# Staging Procedures Fail to Benefit Women with Borderline Ovarian Tumours Who Want to Preserve Fertility: A Retrospective Analysis of 448 cases

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# Abstract

Background This study aimed to evaluate the effect of clinicopathologic and surgical factors on the prognosis and fertility outcomes of patients with borderline ovarian tumour (BOT). Methods We performed a retrospective analysis of BOT patients who underwent surgical procedures in West China Second University Hospital from January 2008 to January 2015. The disease-free survival (DFS) outcomes and potential prognostic factors were evaluated using the Kaplan-Meier method and Cox regression analysis, respectively. Furthermore, fertility outcomes were analysed using Pearson X 2 and Fisher's correlation tests. Results A total of 448 patients were included, with a median age of 37.1 years and a median follow-up time of 113 months; 52 (11.6%) recurrences were observed, with a mean recurrence interval of 80.2 months and four (0.9%) deaths; 118 (26.3%) patients underwent staging surgery and the remaining 330 (73.7%) underwent unstaged surgery. In total, 233 patients undergoing fertility-sparing surgery (FSS) attempted to conceive, and 92 (39.48%) of them achieved pregnancy. No significant differences in fertility outcomes were found between the staging and unstaged surgery groups ( P = 0.691). In univariate analysis, staging surgery was associated with DFS (hazard ratio [HR] = 2.191; P = 0.005), but it was not an independent prognostic factor ( P = 0.600) for DFS on multivariate analysis. Multivariate Cox analysis revealed that advanced FIGO stage (≥stage II), positive ascites\pelvic washings, and laparotomy approach were independent prognostic factors for DFS in patients with BOT, whereas advanced stage (≥stage II), laparotomy approach, cystectomy-related procedures, invasive implants, and bilateral tumours were independent prognostic factors for DFS in patients undergoing FSS. In addition, laparoscopy resulted in better prognosis than laparotomy in patients with early-stage (stage I) tumours and a desire for fertility preservation. Conclusion Patients with BOT fail to benefit from surgical staging in terms of prognosis and fertility outcomes. Laparoscopy is recommended for patients with stage I disease who desire to preserve their fertility. Physicians should pay more attention to the risk of recurrence in patients who want to preserve fertility with advanced stage (≥stage II) disease, invasive implants, and bilateral tumours, and choose FSS carefully.


# Background

Borderline ovarian tumour (BOT) is a peculiar type of tumour with a more favourable prognosis than malignant ovarian tumours. BOT typically occurs in women 10 years younger than those with epithelial ovarian cancer, and the majority of the women with BOT are diagnosed in the earlier stages, with 75% diagnosed at stage I [1, 2]. It was reported that Ki67 (a significant marker for malignant tumors) Labeling Index value ranged from 2% to 40% in BOT specimens [3].

The clinical management of BOT has evolved over the last two decades since our understanding of its biological behaviour has increased. Treatment is based on surgical removal of the tumour, with an emphasis on fertility-sparing surgery (FSS) in women who desire to preserve their fertility. The role of comprehensive surgical staging in the treatment of BOT is still controversial. As peritoneal implants are a significant prognostic index and the most common sites of implants include the omentum and peritoneal surfaces, surgical staging that includes resection of the primary borderline tumour, abdominal/pelvic

cytologic washings, omentectomy, and peritoneal biopsies is recommended. Routine lymphadenectomy is not recommended [4, 5]. However, comprehensive surgical staging, adequate tissue sampling, and adequate follow-up period are essential aspects for gaining additional insights into optimal clinical management [2]. Previous studies have been inconsistent in their support of the benefits of staging surgery, and a recent systematic literature review showed that staging surgery, including hysterectomy and lymphadenectomy for BOT, is not supported by sufficient evidence [6-8]. As the likelihood of uterine or nodal metastasis is low in apparent early-stage BOT, the risk of surgical complications and the benefits of staging information must be balanced carefully.

To evaluate the effect of clinicopathologic factors on the prognosis and fertility outcomes of BOT patients, this study was performed.

# Methods

Clinical data of BOT patients were collected retrospectively in West China Second University Hospital between January 2008 and December 2015. Patients with a pathological diagnosis of BOT who underwent surgery were enrolled in this study. Those with concurrent ovarian cancer, other malignant reproductive tumours, or incomplete data were excluded. This study was approved by the Medical Ethics Committee of West China Second University Hospital. Data were extracted from medical records, telephone interview and out-patient review, including data of age, surgical information, lesion location, International Federation of Gynecology and Obstetrics (FIGO) stage, surgical approach, histological subtype, treatment with chemotherapy, and follow-up information. Although the FIGO ovarian staging classification was revised on 1 January 2014, we used the previous staging (2009) classification for consistency [9]. In addition, histological typology was determined in accordance with the World Health Organization (WHO) system (2003). Pathological specimens were evaluated by two independent pathologists experienced in gynaecologic pathology. The tumours were divided into four histological types: serous, mucinous, endometrioid, and serous/mucinous types. Micropapillary lesions were defined as serous borderline tumours containing complex micropapillary structures [10]. Microinvasion was defined as stromal invasion restricted to an area of no more than 10 $mm^2$ [10]. Several surgical options are mentioned in this study such as FSS, which was performed to conserve the uterus and at least one ovary, and radical resection, which included hysterectomy and bilateral salpingo-oophorectomy [11]. Moreover, the concepts of surgery types need to be clarified: staging, and non-staging surgery. Staging was defined as peritoneal washing and/or biopsies, pelvic and para-aortic lymphadenectomy (sampling or systematic), and omentectomy. Other surgery was considered non-staging surgery [12]. Four types of FSSs are mentioned in this study: unilateral salpingo-oophorectomy, unilateral cystectomy, bilateral cystectomy, and unilateral salpingo-oophorectomy plus contralateral cystectomy. The latter three modalities were defined as cystectomy. Patients were followed-up once every 3 months for the first 2 years, every 6 months for 3–5 years after the surgery, and once per year thereafter. Gynaecological examination, abdominal ultrasonography, and tumour marker evaluation were performed in each follow-

up cycle. In cases of favourable prognosis, disease-free survival (DFS) (defined as the duration from the primary surgery to the first recurrence or the last follow-up) was used to assess oncological outcomes.

Statistical analyses of DFS, recurrence rate, and pregnancy rate were selected as the primary outcomes in this study. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) statistical software (version 20.0). The Student's *t*-test was used for statistical analysis of unpaired data. Univariate and multivariate Cox regression analysis were used to determine the factors affecting recurrence, presented as hazard ratios (HRs). A *P*-Value <0.05 was considered statistically significant.

# Results

### Patient characteristics

A total of 448 patients with BOT were enrolled in this study. The demographics and clinicopathological characteristics are shown in Table 1.

The median age at diagnosis was 37.1 years (range: 11–82 years). The majority of the patients were in FIGO stage I (n = 347, 77.46%), with a few cases of stage II (n = 20, 4.46%), stage III (n = 74, 16.52%), and stage IV (n = 7, 1.56%). The most common pathological type of BOT was serous (n = 258, 57.59%), followed by mucinous (n = 150, 33.48%), serous/mucinous (n = 32, 7.14%), and endometrioid (n = 8, 1.79%). Notably, most patients had unilateral lesions (n = 352, 78.57%), whereas 96 (21.43%) patients had bilateral lesions. Among the patients enrolled, 81 (18.08%) had micropapillary lesions, 88 (19.64%) had microinvasion lesions, and 25 (5.58%) had carcinogenesis lesions.

Regarding surgical approach, 298 patients (66.52%) underwent laparotomy and 150 patients (33.48%) underwent laparoscopy; 118 patients (26.34%) underwent staging surgery, whereas the rest underwent non-staging surgery (330 patients, 73.66%). Abdominal/pelvic washings or ascites were collected prior to surgery for all patients, and positive involvement was identified in 27 patients (6.03%). Lymph node metastasis was detected in 21 of 113 patients (18.58%) who underwent lymphadenectomy. Appendix metastases were detected in 11 of 150 patients (7.33%) who underwent appendectomy. Omentum metastases were detected in 27 of 117 patients (23.08%) who underwent omentectomy. A total of 121 patients (27.01%) received adjuvant chemotherapy for lymph node metastasis, positive abdominal/pelvic washings, invasive implants, and/or other high-risk indicators.

### Oncological outcomes of BOT patients

We carried out a survival analysis. The median follow-up for this study was 113 (range: 14–166) months. At the last follow-up, 42 (11.6%) patients experienced recurrence, with a mean recurrence interval of 80.2 months, and 4 (0.9%) disease-specific deaths were observed. The recurrence rate in patients who underwent non-staging surgery (30/330, 9.09%) was lower than that in those underwent staging surgery

(22/118, 18.64%), with the difference being statistically significant ($P < 0.01$). The results of univariate and multivariate analyses of DFS in all patients are shown in Table 2.

According to the univariate analysis, patients who underwent staging surgery had shorter DFS than those who underwent non-staging surgery. In addition, laparoscopy was strongly associated with improved DFS (HR = 0.292, 95% CI: 0.132–0.647, $P = 0.002$) compared to laparotomy. Other factors found to be associated with DFS were FIGO stage, histology, lesion location, microinvasion, adjuvant chemotherapy, ascites/pelvic washings, cancer antigen (CA)-125 level, appendectomy, and invasive implants (all $P < 0.01$). Micropapillary and carcinogenic lesions were not associated with DFS ($P > 0.05$).

Although several factors were found to be associated with DFS by univariate analysis, only FIGO stage (OR: 6.544, 95% CI: 2.137–20.041), positive ascites/pelvic washings (OR: 3.259, 95% CI: 1.202–8.835), and surgical approach (OR: 0.319, 95% CI: 0.128–0.793) were significantly associated with DFS ($P < 0.001$, $P = 0.014$, $P = 0.043$, respectively) as per multivariate analysis; complete staging surgery was not associated with DFS ($P = 0.600$) as per multivariate analysis. There was no difference in DFS between patients who underwent FSS and radical surgery according to univariate and multivariate analyses.

Subgroup analysis showed that in patients who underwent staging surgery, there was no difference in DFS between those who underwent laparotomy or laparoscopy ($P = 0.349$). Among patients who underwent non-staging surgery, the DFS was longer for patients who underwent laparoscopy than for those who underwent laparotomy ($P = 0.011$; Supplementary Table 1).

### Oncological outcomes in patients with BOT after FSS

Among the patients enrolled, 270 patients underwent FSS. Of these, 32 patients (11.8%) experienced recurrence. To explore the potential risk factors associated with improved DFS in patients who underwent FSS, univariate and multivariate analyses were performed (Table 3).

Univariate analysis with patients who underwent FSS showed that patients who underwent staging surgery had shorter DFS than those who underwent non-staging procedures (OR: 4.290, 95% CI: 1.979–9.298, $P < 0.001$). DFS was better among patients who underwent laparoscopy (OR: 0.332, 95% CI: 0.135–0.820, $P = 0.017$) than among those who underwent laparotomy. In addition, patients who underwent salpingo-oophorectomy had longer DFS than those who underwent a cystectomy procedure (OR: 0.230, 95% CI: 0.168–0.867, $P = 0.021$). Other factors were also associated with DFS in patients who underwent FSS, including FIGO stage, histology, lesion location, microinvasion, adjuvant chemotherapy, positive ascites/pelvic washings, appendectomy, and invasive implants ($P < 0.05$).

In multivariate analysis, there was no difference in DFS between patients who underwent staging and non-staging surgery ($P = 0.358$). There was no difference in DFS between patients with different histological types. Early FIGO stage (OR: 11.586, 95% CI: 4.535–29.602), unilateral lesions (OR: 2.581, 95% CI: 1.061–6.283), laparoscopy (OR: 0.367, 95% CI: 0.148–0.913), salpingo-oophorectomy (OR: 0.367,

95% CI: 0.148–0.913), and no invasive implants (OR: 4.832, 95% CI: 1.663–14.037) were independent factors for improved DFS ($P < 0.05$).

### Reproductive outcomes in patients with BOT after FFS

At the last follow-up, of the 270 patients who underwent FSS, 252 patients had attempted to conceive and 92 achieved pregnancy. The correlation between clinicopathological characteristics and reproductive outcome is shown in Table 4. The pregnancy rate in patients aged <35 years was higher than those aged ≧35, at a statistically significant ($P < 0.001$) level. Of the 30 patients who underwent staging surgery, 13 patients (43.33%) succeeded in conceiving, whereas 79 of 203 patients (38.92%) who underwent non-staging surgery succeeded in conceiving, but these differences were not statistically significant ($P > 0.05$). There was no difference between patients who underwent laparotomy or laparoscopy. Similarly, among patients who underwent salpingo-oophorectomy or cystectomy, there was no difference in the pregnancy rates ($P > 0.05$).

## Discussion

In the present study, we performed a retrospective analysis of 448 patients with BOT in a single centre in China. BOTs are ovarian neoplasms with characteristics of benign or malignant tumours, frequently occurring in young women and associated with favourable prognosis. Within the past two decades, we have begun to understand the biological behaviour of BOTs; however, the optimal therapy for this disease is still controversial. Numerous studies have focused on the oncological and reproductive outcomes of BOT. In the literature, the primary points of discussion regarding BOT include the prognostic factors for overall survival (OS) or DFS, necessity of staging surgery, application of minimally invasive approaches, and outcome of conservative surgery.

Complete staging surgery generally includes resection of the primary borderline tumour (cystectomy or salpingo-oophorectomy), cytologic washings, omentectomy, peritoneal biopsies, and routine lymphadenectomy. Unlike in ovarian cancer, previous studies have shown that the prognosis of patients with BOT is generally favourable, with very low mortality [13, 14]. A Turkish Gynaecologic Oncology Group (GOG) study showed that the five-year survival rate of patients with BOT was 100%, and the median survival time was 120 months [15]. Therefore, DFS and recurrence-free survival (RFS) were defined as the main oncological outcomes. In the present study, complete staging surgery was performed in 26.3% of the patients. Although univariate analysis showed that patients who underwent staging surgery had shorter DFS than those who underwent non-staging surgery, no significant difference was found in the DFS between different surgical approaches as per multivariate analysis. These results were similar to those of previous studies [2, 12, 15-17]. The Turkish GOG study showed that comprehensive surgical staging did not lead to any difference in survival [15]. A retrospective multicentre study showed that there were no differences in the five-year RFS and OS between patients who did and did not undergo complete surgical staging [18]. Another multicentre study showed that surgical staging were not beneficial in the management of BOT [12]. A third multicentre study from Turkey that focused on mucinous BOT showed

that radical surgery, omentectomy, appendectomy, and lymphadenectomy were not independent prognostic factors for progression-free survival and OS [17].

Regarding the correlation between lymphadenectomy and DFS, lymph node involvement does not appear to be a prognostic factor [19, 20]. Univariate analysis by Matsuo et al. showed that surgical staging patterns for hysterectomy and lymphadenectomy were not associated with cause-specific survival ($P$ = 0.19) [2]. A previous study by Qian et al. showed that there were no significant differences between groups with or without lymphatic node involvement ($P$ = 0.778), and between patients who had more or fewer than 10 nodes removed ($P$ = 0.549) [16].

BOT occurs in women of all ages, with a high proportion in the reproductive age [21]. In the present study, the median age at diagnosis was 37.1 years. Therefore, a conservative surgical approach (FSS) was the preferred choice for patients who desired to preserve their fertility. However, the balance between oncological and reproductive outcomes should be assessed adequately; approximately 12%–36% of the patients with BOT who undergo FSS experience recurrence [21], and the most common site of recurrence is the residual ovary [21-24]. Previous studies have shown that the recurrence rate of BOT in patients who underwent FSS was markedly higher than that in patients who underwent radical surgeries (21.4% vs. 6.3%, $P$ < 0.05) [10, 25]. Furthermore, a large proportion of patients who underwent FSS experienced invasive recurrence [14]. In a recent retrospective study, patients with FSS developed more relapse than patients with radical surgeries [26]. In the multivariate analyses, fertility preservation and micropapillary pattern were independently associated with adverse disease-free survival (P = 0.001, 0.03 and 0.026, respectively) [26]. Regarding surgical patterns, a meta-analysis showed that unilateral cystectomy is significantly associated with high recurrence rates [11]. However, another study reported that there was no statistically significant difference between patients who underwent cystectomy or unilateral salpingo-oophorectomy [27]. A recent study involving 6295 patients showed that FSS was associated with worse DFS in patients aged ≥50 years than in those aged <50 years [28]. Another study showed that surgical procedure (conservative vs. radical) was not an independent prognostic factor for DFS or OS [12].

In the present study, both univariate and multivariate analyses results showed no significant difference in the DFS between patients who underwent FSS and those who did not ($P$ > 0.05). In patients who underwent FSS, there was no significant difference in DFS between those who underwent staging and those who did not ($P$ > 0.05), whereas a significant difference was observed between those who underwent laparoscopy and laparotomy ($P$ < 0.05). However, no significant differences were found in the reproductive rates of those who underwent staging surgery or a different surgical approach. Therefore, the balance between oncological and reproductive outcomes in patients of reproductive age should be considered before performing FSS.

The standard treatment for BOT is surgery. Since most patients are of childbearing age, surgeons should consider using a minimally invasive procedure. Laparoscopic surgery has several advantages over open surgery in the management of gynaecologic diseases, including fewer peri-operative complications and superior cosmetic outcomes. In this study, approximately 33.48% of the patients underwent laparoscopic

surgery. As per both univariate and multivariate analyses findings, laparoscopic surgery was more positively associated with improved DFS than laparotomy ($P < 0.05$). Similarly, a previous study by Song et al. also showed that RFS and OS did not differ between the laparoscopy (single-port and multi-port laparoscopy) and laparotomy groups [29]. However, the potential selective bias should be noticed, which means that the characteristic of individual patients might influence the surgery approach. For those patients with smaller mass, younger ages, lower CA125 levels in pre-operative time, laparoscopy may be more favorable, usually getting a better prognosis. However, for those patients with larger mass, older ages, higher CA125 levels, or other signs suspected for malignant tumors in pre-operative time, laparotomy was possibly chosen. This bias could be solved through increasing patients enrolled, or randomized controlled trial.

In a retrospective study of 1069 patients with BOT in Japan, 49% had normal serum CA-125 levels and only 23% had serum CA-125 levels above 100 U/mL [21]. In another study of 198 patients in Singapore, the preoperative serum CA-125 levels of 77 (39%) patients were >35 U/mL [30]. In the present study, the serum level of CA-125 was not an independent prognostic factor for patients with BOT after FSS.

Because an accurate intra-operative diagnosis is important in the management of BOT, frozen-section examination should be performed to help surgeons and patients' families make decisions during intra-operative periods. The accuracy of frozen-section examination is lower than optimal and the availability of reliable frozen-section analysis methods in many hospitals is difficult. Previous studies have shown that the matched rate between the results of frozen-section and definitive histological examination varies from 66.67% to 88.9% [31, 32]. Therefore, it is important for surgeons to counsel patients and their families with regard to possible intra-operative indications.

# Conclusions

Patients with BOT do not benefit from surgical staging procedures in terms of prognosis and fertility outcomes. Laparoscopy, rather than laparotomy, should be recommended for patients with stage I disease who wish to preserve their fertility. In addition, patients with advanced stage disease, invasive implants, and/or bilateral tumours who wish to maintain their fertility should consider the risk of recurrence before choosing FSS. Unilateral salpingo-oophorectomy is an alternative method for patients with BOT to preserve their fertility.

# Abbreviations

| | |
|---|---|
| BOT | Borderline ovarian tumour |
| DFS | Disease-free survival |
| FIGO | Federation of Gynecology and Obstetrics |
| FSS | Fertility-sparing surgery |

| | |
|---|---|
| GOG | Gynaecologic Oncology Group |
| HR | Hazard ratios |
| OS | Overall survival |
| RFS | Recurrence-free survival |
| SPSS | Statistical Package for Social Sciences |
| WHO | World Health Organization |

# Declarations

### Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of West China Second University Hospital, Sichuan University. Due to the nature of retrospective study, no written informed consent was obtained from patients. All follow-up information were approved by telephone review or out-patient review.

### Consent for publication

Not applicable.

### Availability of data and materials

Not applicable. All data were included in the manuscript.

### Competing interests

The authors have no competing interests to declare.


### Funding

Not applicable.


### Authors' contributions

NL, JG were involved in all research activities, data collection, data analysis, development of study document and manuscript drafting. LL, XM, TH contributed to collection of clinical data and data analysis. ZL made the study design. All authors have read and approved the manuscript.


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# Tables

### Table 1

**Demographics of patients with borderline ovarian tumors**

| | Non-staging surgery | Staging surgery | P Value |
|---|---|---|---|
| Total | 330 | 118 | |
| Age (y,mean±Std) | 36.75±14.35 | 38.03±12.49 | 0.363 |
| Time of operation(h, mean) | 127.50 | 255.00 | <0.001 |
| Blood Loss (ml, median) | 80 | 400 | <0.001 |
| Length of stay(d, median) | 6 | 8 | <0.001 |
| FIGO Stage | | | |
| I | 287 (87%) | 60 (50.8%) | <0.001 |
| II | 8 (2.40%) | 12 (10.2%) | |
| III | 32 (9.7%) | 42 (35.6%) | |
| IV | 3 (0.9%) | 4 (3.4%) | |
| Histology | | | 0.038 |
| Serous | 177 (53.6%) | 81 (68.6%) | |
| Mucinous | 119 (36.1%) | 31 (26.3%) | |
| Endometrioid | 7 (2.1%) | 1 (0.8%) | |
| Serous and Mucinous | 27 (8.2%) | 5 (4.2%) | |
| Lesion lateral | | | <0.001 |
| Unilateral | 277 (83.9%) | 75 (63.6%) | |
| Bilateral | 53 (16.1%) | 43 (36.4%) | |
| Micropapillary | | | |
| Yes | 45 (13.6%) | 36 (30.5%) | <0.001 |
| No | 285 (86.4%) | 82 (69.5%) | |
| Microinvasion | | | <0.001 |
| Yes | 31 (9.4%) | 57 (48.3%) | |
| No | 299 (90.6%) | 61 (51.7%) | |
| Carcinogenesis | | | |
| Yes | 14 (4.2%) | 11 (9.3%) | 0.058 |
| No | 316 (95.8%) | 107 (90.7%) | |
| Surgical Approach | | | <0.001 |
| Laparotomy | 192 (58.2%) | 106 (89.8%) | |
| Laparoscopy | 138 (41.8%) | 12 (10.2%) | |
| Ascites/Cytologic washings | | | 0.012 |
| Positive | 14 (4.2%) | 13 (11.0%) | |
| Negative | 316 (95.8%) | 105 (89.0%) | |
| Lymph node involvement | | | NA |
| Yes | NA | 21 (18.6%) | |
| No | NA | 92 (81.4%) | |
| Appendix metastasis | | | |
| Yes | 6 (54.5%) | 5 (45.5%) | 0.05 |
| No | 113 (81.3%) | 26 (18.7%) | |

| | | | |
|---|---|---|---|
| Omentum metastasis | | | NA |
| Yes | NA | 27 (23.1%) | |
| No | NA | 90 (76.9%) | |
| Adjuvant chemotherapy | | | <0.001 |
| Yes | 54 (16.4%) | 67 (56.8%) | |
| No | 276 (83.6%) | 51 (43.2%) | |
| Recurrence | | | 0.007 |
| Yes | 30 (9.1%) | 22 (18.6%) | |
| No | 300 (90.9%) | 96 (81.4%) | |
| Fertility-sparing surgery | | | <0.001 |
| Yes | 240 (72.7%) | 30 (25.4%) | |
| No | 90 (27.3%) | 88 (74.6%) | |
| Achieving pregnancy | | | 0.552 |
| Yes | 79 (35.7%) | 13 (41.9%) | |
| No | 142 (64.3%) | 18 (58.1%) | |

Data were recorded as number (%), mean (±SD), or median (range).

Abbreviations: y, years; h, hours; d, days;

**Table 2**

**Univariate and multivariate analysis of DFS**

| | | Univariate | | P value | Multivariate | | P value |
|---|---|---|---|---|---|---|---|
| | | HR | 95% confidence interval | | HR | 95% confidence interval | |
| FIGO Stage | I | 1 | | | | | |
| | ≧II | 7.204 | 4.093-12.680 | 0.000 | 6.544 | 2.137-20.041 | 0.001 |
| Histology | Serous | 1 | | | | | 0.528 |
| | Mucinous | 0.353 | 0.171-0.726 | 0.005 | 1.215 | 0.275-5.375 | 0.797 |
| | Others | 0.286 | 0.069-1.183 | 0.084 | 0.632 | 0.130-3.066 | 0.569 |
| Lesion lateral | Unilateral | 1 | | | | | |
| | Bilateral | 2.554 | 1.460-4.469 | 0.001 | 1.076 | 0.526-2.202 | 0.840 |
| Micropapillary | Yes | 1.557 | 0.831-2.917 | 0.167 | | | |
| | No | 1 | | | | | |
| Microinvasion | Yes | 5.092 | 2.954-8.779 | 0.000 | 0.478 | 0.181-1.261 | 0.136 |
| | No | 1 | | | | | |
| Carcinogenesis | Yes | 1.049 | 0.327-3.366 | 0.936 | | | NA |
| | No | 1 | | | | | |
| Staging surgery | Yes | 2.191 | 1.263-3.801 | 0.005 | 0.810 | 0.393-1.669 | 0.567 |
| | No | 1 | | | | | |
| Adjuvant chemotherapy | Yes | 5.281 | 3.002-9.289 | 0.000 | 2.031 | 0.913-4.519 | 0.083 |
| | No | 1 | | | | | |
| Ascites/Pelvic washings | Positive | 5.442 | 2.850-10.391 | 0.000 | 3.259 | 1.202-8.835 | 0.020 |
| | Negative | 1 | | | | | |
| Surgical Approach | laparotomy | 1 | | | | | |
| | laparoscopy | 0.292 | 0.132-0.647 | 0.002 | 0.319 | 0.128-0.793 | 0.014 |
| CA-125 | Normal | 1 | | | | | |
| | Elevated | 2.201 | 1.224-3.960 | 0.008 | 0.825 | 0.422-1.611 | 0.572 |
| Fertility sparing surgery | No | 1 | | | | | |
| | Yes | 1.055 | 0.063-1.845 | 0.851 | | | NA |
| Appendectomy | No | 1 | | | | | |
| | Yes | 0.394 | 0.192-0.808 | 0.011 | | | NA |
| Invasive implants | NO | 1 | | | | | |
| | Yes | 4.105 | 2.222-7.583 | 0.000 | 0.566 | 0.208-1.539 | 0.265 |

**Table 3**

**Univariate and multivariate analysis of DFS in fertility desiring patients after fertility-sparing surgery**

| | | Univariate | | P | Multivariate | | P |
|---|---|---|---|---|---|---|---|
| | | OR | 95% confidence interval | Value | OR | 95% confidence interval | Value |
| FIGO Stage | I | 1 | | | | | |
| | ≧II | 21.061 | 9.662-45.909 | 0.000 | 11.586 | 4.535-29.602 | 0.000 |
| Histology | Serous | 1 | | 0.010 | | | 0.155 |
| | Mucinous | 0.196 | 0.068-0.654 | 0.003 | | | 0.189 |
| | others | 0.000 | | 0.975 | | | NA |
| Lesion lateral | unilateral | 1 | | | | | |
| | Bilateral | 5.491 | 2.570-11.73 | 0.000 | 2.581 | 1.061-6.283 | 0.037 |
| Micropapillary | Yes | 1.976 | 0.840-4.649 | 0.119 | | | NA |
| | No | 1 | | | | | |
| Microinvasion | Yes | 14.644 | 6.940-30.903 | 0.000 | | | 0.955 |
| | No | 1 | | | | | |
| Carcinogenesis | Yes | 0.609 | 0.083-4.483 | 0.626 | | | NA |
| | No | 1 | | | | | |
| Staging surgery | Yes | 4.290 | 1.979-9.298 | 0.000 | | | 0.358 |
| | No | 1 | | | | | |
| Adjuvant chemotherapy | Yes | 7.797 | 3.648-16.664 | 0.000 | | | 0.391 |
| | No | 1 | | | | | |
| Ascites/Pelivic washings | Positive | 13.350 | 5.612-31.770 | 0.000 | | | 0.888 |
| | Negative | 1 | | | | | |
| Surgical Approach | laparotomy | 1 | | | | | |
| | laparoscopy | 0.332 | 0.135-0.820 | 0.017 | 0.367 | 0.148-0.913 | 0.031 |
| CA-125 | Normal | 1 | | | | | |
| | Elevated | 1.649 | 0.748-3.632 | 0.215 | | | NA |
| Fertility sparing surgery | Cystectomy-included | 1 | | | | | |
| | Adnexectomy | 0.382 | 0.168-0.867 | 0.021 | 0.367 | 0.148-0.913 | 0.014 |
| Appendectomy | No | 1 | | | | | |
| | Yes | 0.240 | 0.083-0.692 | 0.008 | | | 0.189 |
| Invasive implants | NO | 1 | | | | | |
| | Yes | 14.289 | 6.400-31.902 | 0.000 | 4.832 | 1.663-14.037 | 0.004 |

## Table 4

**Correlation between pregnant outcomes and clinicopathological indexes in patients after fertility-sparing surgery**

| | | Fertility outcome | | P value |
|---|---|---|---|---|
| | | No | Yes | |
| | | (n,%) | (n,%) | |
| Staging surgery | No | 124(87.9) | 79(85.9) | 0.691 |
| | Yes | 17(12.1) | 13(14.1) | |
| Surgical approach | laparoscopy | 65(46.1) | 37(40.2) | 0.419 |
| | laparotomy | 76(53.9) | 55(59.8) | |
| Surgical procedure | Cystectomy | 76(53.9) | 41(44.6) | 0.181 |
| | Salpingo-oophorectomy | 65(46.1) | 51(55.4) | |
| Adjuvant chemotherapy | No | 110(78.0) | 77(83.7) | 0.316 |
| | Yes | 31(22.0) | 15(16.3) | |
| FIGO Stage | I | 121(85.8) | 84(91.3) | 0.225 |
| | ≧II | 20(14.2) | 8(8.7) | |
| Histology | Serous | 79(56.0) | 39(42.4) | 0.08 |
| | Mucinous | 47(33.3) | 44(47.8) | |
| | others | 15(10.6) | 9(9.8) | |
| Lesion lateral | unilateral | 122(86.5) | 82(89.1) | 0.686 |
| | Bilateral | 19(13.5) | 10(10.9) | |
| Micropapillary | No | 23(16.3) | 12(13.0) | 0.576 |
| | Yes | 118(83.7) | 80(87.0) | |
| Microinvasion | No | 126(89.4) | 85(92.4) | 0.499 |
| | Yes | 15(10.6) | 7(7.6) | |
| Carcinogenesis | No | 134(95.0) | 86(93.5) | 0.771 |
| | Yes | 7(5.0) | 6(6.5) | |
| Ascites/Pelvic washings | Positive | 7(5.0) | 3(3.3) | 0.744 |
| | Negative | 134(95.0) | 89(96.7) | |
| CA-125 | Normal | 82(65.6) | 60(69.8) | 0.553 |
| | Elevated | 43(34.4) | 26(30.2) | |
| nvasive implants | No | 132(93.6) | 88(95.7) | 0.574 |
| | Yes | 9(6.4) | 4(4.3) | |
| Age | <35 | 107(75.9) | 92(100) | 0.000 |
| | ≧35 | 34(24.1) | 0 | |

# Supplementary Table

**Supplementary table 1**

Subgroup analysis of staging surgery in DFS of patients undergoing laparoscopy or laparotomy

| | Laparoscopy | | Laparotomy | | P Valve |
|---|---|---|---|---|---|
| | mean | 95% Confidence interval | mean | 95% Confidence interval | |
| Complete staging | 120.167±8.457 | 103.590-136.743 | 107.379±4.079 | 99.385-115.373 | 0.349 |
| Incomplete staging/unstaged | 150.920±2.430 | 146.158-155.683 | 141.914±3.478 | 135.098-148.731 | 0.011 |