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Systematic Review

Outcomes of fertility-sparing surgery in early-stage ovarian cancer; systematic review

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ABSTRACT

Background: Fertility sparing surgery (FSS) is used in women with early-stage ovarian malignancies who aim to preserve fertility, but its oncologic safety still debated. Our review examined oncologic and reproductive outcomes after FSS. **Methods:** We conduct A PRISMA 2020-based systematic review in PubMed, Web of Science, Scopus, Embase, and the Cochrane Library from inception to early 2024. We include observational and registry-based analyses of reproductive-age women with early-stage epithelial ovarian cancer (EOC), malignant ovarian germ cell tumors (MOGCT), or sex cord-stromal tumors (SCST) treated with FSS. Primary outcomes were OS, disease-free survival, and recurrence; secondary outcomes were pregnancy, menstrual recovery, and live birth. **Results:** We include 24 studies published between 2002 and 2024, mainly retrospective and included EOC, MOGCT, and SCST. In stage I EOC, large population-based studies showed no significant survival disadvantage with FSS, with 5-year overall survival above 95%. Recurrence

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after FSS ranged from 2.0% to 27.8%, with higher risk in grade 3 tumors, clear-cell carcinoma, and selected stage IC cases. In women attempting conception, pregnancy rates reached 91.2% in MOGCT and 92.3% in EOC, with live birth rates of 65% to 100% in those who conceived. **Conclusion:** FSS provide positive oncologic and reproductive outcomes in some women, although epithelial high-risk subgroups and SCST require special counseling and long surveillance.

Keywords: Fertility-sparing surgery; Early-stage ovarian cancer; Epithelial ovarian cancer; Reproductive outcomes; Oncologic outcomes

Introduction

Ovarian cancer is a significant health problem worldwide, mainly when diagnosed in women of reproductive age. While the majority of cases occur in postmenopausal women, 12% to 15% of epithelial ovarian cancers (EOC) are diagnosed in patients under 40 years old (Guan et al. 2024). Non-epithelial malignancies, malignant ovarian germ cell tumors (MOGCT) and sex cord-stromal tumors (SCST), affect even younger populations (Bercow et al. 2021). The standard treatment for ovarian cancer is been radical surgery (RS), total abdominal hysterectomy and bilateral salpingo-oophorectomy. This approach leads to permanent loss of fertility, impacting the Qol and psychological well-being of young survivors (Canlorbe et al. 2021).

FSS has emerged as alternative for women wishing to maintain reproductive possibility (Schuurman et al. 2021). Current guidelines support FSS for stage I EOC, mainly FIGO stage IA or IC1 low-grade tumors, and for most stages of MOGCT and SCST (Canlorbe et al. 2021). The oncological safety of FSS compared to RS is a subject of intensive debate, mainly in recurrence rates and long-term survival in high-grade or more advanced early-stage epithelial tumors (Chatziioannou et al. 2025).

Liu et al. (2020) show no significant difference in overall survival between patients undergoing FSS and RS for stage I EOC, with a pooled hazard ratio of 1.03. Zhang et al. (2022) found that the pooled recurrence rate for EOC after FSS was 12%, which did not differ from radical management. Despite these survival figures, reproductive outcomes vary; while some reports show pregnancy rates of 30% (Zhang et al. 2022). Our systematic review aims to evaluate the oncologic safety and reproductive outcomes of FSS compared to RS in young women diagnosed with early-stage EOC, MOGCT, and SCST.

Methodology

Study design

This systematic review was conducted in according to the PRISMA 2020 statement to ensure a transparent reporting process. The protocol focused on the evaluation of oncologic safety and reproductive outcomes of FSS compared to RS in young women with ovarian malignancies (EOC, MOGCT, and SCST).

Search strategy and information sources

A comprehensive systematic search was performed in five major electronic databases: PubMed, Web of Science (WoS), Scopus, Embase, and the Cochrane Library. The search was conducted from database inception through early 2024. The search strategy utilized a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to: "ovarian cancer," "epithelial ovarian cancer," "malignant germ cell tumors," "sex cord-stromal tumors." "fertility-sparing surgery," "conservative surgery," "unilateral salpingo-oophorectomy," "ovarian cystectomy." "oncologic outcome," "overall survival," "recurrence," "pregnancy rate," "live birth." References of relevant articles were

manually screened to identify additional eligible studies.

Eligibility criteria

Studies were included based on the following PICOS criteria:

Population: Women of reproductive age defined as <40, <45, or <50 years depending on the study diagnosed with early-stage EOC, or MOGCT/SCST of any stage.

Intervention: Fertility-sparing surgery preservation of the uterus and at least part of one ovary.

Comparison: Radical surgery total abdominal hysterectomy and bilateral salpingo-oophorectomy or no comparison group.

Outcomes: Primary outcomes included overall survival (OS), disease-free survival (DFS), and recurrence rates. Secondary outcomes included pregnancy rates, menstrual function, and live birth rates.

Study design: Retrospective cohorts, prospective observational studies, and population-based registry analyses.

Exclusion criteria: Case reports with fewer than 10 patients, literature reviews, meta-analyses, and studies published in languages other than English without available translations.

Study selection and data extraction

The selection process followed a multi-stage approach. 450 articles were identified through the database search. After the removal of duplicates using reference management software, titles and abstracts were screened for relevance. Studies that did not meet the inclusion criteria were excluded.

Full-text versions of the remaining articles were retrieved and assessed for eligibility. This process resulted in a final cohort of 24 eligible studies. Data extraction was performed using a standardized form, capturing: author, year, study design, histology, sample size, staging, follow-up duration, recurrence rates, and reproductive metrics.

Quality assessment

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS) for non-randomized studies. This tool evaluates studies in the selection of the study groups, the comparability of the groups, and the ascertainment of the outcome of interest. Studies scoring ≥ 7 were considered high quality. Given the heterogeneity in histological types, staging, and outcome reporting across the 24 studies, a qualitative synthesis was performed. Data were categorized by tumor histology to allow for a nuanced analysis of survival and fertility outcomes specific to each malignancy type.

Results

A total of 24 studies published between 2002 and 2024 were included in this systematic review, including a range of histological types, epithelial ovarian cancer (EOC), malignant ovarian germ cell tumors (MOGCT), and sex cord-stromal tumors (SCST). Most of the included studies used a retrospective cohort design, including population-based analyses from the SEER and NCDB databases. The patient populations consisted of reproductive-age women, with median ages typically ranging from 21 to 33 years. Follow-up durations were

extensive, with several studies reporting median follow-up periods exceeding 80 months, providing data on long-term survival and late recurrences.

For patients with Stage IA–IC EOC, FSS show high oncologic safety. Large population-based studies (Wright et al., 2009; Melamed et al., 2017; Xie et al., 2022) found no significant difference in OS or CSS between patients undergoing FSS and those undergoing radical surgery (RS). Five year OS rates for Stage I EOC exceeded 95%. Histological subtype and grade significantly impact outcomes; Jiang et al. (2017) and others identified Grade 3 tumors and clear-cell carcinoma as independent risk factors for decreased DFS.

Tamauchi et al. (2018) and Park et al. (2017) reported 5-year OS rates as high as 98.1% and 97.0%, respectively, even when including advanced-stage patients. Recurrence rates in MOGCT were low (5.7% to 12.5%), with most recurrences managed with salvage chemotherapy. For SCST, Granulosa cell tumors, survival remained high (96.8% CSS), though Sun et al. (2022) observed a recurrence rate of 12.1% in Stage I cases, showing the need for long-term surveillance due to the risk for late relapse.

Among women who attempted to conceive following FSS and adjuvant chemotherapy, pregnancy rates were high. in the MOGCT group, Tamauchi et al. (2018) reported that 61 out of 105 survivors achieved pregnancy in the MOGCT group, resulting in 108 live births. Schilder et al. (2002) found a 92.3% pregnancy rate in EOC survivors who attempted conception.

Live birth rates in those who conceived ranged from 65% to 100%. While adjuvant chemotherapy caused transient amenorrhea, the majority of patients regained normal menstrual function within 6 to 12 months post-treatment. Obstetric complications were not higher than in the general population, and the health of the offspring was reported as normal, with no increased risk of congenital anomalies related to prior chemotherapy.

Kashima et al. (2013) found a higher recurrence rate (27.8%) in a small Stage IC cohort, which suggest that while FSS is safe, these patients require individualized counseling and strict monitoring. For non-epithelial tumors, residual disease and incomplete surgical staging were identified as primary drivers of recurrence. Characteristics of the included studies and main findings presented in Tables 1 and 2 respectively.

Table 1: characteristics of the included studies

Author	Study design	Histology type	Sample size	Patient age	Follow-up
Tamauchi (2018)	Multicenter Retrospective	MOGCT	105	Median: 22.8 yrs	Median: 120

Author	Study design	Histology type	Sample size	Patient age	Follow-up
Wright (2009)	SEER Population Study	EOC (Stage IA/IC)	432	≤ 50 years	Median: 48
Xie (2022)	SEER Propensity Match	EOC (Stage I)	625	≤ 50 years	Median: 85
Schilder (2002)	Multicenter Retrospective	EOC (Stage IA/IC)	52	Range: 14–39 yrs	Median: 68
Jorgensen (2023)	SEER & NCDB Cohort	EOC (Stage IA/IC)	390 (SEER) / 393 (NCDB)	18–45 years	50.8 / 76.8
Swift (2022)	Retrospective Cohort	Endometrioid (Low-grade)	26	Range: 22–44 yrs	Median: 56
Sun (2022)	SEER Cohort	SCST (Stage I)	165	Range: 18–49 yrs	Median: 92
Zamani (2021)	Retrospective Cohort	MOGCT	72	Mean: 23 yrs	Median: 84
Crafton (2020)	SEER & NCDB Cohort	EOC (Reproductive Age)	1,185	≤ 44 years	Median: 64
Kajiyama (2019)	Propensity Score Matched	EOC (Stage I)	101	Range: 19–40 yrs	Median: 66
Melamed (2017)	NCDB Propensity Match	EOC (Stage IA/IC)	825	≤ 40 years	Median: 55
Jiang (2017)	Retrospective Cohort	EOC (Stage I)	52	≤ 40 years	Median: 83

Author	Study design	Histology type	Sample size	Patient age	Follow-up
Zhang (2017)	Retrospective Cohort	MOGCT & SCST	41	Range: 18–35 yrs	Mean: 86.3
Nasioudis (2017)	SEER Cohort	SCST (Stage I)	161	Range: 18–49 yrs	Median: 104
Park (2017)	Retrospective Cohort	MOGCT	171	Mean: 21 yrs	Median: 79
Lee (2015)	Retrospective Cohort	Mucinous EOC	42	Range: 16–40 yrs	Mean: 71
Kajiyama (2014)	Multi-institutional	EOC (Stage I)	148	Mean: 31.2 yrs	Median: 76
Gouy (2017)	Retrospective (G. Roussy)	Mucinous (Expansile vs Infilt.)	47	Range: 15–39 yrs	Median: 102
Kashima (2013)	Retrospective Cohort	EOC (Stage IC)	18	Range: 23–38 yrs	Median: 78
Hu (2011)	Multicenter Retrospective	EOC (Stage I)	38	Range: 18–40 yrs	Mean: 58
Satoh (2010)	Multicenter Retrospective	EOC (Stage I)	211	Range: 16–40 yrs	Median: 81
Kwon (2009)	Retrospective Cohort	EOC (Stage I)	21	Mean: 26.7 yrs	Mean: 43

Author	Study design	Histology type	Sample size	Patient age	Follow-up
Park (2008)	Retrospective Cohort	EOC (Stage I)	62	Range: 13–40 yrs	Median: 58
Lee (2024)	Nationwide Pop-based	EOC (Stage I)	158	Range: 18–45 yrs	Median: 88

Table 2: main findings and outcomes

Author	Recurrence rate (FSS)	Survival outcome	Pregnancy rate	Live birth rate
Tamauchi (2018)	5.7%	5-yr OS: 98.1%	58.1% (61/105 total)	108 Live Births
Wright (2009)	N/A	5-yr OS: 96.2%	N/A	N/A
Xie (2022)	N/A	5-yr OS: 96.3%; CSS: 97.5%	N/A	N/A
Schilder (2002)	2.0% (1/52)	5-yr OS: 98%	92.3% (24/26 attempted)	80.8% (21/26)
Jorgensen (2023)	N/A	5-yr OS: 94% (FSS)	N/A	N/A
Swift (2022)	11.5%	10-yr OS: 100%	85.7% (6/7 attempted)	100% (6/6)

Author	Recurrence rate (FSS)	Survival outcome	Pregnancy rate	Live birth rate
Sun (2022)	12.1%	5-yr CSS: 96.8%	N/A	N/A
Zamani (2021)	12.5%	10-yr DFS: 94.4%	91.2% (31/34 attempted)	88.2% (30/34)
Kajiyama (2019)	13.9%	5-yr OS: 97.4%	N/A	N/A
Jiang (2017)	13.5%	5-yr OS: 98.1%	33.3% (3/9 attempted)	22.2% (2/9)
Melamed (2017)	N/A	5-yr OS: 95.8%	N/A	N/A
Zhang (2017)	0%	5-yr OS: 100%	83.3% (10/12 attempted)	66.7% (8/12)
Park (2017)	12.3%	5-yr OS: 97.0%	75.0% (45/60 attempted)	65.0% (39/60)
Nasioudis (2017)	N/A	5-yr OS: 97.4%	N/A	N/A
Gouy (2017)	8.5%	5-yr OS: 93.0%	52.6% (10/19 attempted)	42.1% (8/19)
Lee (2015)	9.5%	5-yr OS: 97.6%	33.3% (2/6 attempted)	33.3% (2/6)
Kajiyama (2014)	10.1%	5-yr OS: 98.0%	N/A	N/A
Kashima (2013)	27.8%	5-yr OS: 100%	41.7% (5/12 attempted)	33.3% (4/12)
Hu (2011)	10.5%	5-yr OS: 100%	62.5% (10/16 attempted)	56.3% (9/16)
Satoh (2010)	8.5%	5-yr OS: 99.1%	80.0% (24/30 attempted)	70.0% (21/30)

Author	Recurrence rate (FSS)	Survival outcome	Pregnancy rate	Live birth rate
Kwon (2009)	4.8%	5-yr OS: 100%	23.8% (5/21 total)	23.8% (5/21)
Park (2008)	11.3%	5-yr OS: 91.3%	81.3% (13/16 attempted)	75.0% (12/16)
Lee (2024)		10-yr OS: 90.7%	N/A	N/A

Discussion

The findings of this systematic review show that FSS is a safe and effective treatment modality for young women with early-stage ovarian malignancies, including EOC, MOGCT, and SCST. Oncological safety indicated by high survival rates and recurrence rates, while reproductive outcomes were encouraging for patients seeking to preserve their fertility.

Our analysis of oncological outcomes showed that OS after FSS is comparable to RS. This is represented by findings from Wright et al. (2009) and Xie et al. (2022), who reported 5-year OS rates of 96.2% and 96.3%, respectively. These results are supported by the meta-analysis of Liu et al. (2020), which found no significant difference in OS between FSS and RS (HR 1.03), the preservation of the uterus and contralateral ovary does not compromise life expectancy in stage I EOC.

Recurrence rates in our findings ranged from 2% in earlier cohorts like Schilder et al. (2002) to 13.9% in Kajiyama et al. (2019). The pooled recurrence rate of 12% reported by Zhang et al. (2022) aligns with the upper end of our findings and confirms that recurrence is a risk, but it does not significantly differ from rates observed following radical management. Our results indicate the need for histological specificity. In sex cord-stromal tumors, Nasioudis et al. (2017) noted that OS did not differ between surgical groups, and CSS was better for patients undergoing definitive surgery (P=0.015). Sun et al. (2022) observed a 5-year CSS of 96.8% for SCST patients after FSS.

Reproductive success is the primary driver for FSS, and our synthesized data show highly favorable pregnancy and live birth rates. While Zhang et al. (2022) reported a pooled pregnancy rate of 30% in a broad EOC population, several studies in our review showcased even higher success in those actively attempting to conceive. Zamani et al. (2021) and Schilder et al. (2002) reported pregnancy rates of 91.2% and 92.3%, respectively, with high corresponding live birth rates.

Conclusion

Our findings indicate that FSS provides excellent oncological and reproductive outcomes for young

women with early-stage ovarian cancer. While high-grade epithelial tumors and SCST require more cautious counseling, the findings supports FSS as a standard of care for fertility preservation. Future prospective research should focus on refining selection criteria and long-term reproductive health after adjuvant chemotherapy.

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