducted in 11 and 102 patients, respectively. Of the patients aged ≤ 35 years, 86.1% underwent FSS, compared with only 21% of those aged > 35 years (p<.001, Table 1). Among patients aged ≤ 35 years, approximately 20% had a successful pregnancy after FSS, compared with only 0.9% of those aged > 35 years (p<.001). Owing to preserving fertility, 10.1% of patients aged ≤ 35 years experienced recurrence, compared with only 1.8% of those aged > 35 years (p<.005). PFS was significantly inferior in those who underwent FSS (p<.001), whereas OS was comparable between the two age groups (Figure 2B).

As a summary of document reviews, a multivariate binomial logistic regression analysis of clinicopathological factors accounting for recurrence was conducted (Table 2), which revealed that pregnancy at diagnosis, fertility-sparing surgery (FSS), and treatment at non-university institutes as well as advanced stage and large tumor diameter were independent risk factors of recurrence ($p<.05$), but not age, parity, CA125, macroscopic findings such as gross tumor findings and tumor laterality, and microscopic findings such as microinvasion, implants, and micropapillary architecture.

CPR for recurrent or metastatic SBTs treated in JCOG-GCSG accredited institutes

The review revealed that SBT could recur. Furthermore, it also showed that it recurred more frequently in young patients who underwent FSS, evoking questions such as “Is the pathological diagnosis properly provided with or without oncologically satisfactory excision?” Do these so-called pathological factors really affect the clinical outcomes of SBT patients?” To address these questions, central pathological reviews (CPR) were conducted. Among the 289 documented reviewed cases, 38 specimens from stage II–IV patients and 11 specimens from stage I patients with recurrence or death were provided.. The number of additionally recruited cases for CPR was 10 and 8, and specimens from 48 Category 1 and 19 Category 2 cases were evaluated. Four out of total 67 cases were excluded because of no specimen of primary tumor or out of criteria, glass slides of 63 patients were reevaluated by 3 gynecological pathologists to confirm the accuracy of the histopathological diagnosis and the significance of the pathological features (Figure 3A).

Through CPR, 63 reviewed cases were diagnosed with benign lesions (n=2), BTs other than SBT (other BT, n=5), SBT (n=50), LGSC (n=2), and other malignancies (n=4). Among other malignancies, there were two cases each of endometrial cancer and colon cancer. Four seromucinous BT and one endometrioid BT were included among the BTs other than SBT. In this study, the diagnoses of Category 1 and 2 high-risk SBT were made at university hospitals (n=39) and non-university hospitals (n=24). Through CPR, diagnoses other than SBT or LGSC were made for eight cases at non-university hospitals, which is more frequent than those made at university hospitals (n=3, $p<.05$, Supplementary Table 2).

The clinical effects of the established poor prognostic indicators were then investigated in 50 pathologically-confirmed SBT cases. Only seven of the 28 SBT cases originally thought to display the micropapillary pattern were diagnosed as micropapillary variants (25%). Among the 50 reviewed cases, 7 and 20 were designated as having invasive and noninvasive implants, respectively. However, through CPR, 3 and 16 patients were diagnosed as having invasive and desmoplastic implants, respectively. Based on these pathological findings, the clinical effects of characteristic pathological indicators were assessed. After CPR, the stage distribution of these 50 cases changed, with a tendency to be downmigrated (up: n=3, down: n=19). Seven cases could not be classified because of insufficient pathological specimens for precise surgical staging (Figure 3B). This migration was mainly due to the revision of the FIGO of Gynecology and Obstetrics surgical staging system. CPR also revealed that in

stage IA cases, recurrence was mainly found in the contralateral ovary, and only one stage IA patient died of the disease after recurrence as an LGSC, whereas four stage IA patients died of other malignancies or from heart failure. Among the true 50 cases of SBT, PFS was not influenced by the presence of a micropapillary pattern, invasive implants, stromal invasion, or nuclear atypia (Figure 4).

Discussion

For this Japanese, nationwide, retrospective surveillance of patients with SBT, more than 300 cases were included from 25 institutions, and 289 cases were centrally reviewed. The prognosis for SBT is favorable, such as mucinous BT (MBT), another borderline ovarian malignancy. However, SBT is associated with a lower average patient age than MBT, and several patients prefer fertility-sparing treatment rather than radical surgery. Because of the diversity in patients' backgrounds, their need to preserve fertility and their tumor growth patterns, clinical behaviors, and treatment of SBT should be carefully determined for each patient. The revision of the WHO classification for SBT and LGSC made the diagnostic boundaries of these entities somewhat clearer. The revised guidelines classify invasive implants as LGSC. However, with the underestimation of the clinical stage and frequent undertreatment due to fertility preservation, the actual prognosis of patients with SBT remains unclear, even though their realistic outcomes seem generally favorable. A large-scale Danish surveillance of ovarian borderline malignancies, including 2787 SBT cases, during the past 24 years [10], exhibited a historical trend of diagnostic shift in SBT owing to the revision of the WHO guidelines. This indicates a low risk of the subsequent development of ovarian cancer. Owing to the nature of chart review, it is difficult to determine the diagnostic accuracy and assess the clinical significance of the established pathological risk factors for survival.

In this study, the following findings were revealed through the central document review: a) most cases diagnosed with SBT are at stage I, b) subtotal resections are more common in young women who wish to retain fertility, c) recurrence does not occur in most patients, and d) patients in whom ovaries are retained are at a higher risk of recurrence.

One of the major established determinants of the prognostic outcome in patients with SBT is whether the lesion was completely resected, and this was also true in this study (Table 2). The Dutch national survey showed that 85% of patients had confined lesions on the unilateral ovary, and the 10-year survival rate of patients with SBT was 94.4% [10]. The recurrence rate of stage I cases in a Korean cohort was reported to be 9.9% [11], whereas that in our JCOG-GCSG cohort was 3.2%. Even though the patients at stage IA constituted only 63.3% in this study, complete excision was achieved in 96.9%, and the 10-year survival rate was as high as 98.6%. In the present study, the rate of complete resection was not altered based on tumor diameter but possibly based on the nature of the tumor growth pattern. Incomplete resection was more frequent among those with papillae on the external tumor surface (11.8%) than among those with papillae on the internal surface (0.6%, $p < .05$). The tumor morphology of SBTs and LGSCs differs based on the presence or absence of *BRAF* or *KRAS* [12]. Further investigation of tumor biology is mandatory, but there may be genetic alterations that produce differences in tumor growth and appearance.

In terms of complete resection, FSS including surgery during pregnancy is a risk factor for incomplete resections. In previous reports, the recurrence rate was 35.3% among patients who underwent FSS [13], and it was much higher (73.4%) in a study assessing the efficacy of FSS for bilateral ovarian lesions [14]. In a recent study in Germany, among 95 ovarian borderline tumor patients who underwent FSS, 13 relapsed (13.7%), but 29 gave birth to live babies (30.5%) [15]. In this study, 86.1% of patients aged < 35 years underwent FSS, and 10.1% experienced recurrence, while only 19.0% became pregnant postoperatively. These results are considered satisfactory as oncologic outcomes, but not as fertile outcomes. Given that retained ovaries were the most frequent site of recurrence, there was a definite risk of leaving invisible disseminated lesions over the preserved ovaries and uterus. Although the recurrence rate was low, a few patients succumbed to the disease. FSS has been shown to be a risk factor for recurrence, as in previous reports, but the true recurrence and metastatic mechanisms of SBT are unclear because FSS did not increase the risk of death.

To shed some light on this fundamental question, CPR was conducted in cases with extraovarian lesions or recurrence. CPR revealed that expert pathological investigation is vital for accurate diagnosis, assessment of micropapillary and invasive implants, and counseling, and that survivorship is high, even among true SBTs with recurrences. Unexpectedly, 11 (17.5%) of the 63 CPR cases that were considered to have metastases or recurrences involved neither SBT nor LGSC. Despite the WHO 2014 revision for pathological diagnostic criteria of SBT, the accurate diagnosis of SBT owing to a busy routine is challenging in Japanese high-volume cancer centers. Thus, it is difficult to diagnose SBT considering its high quality worldwide. Among these 50 SBTs, 8% of patients died of other malignancies or heart failure, and as previous report also noted [16], the cause of death was difficult to accurately ascertain in SBT case-series studies. In terms of accurate diagnosis and cause of death, careful attention should be paid to interpreting the survival analysis in previous reports without CPR or close follow-up.

Some of the reviewed cases showed characteristic pathological findings, including focal changes. Among the 50 pathologically confirmed SBTs, the outcomes were good even when high-risk histological characteristics were present (Fig. 4). This was because the micropapillary pattern, a high-risk characteristic, is not reportedly associated with poor outcomes [17]. A large-scale Danish population-based clinicopathological study showed that SBTs with micropapillary architecture have a higher risk of developing subsequent serous carcinoma (subSeCa) than those without it (hazard ratio [HR]:3.8, 95% confidence interval [CI]:1.7–8.2) [16], after the WHO 2020 revision, SBTs were classified into conventional SBT or micropapillary/cribriform SBT. Nonetheless, the pathogenic signalling pathway for subSeCa development remains unclear. This is because there is a discrepancy in the *BRAF/KRAS* mutational status between subSeCas derived from SBTs with and without a micropapillary architecture. Nearly 80% of SBTs without micropapillary architecture that develop into subSeCa involve *BRAF/KRAS* mutations, whereas > 80% of SBTs with micropapillary architecture that develop subSeCa do not involve such mutations [18]. Furthermore, as there was no difference in all-cause mortality when SBT was with and without micropapillary architecture (HR:1.2, 95% CI:0.8–1.9) [16], the clinical significance of various characteristic pathological findings can be considered undetermined in terms of the epidemiology and etiology of SBTs. To date, studies on SBT conducted in Japan and other Asian countries have involved

single centers or a small number of patients. Population-based data may provide important information for the individualized counseling of such patients. Further, the results of this study will be useful for future SBT treatment in East Asian countries, where SBT is more common than MBT.

In conclusion, this Japanese, population-based surveillance of SBTs involving JCOG-accredited hospitals not only exhibits the fundamentally favorable clinical outcomes of SBT but also serves as a reminder of the importance of maintaining a premium on expert pathology. Pregnancy is attainable in women who wish to preserve fertility, but there is a definite risk of recurrence due to incomplete resection. Although patients with SBT have a good prognosis, other life-threatening factors tend to affect patients over a long follow-up period, and careful interpretation of prognosis is mandatory.

Declarations

Conflicts of Interest and Sources of Funding: This study was designed and executed by the participating and standby centers of the JCOG Gynecologic Oncology Group. The authors declare no conflicts of interest associated with any particular company. The National Cancer Center Research and Development Fund (23-A-17) was involved in the collection and analysis of data, CPR, writing of the report, and decision to submit the article for publication.

Data Access Statement: All relevant data are within the paper and *Supplementary material*.

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T.B., M.K., M.K., T.S., I. K., and N.Y. contributed to study conception, study design, quality control of data, data analysis, interpretation, and manuscript preparation. S.M., Y.M., and S.M. contributed to the CPR. All authors contributed to the data acquisition, manuscript editing, and manuscript review.

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Tables

Table 1. Summary of the patients’ choice of treatment and outcomes by age (y.o.: years old)

		≤35y.o. (n=79)	>35y.o. (n=210)	p value
parity	0	64	51	<0.0001
	≥1	15	159	
pregnancy at diagnosis	no	73	208	0.0062
	yes	6	2	
FSS	non-FSS	11	165	<0.0001
	cystectomy	6	5	
	unilateral-SO	62	40	
post-treatment delivery	yes	15	2	<0.0001
	no	64	208	
recurrence	yes	8	4	0.0043
	no	71	206	

FSS: fertility sparing surgery, SO: salpingo-oophrectomy

Table 2. A multivariate binomial logistic regression analysis for recurrence of 289 SBT cases on fourteen clinical or pathological factors.

	characteristics	parameter	NED	recurrence	total	Odds Ratio (95% CI)	p value
background	age	≤ 35	67	12	79	4.02 (0.61-26.62)	0.15
		> 35	210	0	210		
	parity	0	100	9	109	0.69 (0.27-1.73)	0.427
		1	51	2	53		
		2	86	0	86		
		≥ 3	35	0	35		
	pregnancy at diagnosis	no	170	9	179	8.84 (0.22-2.34)	0.048
		yes	7	3	10		
	CA125	≤ 35	93	3	96	0.71 (0.22-2.34)	0.578
		> 35	159	8	167		
Institute	university hospital	yes	165	11	176	3.1 (1.27-7.55)	0.013
		no	112	1	113		
Operation	tumor resection	complete	271	9	280	1.94 (0.47-8.01)	0.362
		incomplete	6	3	9		
	fertility sparing	FSS	78	10	88	0.02 (0.0-0.24)	0.001
		non-FSS	199	2	201		
Tumor	Gross findings	solid mass	56	4	60	0.89 (0.50-1.57)	0.673
		papillae int	156	2	158		
		papillae ext	16	2	18		
		mix	24	1	25		
	tumor diameter	≤ 5cm	43	1	44	2.17 (1.11-4.24)	0.024
		5-10cm	115	4	119		
		10-15cm	63	6	66		
		≥ 15cm	40	2	42		
	laterality	unilateral	227	8	235	1.9 (0.84-4.28)	0.122
		bilateral	39	3	42		

Microscopic findings	microinvasion	absent	221	9	230	2.42 (0.73-8.03)	0.15
		present	23	2	25		
	implants	absent	239	9	248	0.97 (0.25-3.77)	0.966
		present	28	2	30		
	micropapillary pattern	absent	126	9	135	0.65 (0.22-1.90)	0.435
		present	85	2	87		
Stage	FIGO stage	IA	177	6	183	4.13 (1.35-12.61)	0.013
		IB-IC	65	2	67		
		II, III, IV	35	4	39		

papillae int: papillae on the internal surface, papillae ext: papillae on the external surface

Figures

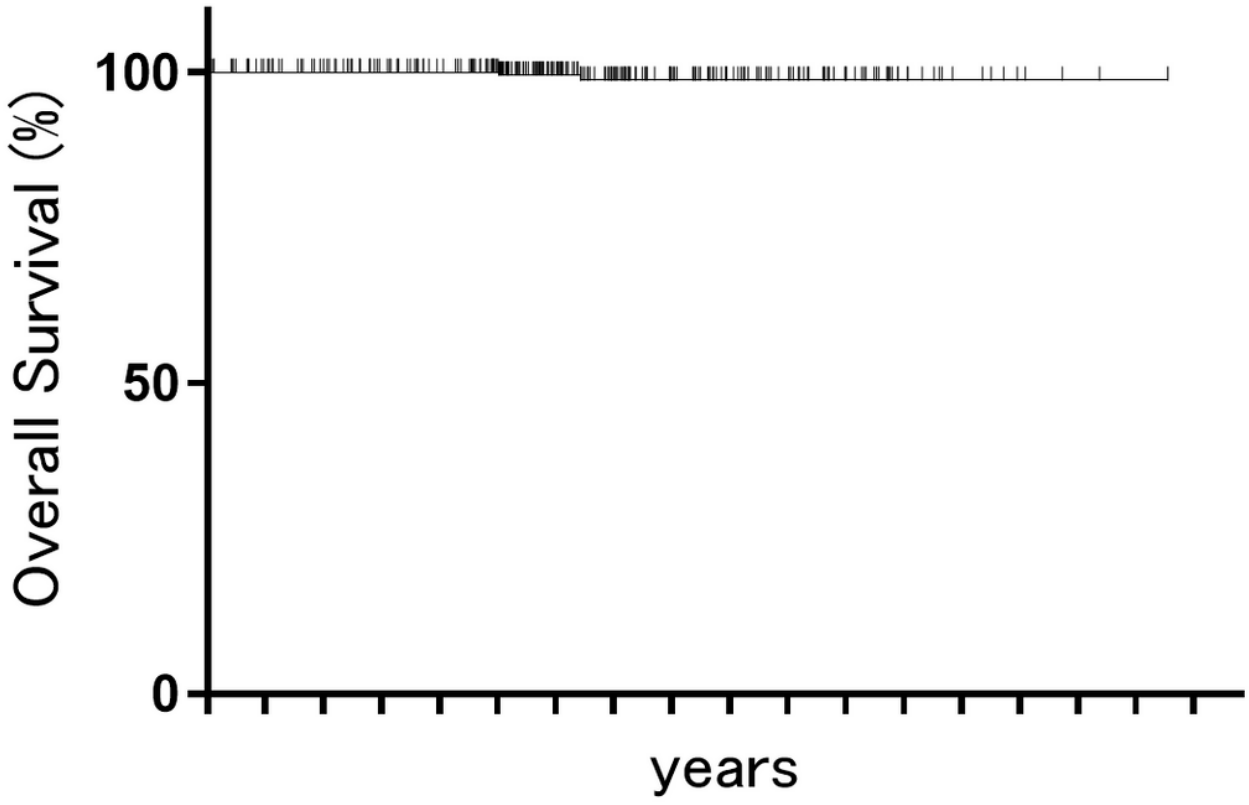

Figure 1

Overall survival of the document reviewed cases treated as serous borderline tumors in Gynecologic Cancer Study Group of Japan Clinical Oncology Group member hospitals during 1999–2008

Figure 2

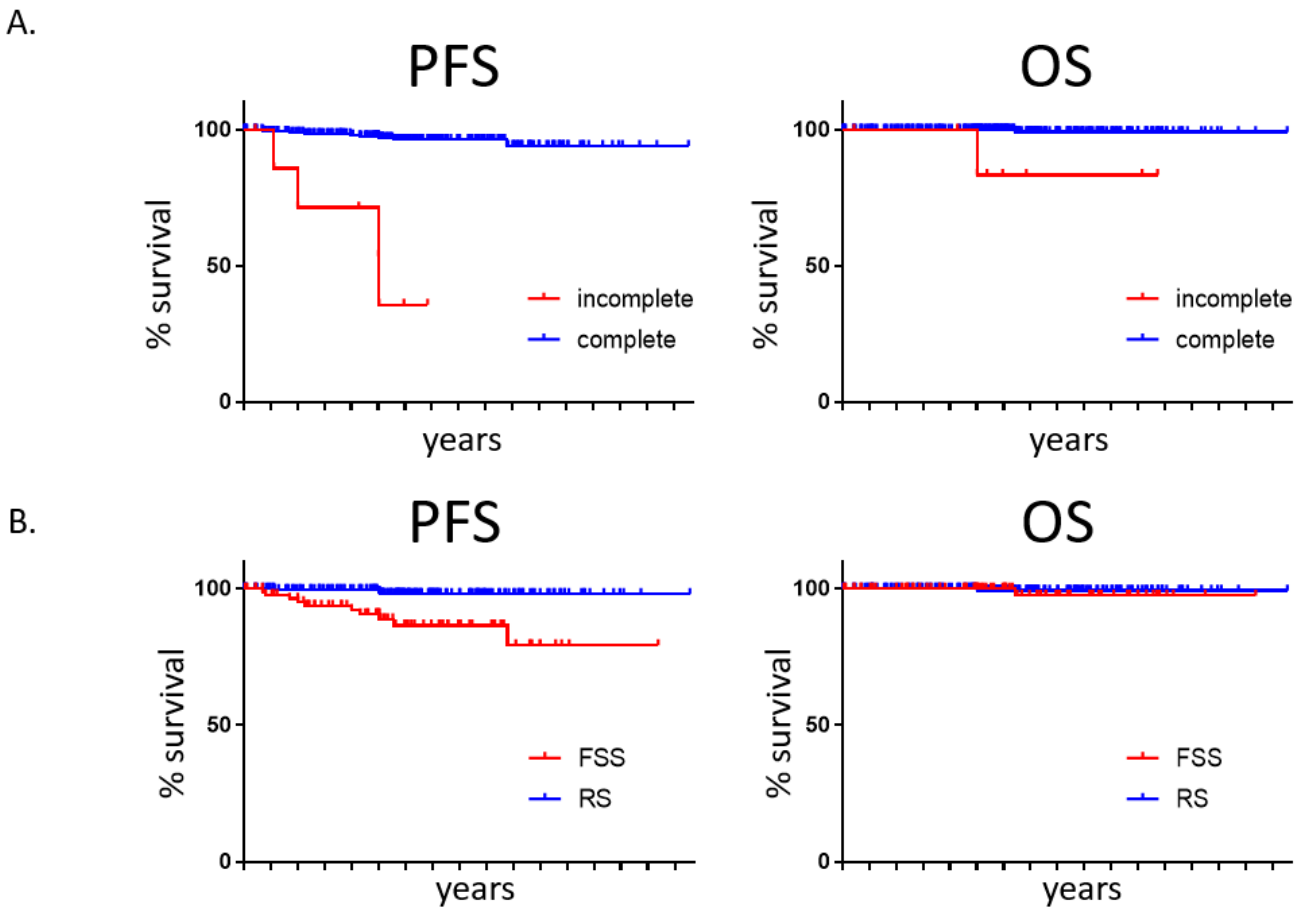

Figure 2

Surgical effect on the clinical outcome of the cases treated as serous borderline tumors (SBTs) in Gynecologic Cancer Study Group of Japan Clinical Oncology Group member hospitals during 1999–2008

A. Progression free survival (PFS) (left) and overall survival (OS) (right) of the included SBT cases with and without complete tumor excision. Both PFS and OS were significantly superior in the cases that involved complete excision (p<.001). complete: complete excision without residual tumor, incomplete: incomplete excision with gross tumor

B. PFS (left) and OS (right) of the included SBT cases with and without a fertility-sparing surgery (FSS). PFS was significantly inferior in the cases involving FSS (p<.001), while OS was not (p=.07). RS: radical

surgery.

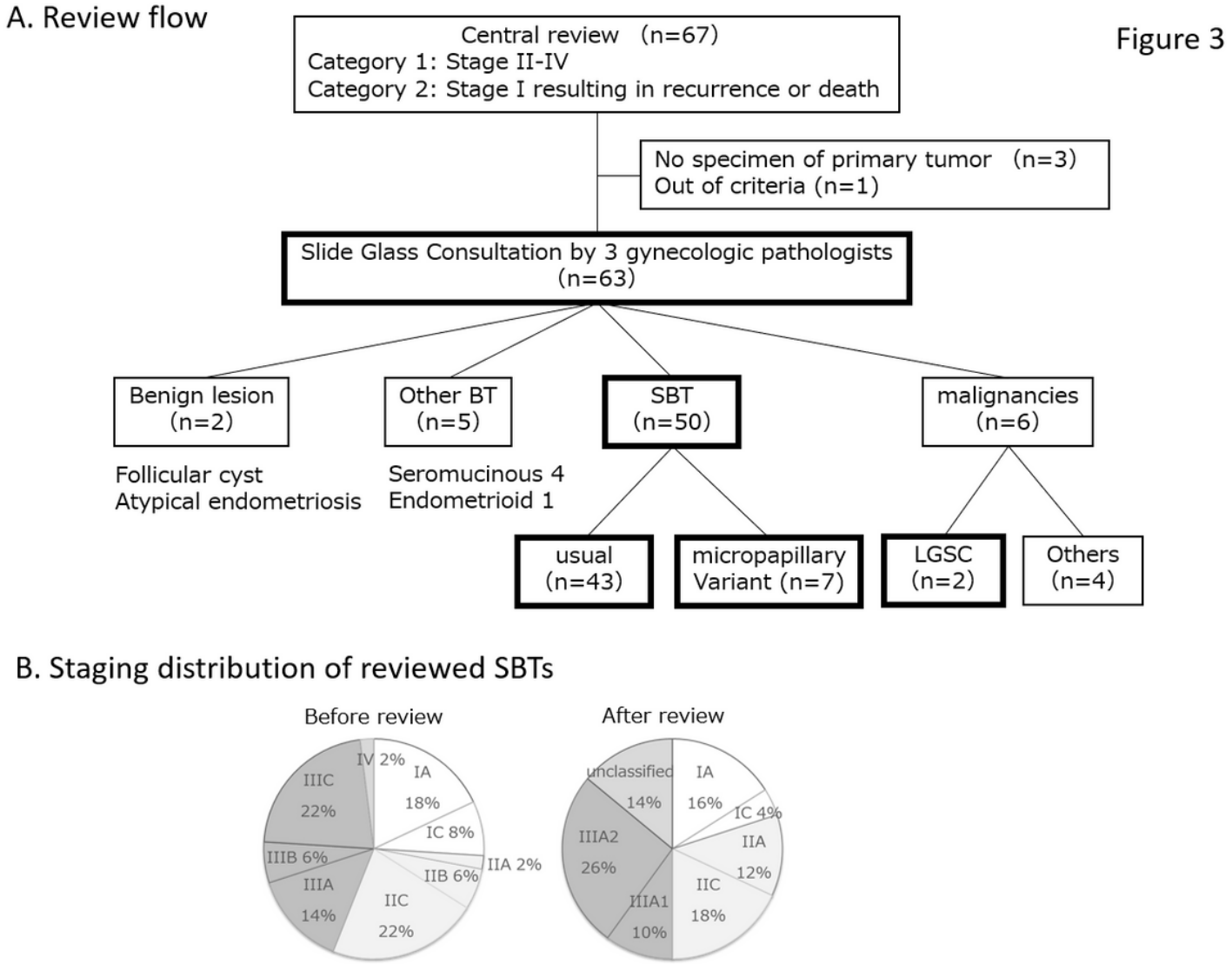

Figure 3

Figure 3

Central pathological review (CPR) of the cases treated as serous borderline tumors (SBTs) with recurrence and/or extraovarian metastasis in Gynecologic Cancer Study Group of Japan Clinical Oncology Group member hospitals during 1999–2008

A. Flow chart of CPR. Four of the seven high-risk cases were excluded from CPR because of lack of specimen or the inclusion criteria not being met.

B. FIGO staging distribution of 50 SBT cases. More than half the cases have stage migration through CPR.

Figure4

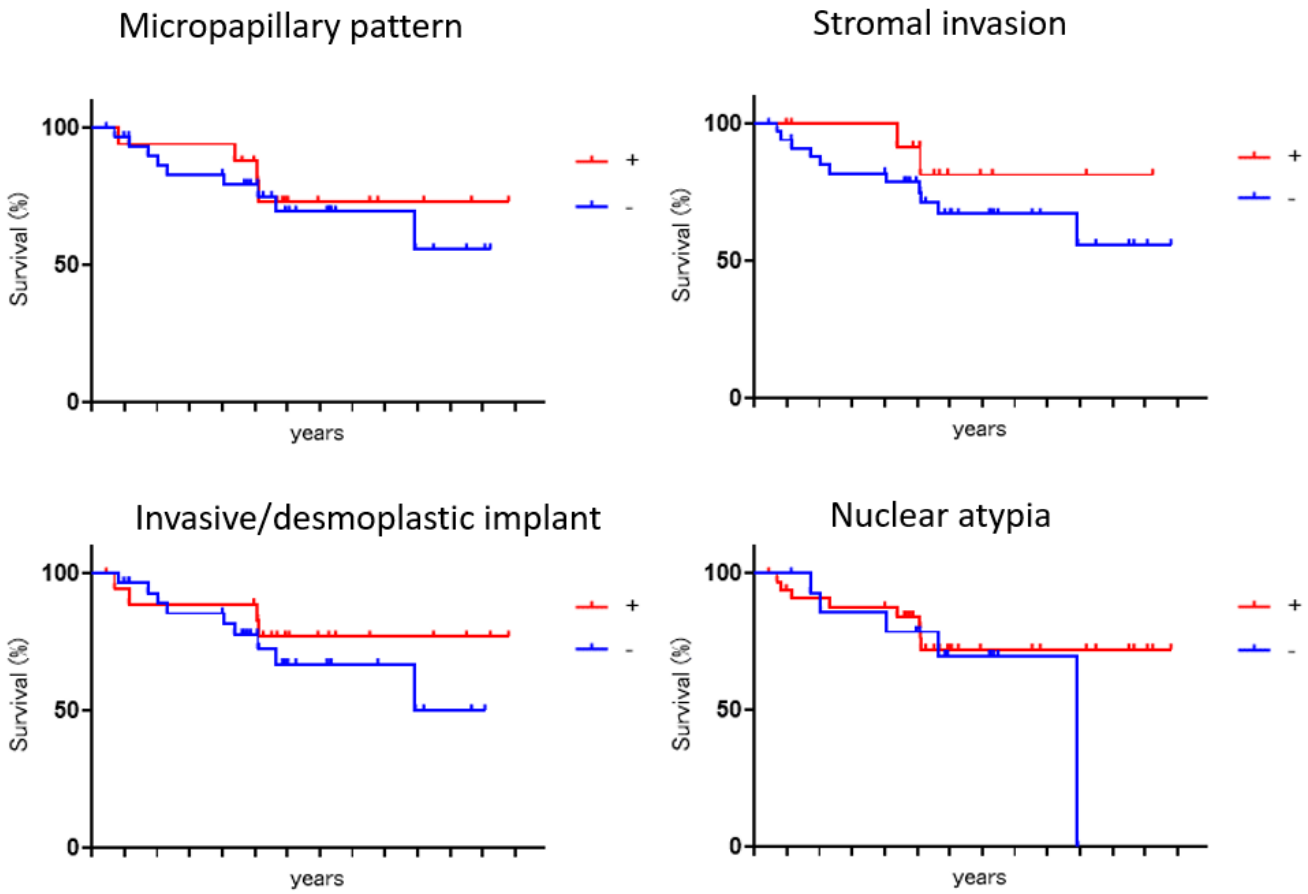

Figure 4

Clinical effects of characteristic pathological findings observed in the 50 serous borderline tumor (SBT) cases with central pathological review. Progression free survival was compared and not found to be significant between the cases involving serous borderline tumors with and without micropapillary architecture (p=0.59), stromal invasion (p=0.26), invasive and/or desmoplastic implants (p=0.37), and nuclear atypia (p=0.52).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable1.docx
- SupplementaryTable2.docx