

Original

Oncologic Outcomes of Fertility-Sparing Surgery versus Radical Surgery for Stage I Epithelial Ovarian Cancer

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Background: Epithelial ovarian cancer (EOC) is increasingly affecting women of reproductive age. Fertility-sparing surgery (FSS) is an option for patients with early EOC who want to preserve their fertility, but the oncologic safety of FSS requires rigorous evaluation. This study retrospectively compared the oncologic outcomes of FSS with those of radical surgery (non-FSS) for patients with FIGO 2014 Stage I EOC at our institution.

Methods: We retrospectively reviewed the medical records of patients younger than 45 years diagnosed with FIGO 2014 Stage I EOC (April 2010–June 2024). Patients were categorized into FSS (n=11) and non-FSS (n=9) groups. Baseline characteristics, recurrence rates, progression-free survival (PFS), and overall survival (OS) were compared.

Results: Twenty patients were included. The FSS group was significantly younger (median age 29.2 vs 40.8 years, $p=0.043$). Recurrence was more frequent in the FSS group (36.4% vs 11.1%), although this difference was not significant ($p=0.077$). Kaplan–Meier analysis showed no significant difference in PFS (HR 3.24, 95% CI: 0.56–18.74, $p=0.19$) or OS (HR 1.78, 95% CI: 0.18–16.9, $p=0.63$).

Conclusion: In this small cohort, FSS for Stage I EOC yielded a higher recurrence rate, but no significant difference in survival, as compared with radical surgery. Because of the small size and inherent stage-migration bias from incomplete surgical staging in the FSS group, these findings should be interpreted with extreme caution. Careful patient selection, thorough staging, and strict surveillance are crucial when implementing FSS.

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Introduction

Although epithelial ovarian cancer (EOC) predominantly affects postmenopausal women, a significant number of women of reproductive age are affected¹. For these younger patients, preserving fertility is often an important consideration, particularly given societal trends toward delayed childbearing, consequently increasing the

demand for fertility preservation options after an EOC diagnosis². Fertility-sparing surgery (FSS), typically involving unilateral salpingo-oophorectomy and comprehensive surgical staging, is an option for some patients with early EOC. International guidelines generally recommend considering FSS for women desiring future fertility and presenting with International Federation of Gy-

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necology and Obstetrics (FIGO) Stage IA or IC grade 1 or 2 tumors with favorable histologic characteristics^{3,4}.

Studies and meta-analyses indicate that FSS yields comparable oncologic outcomes to standard radical surgery (hysterectomy and bilateral salpingo-oophorectomy) in selected patients^{5,6}. However, the indications for FSS are limited, and oncologic safety is a concern in certain subgroups⁷. A cautious approach to FSS patient selection is crucial, and the procedure is typically limited to FIGO Stage IA/IC1, low-grade (G1/2), and non-clear cell carcinoma histologies. Conversely, the oncologic safety of FSS in patients with FIGO Stage IC2 (intraoperative capsule rupture) or IC3 (positive peritoneal cytology) and in specific histologic subtypes such as clear cell carcinoma (CCC) remains a subject of ongoing debate⁸⁻¹⁰. CCC is often associated with chemoresistance and poorer prognosis and is more prevalent in Japan and other Asian countries than in Western populations^{11,12}. Thus, careful consideration is required when selecting FSS for Japanese patients.

Although multiple guidelines suggest an age limit of 40 years for FSS³, an increasing number of women in their early forties are seeking fertility treatment, thus highlighting the need to evaluate the safety and efficacy of FSS in this older age group. Our cohort included patients up to 45 years of age. Against this background, our study retrospectively compared recurrence rate, progression-free survival (PFS), and overall survival (OS) between FSS and standard radical surgery for women younger than 45 years with FIGO 2014 Stage I EOC.

Materials and Methods

Study Design and Population

This was a retrospective cohort study conducted at the Nippon Medical School Hospital. The study protocol was approved by the Institutional Review Board of Nippon Medical School¹³ (approval number: M-2025-294) and complied with the ethical principles outlined in the Declaration of Helsinki. We reviewed the medical records of patients diagnosed with FIGO 2014 Stage I EOC during the period April 2010 through June 2024. The inclusion criteria were (1) histologically confirmed EOC, (2) FIGO 2014 Stage I disease, (3) age <45 years at diagnosis, and (4) receipt of primary surgical treatment at our institution. The exclusion criteria were (1) nonepithelial ovarian tumors, (2) receipt of primary treatment elsewhere, and (3) insufficient data for outcome assessment. Patients with synchronous endometrial cancer were included if the primary surgical treatment was for EOC and the in-

clusion criteria were met. Written informed consent for research use of patient data was obtained from all patients, in accordance with the institutional review board guidelines.

Patient Selection for FSS

FSS was offered to patients who had (1) FIGO 2014 Stage IA or IC disease, (2) low-grade (G1 or G2) non-CCC histology or Stage IA CCC, and (3) a strong desire for future fertility⁴. Although an age of 40 years was used as the cutoff in principle, the final decision was made on an individualized basis in discussion with the patient, and considered factors such as the patient's partner status and the intensity of their desire for a child.

Data Collection

Data were extracted from electronic medical records and included patient demographics (age at surgery, body mass index [BMI]), tumor characteristics (FIGO stage, histologic type, grade, and maximum tumor diameter), preoperative serum tumor markers (cancer antigen 125 [CA125], carbohydrate antigen 19-9 [CA19-9]), presence of endometriosis, type of surgery performed (FSS or non-FSS), details of surgical staging (omentectomy [OMT], lymphadenectomy—pelvic/para-aortic [PLN/PAN]), adjuvant chemotherapy, date of recurrence, site of recurrence, date of last follow-up, and survival status. The data cutoff was October 24, 2025.

Recurrence and Surveillance

Recurrence was defined as any new or progressive disease confirmed by imaging, ie, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography/CT (PET/CT), and/or biopsy after the primary treatment. The postoperative surveillance schedule for all patients consisted of clinical examinations, serum CA125 measurements every 3 months for the first 2 years, every 6 months for the next 3 years, and annually thereafter. Imaging (CT, MRI, PET/CT) was performed annually or as clinically indicated by the presence of elevated tumor markers.

Definition of Groups

Patients were divided into 2 groups based on the surgery received. The FSS group comprised patients who underwent preservation of the uterus and at least part of 1 ovary (typically unilateral salpingo-oophorectomy plus contralateral ovary preservation) with selected staging procedures. The non-FSS group comprised patients who

Table 1 Clinical and pathological characteristics of patients

	FSS (N=11)	non-FSS (N=9)	P value
Age at start of treatment (years)	29.2 (22–37)	40.8 (35–44)	0.043
FIGO Stage			
IA	6	3	
IC1	3	1	
IC2	1	1	
IC3	1	4	
Histology			
Mucinous	6	2	
Endometrioid	5	2	
Clear Cell	0	4	
Serous	0	1	
BMI (kg/m ²)	21.8 (21.0–31.2)	20.3 (15.4–27.8)	0.145
CA125 (U/mL)	81.8 (11.7–1,619.4)	57.3 (15.8–5,832.4)	0.501
CA19-9 (U/mL)	17.3 (4.6–3,353.3)	81.0 (1.6–5,827.1)	0.647
Tumor size (cm)	13.0 (6.0–32.0)	13.4 (5.7–20.0)	0.416
Endometriosis (N)	4 (36.4%)	1 (11.1%)	0.077
Recurrence (N)	4 (36.4%)	1 (11.1%)	0.077

Median (range) values are shown for age at start of treatment, BMI, CA125, CA19-9, and tumor size.

FSS: Fertility-Sparing Surgery, FIGO: International Federation of Gynecology and Obstetrics, BMI: Body mass index, CA125: Cancer antigen 125, CA19-9: Carbohydrate antigen 19-9.

underwent radical surgery (typically total abdominal hysterectomy plus bilateral salpingo-oophorectomy) along with surgical staging procedures.

Outcomes

The primary outcomes were PFS, defined as the time from primary surgery to the first documented recurrence or death from any cause, and OS, defined as the time from primary surgery to death from any cause. The secondary outcome was recurrence rate.

Statistical Analysis

Continuous variables were compared with the Mann-Whitney U test and reported as median (range) because of the small sample size. Categorical variables were compared using Fisher's exact test. Survival analyses were performed using the Cox proportional hazards model to estimate hazard ratios (HRs) with 95% confidence intervals (CIs). The proportional hazards assumption was verified visually with log-minus-log plots and was not violated. Survival curves for PFS and OS were estimated using the Kaplan-Meier method, and differences between groups were determined using the log-rank test. A *p*-value of <0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS

version 29.0.2. (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 5.03 (GraphPad Software, San Diego, CA, USA).

Results

A total of 20 patients met the inclusion criteria: 11 underwent FSS and 9 underwent non-FSS. The median (interquartile range) follow-up period was 2,209 (849–3,369) days in the FSS group and 2,970 (2,458–3,720) days in the non-FSS group. The baseline characteristics of the patients are shown in **Table 1**. The median age was significantly lower in the FSS group than in the non-FSS group (29.2 [range 22–37] vs 40.8 [range 35–44] years, *p* = 0.043). There was no significant difference between the groups in BMI, median preoperative CA125, CA19-9, median tumor size, or rate of concurrent endometriosis.

Recurrence occurred in 4 of 11 patients (36.4%) in the FSS group and 1 of 9 patients (11.1%) in the non-FSS group. All recurrences in the FSS group occurred within 4 years of the initial surgery. The detailed clinical course of the FSS group is shown in **Table 2**. Only 1 of the 11 patients in the FSS group received adjuvant chemotherapy (Patient 6). The patient had a positive result for peritoneal cytology and was thus upstaged to FIGO Stage IC 3. Details regarding the surgical staging of the FSS group

Table 2 Clinical course of the FSS group

No	Age (years)	Parity and Gravidity	Surgical procedure	Histology	FIGO stage	Peritoneal cytology	LVSI	Endometriosis	Chemotherapy	Recurrence	Time to recurrence (months)	Site of recurrence	Final outcome	Delivery after FSS
1	36	G1P0	USO+OMT (Preg 8w)	Endometrioid	IA	Negative	Negative	No	No				NED	NVD
2	22	G0P0	USO+OMT	Mucinous	IA	Negative	Negative	Yes	No				NED	
3	23	G0P0	USO+OMT	Mucinous	IA	Negative	Negative	No	No	Yes	26	ovary/liver/PC	DOD	
4	23	G0P0	USO+OMT	Mucinous	IC1	Negative	Negative	Yes	No	Yes	43	ovary/PC	NED	NVD (IVF)
5	23	G0P0	USO+OMT	Endometrioid	IC1	Negative	Negative	No	No	Yes	35	ovary/lung/liver/multiple LN/PC	DOD	
6	27	G0P0	USO+OMT	Endometrioid	IC3	Positive	Negative	No	TC				NED	
7	33	G0P0	USO+OMT	Mucinous	IA	Negative	Negative	No	No				NED	
8	35	G0P0	USO+OMT	Mucinous	IC1	Negative	Negative	Yes	No				NED	
9	31	G0P0	USO+OMT	Mucinous	IA	Negative	Negative	No	No				NED	
10	37	G0P0	USO+OMT	Endometrioid	IC2	Negative	Negative	Yes	No	Yes	1	ovary	NED	
11	31	G0P0	USO	Endometrioid	IA	Negative	Negative	No	No				NED	

FSS: Fertility-Sparing Surgery, FIGO: International Federation of Gynecology and Obstetrics, LVSI: LymphoVascular Space Invasion, USO: Unilateral Salpingo-Oophorectomy, OMT: Omentectomy, TC: Paclitaxel + Carboplatin, PC: Peritonitis Carcinomatosa, LN: Lymph Node, NED: No Evidence of Disease, DOD: Died of Disease, NVD: Normal Vaginal Delivery, IVF: In Vitro Fertilization.

Table 3 Clinical course of the non-FSS group

No	Age (years)	Parity and Gravidity	Surgical procedure	Histology	FIGO stage	Peritoneal cytology	LVSI	Endometriosis	Chemotherapy	Recurrence	Time to recurrence (months)	Site of recurrence	Final outcome
1	43	G0P0	TAH+BSO+OMT	Serous	IC3	Positive	No	No	TC				NED
2	42	G0P0	TAH+BSO+OMT	Endometrioid	IC2	Negative	No	No	TC				NED
3	35	G2P2	TAH+BSO+OMT+PLN+PAN	mucinous	IC3	Positive	No	Yes	ddTC				NED
4*	42	G1P1	TAH+BSO+OMT+PLN+PAN	Clear cell	IA	Negative	No	No	DC				NED
5	42	G0P0	TAH+BSO+OMT+PLN+PAN	Mucinous	IA	Negative	No	No	No				NED
6	43	G0P0	TAH+BSO+OMT+PLN+PAN	Clear cell	IA	Negative	No	No	TC				NED
7	37	G0P0	TAH+BSO+OMT+PLN+PAN	Clear cell	IC3	Positive	No	No	ddTC				NED
8	39	G0P0	TAH+BSO+OMT+PLN+PAN	Clear cell	IC3	Positive	No	No	TC	Yes	9	PC	DOD
9	44	G0P0	TAH+BSO+OMT+PLN+PAN	Endometrioid	IC1	Negative	No	No	No				NED

* Patient 4 had concurrent endometrial cancer

FSS: Fertility-Sparing Surgery, LVSI: LymphoVascular Space Invasion, FIGO: International Federation of Gynecology and Obstetrics, TAH: Total Abdominal Hysterectomy, BSO: Bilateral Salpingo-Oophorectomy, OMT: Omentectomy, PLN: Pelvic Lymphadenectomy, PAN: Para-Aortic Lymphadenectomy, TC: Paclitaxel + Carboplatin, ddTC: dose dense TC, DC: Docetaxel + Carboplatin, PC: Peritonitis Carcinomatosa, NED: No Evidence of Disease, DOD: Died of Disease.

were limited because lymphadenectomy was not performed in any patient in this group. Two patients experienced successful deliveries after undergoing FSS.

The clinical course of the non-FSS patients is detailed in **Table 3**. With the exception of 2 patients (Patients 1 and 2), surgical staging, including pelvic and para-aortic

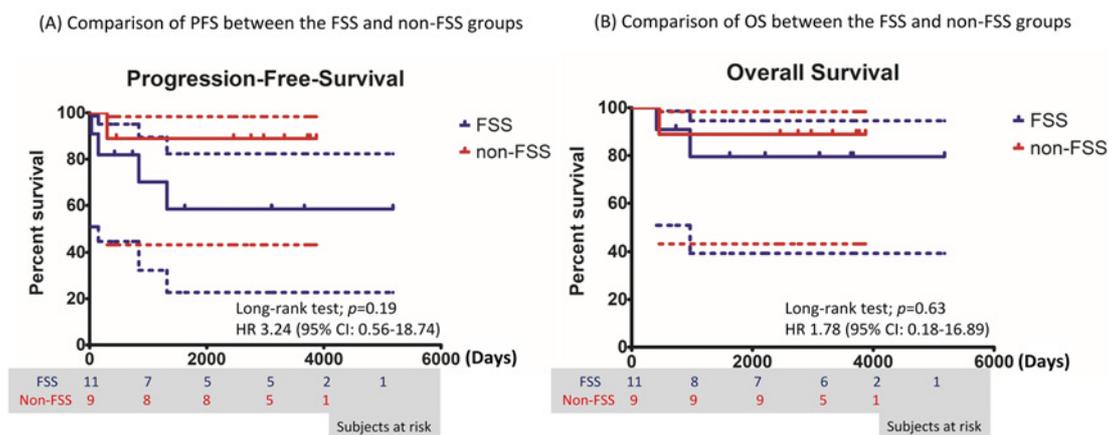


Figure 1 Kaplan–Meier analysis of progression-free survival (PFS) (A) and overall survival (OS) (B) in the FSS and non-FSS groups
Numbers at risk are shown below each panel; 95% confidence intervals (CIs) are displayed as dashed bands. Comparisons were made using the log-rank test.

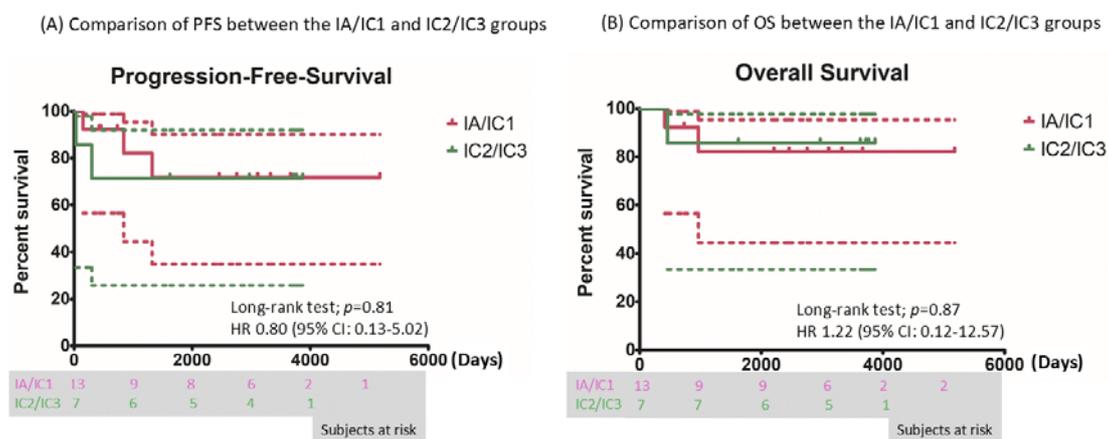


Figure 2 Kaplan–Meier analysis of PFS (A) and OS (B) in the Stage IA/IC1 and Stage IC2/IC3 groups
Numbers at risk are shown below each panel; 95% CIs are displayed as dashed bands. Comparisons were made using the log-rank test.

lymphadenectomy, was performed. Adjuvant chemotherapy was administered to all but 2 patients (Patients 5 and 9). The non-FSS group also included 1 patient with concurrent endometrial cancer (Patient 4). As this patient underwent non-FSS surgery and had no evidence of disease, her inclusion is not likely to materially change the primary oncologic outcomes of this study.

Three deaths occurred during the follow-up period (2 in the FSS group and 1 in the non-FSS group). Kaplan–Meier curves for PFS and OS are shown in **Figure 1**. There was no significant difference in PFS (HR 3.24, 95% CI: 0.56–18.74, $p=0.19$) or OS (HR 1.78, 95% CI: 0.18–16.9, $p=0.63$) between the FSS and non-FSS groups; however, visual inspection of the curves suggests a trend toward lower PFS and OS in the FSS group. To further investigate the influence of high-risk stage characteristics, we

conducted a subgroup analysis comparing oncologic outcomes between patients with low-risk disease (Stage IA/IC1, $n=13$) and those with high-risk disease (Stage IC2/IC3, $n=7$). This analysis showed no significant difference in survival in relation to stage grouping (**Figure 2**). PFS did not significantly differ between the low-risk and high-risk groups (HR 0.80, 95% CI: 0.13–5.02, $p=0.81$). Similarly, OS showed no significant difference (HR 1.22, 95% CI: 0.12–12.57, $p=0.87$).

To address potential stage-migration bias from the inclusion of higher-risk IC2/IC3 cases, we performed a sensitivity analysis restricted to patients with Stage IA and IC1 disease ($n=9$ for FSS, $n=4$ for non-FSS). In this subgroup, the differences remained nonsignificant for both PFS (HR 4.56, 95% CI: 0.41–50.03, $p=0.21$) and OS (HR 4.36, 95% CI: 0.22–85.09, $p=0.33$) (**Supplementary**

Table 4 Patient characteristics in relation to recurrence status in the FSS group

	Recurrence (N=4)	Non-Recurrence (N=7)	P value
Age at start of treatment (years)	23 (± 6.5)	31 (± 5.2)	0.736
BMI (kg/m ²)	22.6 (± 4.86)	21.9 (± 1.08)	0.617
CA125 (U/mL)	506.3 (± 638.76)	51.3 (± 34.22)	0.192
CA19-9 (U/mL)	541.4 ($\pm 1,363.47$)	16 (± 20.87)	0.26
Tumor size (cm)	13 (± 9.10)	16 (± 9.42)	0.747
Endometriosis (N)	2 (50%)	2 (28.6%)	0.617

Median (range) values are shown for age at start of treatment, BMI, CA125, CA19-9, and tumor size. FSS: Fertility-Sparing Surgery, BMI: Body mass index, CA125: Cancer antigen 125, CA19-9: Carbohydrate antigen 19-9.

Figure 1).

We compared the clinicopathological factors between patients with and without recurrence in the FSS group (Table 4). No significant difference was observed in average age at the start of treatment, BMI, CA125, CA19-9, tumor size, or the presence of endometriosis between the recurrence and non-recurrence groups within the FSS cohort.

Discussion

This single-center, retrospective study compared oncologic outcomes between FSS and radical surgery in patients younger than 45 years with FIGO 2014 Stage I EOC. There was no significant difference in PFS or OS between these groups; however, the FSS group had a higher recurrence rate (36.4% vs. 11.1%) and a trend toward poorer survival outcomes. There were 3 deaths during the observation period: 2 in the FSS group and 1 in the non-FSS group.

The nonsignificant differences in PFS and OS are consistent with the findings from some large-scale studies and meta-analyses, which suggests that survival rates with FSS are comparable for carefully selected patients with early EOC^{5,14,15}. However, these studies often use large databases, like the Surveillance, Epidemiology, and End Results database, or employ statistical adjustments such as inverse probability of treatment weighting to mitigate selection bias, neither of which was feasible for our small cohort. The lack of statistical significance in the present study is likely attributable to the limited statistical power resulting from the small sample size (n=20), as confirmed by a post hoc power analysis.

The trend toward lower survival and more deaths in the FSS group is consistent with the findings of a previous study¹⁶ that reported higher cancer-specific mortality rates for Stage IC patients undergoing FSS, despite similar overall OS. This highlights the importance of inter-

preting nonsignificant survival results with caution, particularly in underpowered studies. The 36.4% recurrence rate in our FSS group is a concern. Although recurrence confined to the preserved ovary may be amenable to salvage surgery, it requires careful long-term surveillance. Further studies should attempt to identify potential risk factors for recurrence in patients undergoing FSS at our institution.

Ovarian cancer histology is an important prognostic factor. FSS is generally considered appropriate for low-grade serous or endometrioid subtypes; however, its use in CCC or high-grade (G3) tumors remains controversial because of the increased risk of recurrence^{9,10}. In our FSS cohort, the histologic subtypes included endometrioid and mucinous carcinomas. Similarly, FIGO Stage IC EOC, particularly IC2 (capsule rupture) and IC3 (positive cytology), is associated with a higher risk of recurrence than stage IA disease⁸. Among our FSS patients, approximately half (5 of 11) had Stage IC disease, and 2 were classified as IC2 and IC3, respectively. The outcomes for patients with these specific risk factors in our FSS group should be interpreted with caution, and these factors should be carefully considered when counseling patients.

Current guidelines suggest an age limit of 40 years for FSS in EOC, and all FSS patients in our cohort were under 40³. However, because of the increasing demand for fertility preservation and advances in assisted reproductive technologies, the appropriateness of a strict age cutoff of 40 years may need to be re-evaluated. Future studies should examine the oncologic safety of FSS in carefully selected patients older than 40 years.

Determining the optimal criteria for offering FSS to patients is challenging. Complete surgical staging, including peritoneal cytology, OMT, biopsies, and lymph node assessment (PLN/PAN), is essential for accurate prognosis and treatment planning. Yet, in our FSS group, no patients underwent lymphadenectomy, and the details of

surgical staging were limited. The omission of lymphadenectomy, even if lymph nodes are visually normal, significantly increases the risk of incomplete staging⁸. While minimally invasive surgery is now increasingly used for FSS, adherence to oncologic principles, including complete staging and avoiding intra-abdominal spillage of the tumor, is of paramount importance. Intraoperative capsule rupture (FIGO IC2) is associated with poor prognosis, especially in CCC and endometrioid carcinoma¹⁷. Currently, a prospective phase III trial, the Japan Clinical Oncology Group 1203 trial, is analyzing the utility of FSS for Stage IA CCC and Stage IC, well-differentiated or moderately differentiated (G1/2), non-CCC patients¹⁸.

Only 1 of the present 11 FSS patients received adjuvant chemotherapy. This low rate is primarily attributable to the initial assessment of the patients as low-risk and their preference for immediate conception. Significantly, none of the 4 patients who developed a recurrence in the FSS group had received adjuvant chemotherapy. While adjuvant TC chemotherapy is the standard of care for high-risk Stage I EOC¹⁹, concerns regarding ovarian toxicity frequently lead to its omission in the FSS setting. Although chemotherapy can impair ovarian function, recovery is possible, particularly in younger women^{20,21}. Given the potential for incomplete staging with FSS, caution is warranted when omitting adjuvant chemotherapy in patients who meet the criteria for its use. Consequently, the risks and benefits of adjuvant chemotherapy must be carefully weighed in the context of fertility preservation.

Several limitations of this study must be acknowledged. First, its retrospective design, single-center setting, and small sample size limit statistical power and generalizability. Specifically, we opted not to include the estimated sample size from a post-hoc power analysis, given that the primary objective was to report trends observed in a limited institutional cohort rather than conduct a large-scale study with sufficient statistical power. Second, significant selection bias is likely, as evidenced by the age difference between the groups. Third, the effect of confounding factors, such as variations in staging completeness and chemotherapy administration, could not be fully addressed. Specifically, the systematic under-staging in the FSS cohort, particularly the lack of systematic pelvic and para-aortic lymphadenectomy (as confirmed in **Supplementary Table 1**), must be acknowledged as a significant source of stage-migration bias. This incomplete staging is the likely driver for the potentially inflated re-

currence rate observed in the FSS group and necessitates cautious interpretation of the oncologic outcomes. Fourth, detailed subgroup analyses were severely limited by the small sample size. Future large, multicenter, prospective studies, or well-controlled retrospective studies incorporating appropriate statistical adjustments (e.g., propensity score matching), are thus required.

Our findings emphasize the importance of comprehensive patient counseling. When discussing FSS, clinicians must provide a balanced presentation of the potential benefits of fertility preservation with the associated oncologic risks, including the possibility of recurrence (as observed in our cohort) and the need for meticulous staging and surveillance. Shared decision-making that incorporates the patient's values and priorities is essential.

Conclusion

In conclusion, this single-center retrospective study suggests that, as compared with radical surgery, FSS for Stage I EOC is associated with a higher recurrence rate and a trend toward poorer survival. However, these differences were not significant and are likely the result of the small sample size and the study's inherent limitations. Therefore, the results should be interpreted with caution. Accordingly, careful patient selection, comprehensive surgical staging, and rigorous postoperative surveillance remain critical considerations for FSS.

Author Contributions: Y.K. contributed to data collection, data analysis, and the preparation of tables. M.T. was involved in patient management, data analysis, writing the manuscript, and the preparation of figures and tables. A.S. contributed to data analysis. M.I., A.Y., R.K., and K.K. were involved in patient management. S.S. supervised the study.

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Data Availability: The datasets generated during and/or analyzed during the current study are not publicly available due to patient confidentiality concerns but are available from the corresponding author on reasonable request.

Supplementary Material: Supplementary material associated with this article is available at https://doi.org/10.1272/jnms.JNMS.2026_93-114.

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