Fertility sparing surgery for malignant ovarian sex-cord stromal tumors: long-term obstetric and oncologic outcomes

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Abstract

Objective: To evaluate the oncological and reproductive outcomes of patients with ovarian sex-cord stromal tumors (SCSTs) treated with fertility sparing surgery (FSS).

Material and Methods: This retrospective study included patients diagnosed with malignant ovarian SCSTs between February 2007 and June 2020 at Başkent University Hospital, Ankara. All patients underwent FSS, which preserved at least one ovary and the uterus. Data on demographics, surgical and pathological features, adjuvant treatments, follow-up, recurrence, survival, and obstetric outcomes were collected. Follow-up continued until September 2025, with survival analyses performed using Kaplan-Meier and Cox regression methods.

Results: The median age of the 35 included patients was 29.0 years, with a median follow-up of 141.0 months. Recurrence occurred in 17.1%, and disease-related mortality was 8.6%. The 5-year disease-free survival (DFS) and overall survival (OS) rates were 85.7% and 97.1%, respectively. No significant factors influenced DFS, while adjuvant therapy impacted OS in univariate analysis. All patients maintained regular menstrual cycles post-treatment. Nine patients conceived (36.0%), resulting in 12 pregnancies and 6 live births (50.0%). Chemotherapy did not significantly affect fertility outcomes.

Conclusion: FSS in patients with ovarian SCSTs demonstrated favorable oncologic and reproductive outcomes. Larger, prospective multicenter studies are necessary to optimize management strategies and establish definitive guidelines for fertility preservation in this patient population. [J Turk Ger Gynecol Assoc. 2025; 26(4): 297-303]

Keywords: Sex-cord stromal tumors, granulosa cell tumors, sertoli-leydig cell tumors, fertility preservation, fertility sparing

Received: 22 September, 2025 **Accepted:** 06 October, 2025 **Epub:** 15 October, 2025 **Publication Date:** 03 December, 2025

Introduction

Ovarian sex-cord stromal tumors (SCSTs) are a group of benign and malignant neoplasms originating from sex-cords or ovarian stroma (1). They can occur across a wide age range. For example, adult-type granulosa cell tumors, the most common subtype of SCST, occur in perimenopausal and postmenopausal women, while Sertoli-Leydig cell tumors typically affect adolescents and young women. SCSTs account for less than 5% of all ovarian malignancies (2-4).

Compared to epithelial ovarian cancers, SCSTs generally have a better prognosis (5). In addition, malignant ovarian SCSTs (MOSCSTs) are often diagnosed at stage I (6). Standard surgical treatment includes hysterectomy with bilateral salpingo-oophorectomy, along with surgical staging procedures, such as omentectomy, peritoneal biopsies, and peritoneal washing (6).

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DOI: *10.4274/jtgga.galenos.2025.2025-9-11*

Cite this article as: *Tunç M, Akıllı H, Haberal Reyhan AN, Kuşçu E, Önalan G, Özgül N, et al. Fertility sparing surgery for malignant ovarian sex-cord stromal tumors: long-term obstetric and oncologic outcomes. J Turk Ger Gynecol Assoc. 2025; 26(4): 297-303*

With the exception of adult-type granulosa cell tumors, these tumors tend to occur in younger women so fertility preservation is often a key concern and has been shown to have similar survival outcomes compared to more extensive surgical approaches. However, evidence regarding the prognosis after fertility-sparing surgery (FSS) for MOSCSTs is limited, because of the rarity of this entity and the scarcity of multicenter, randomized, prospective studies (7).

Therefore, the aim of this study was to evaluate the oncological and obstetric outcomes of patients with MOSCSTs who underwent FSS.

Materials and Methods

This retrospective study included patients diagnosed with MOSCSTs between February 2007 and June 2020 at the Department of Obstetrics and Gynecology, Başkent University Hospital, Ankara. This study was approved by the Başkent University Medical and Health Sciences Research Board (approval number: KA25/336, date: 18.09.2025). Informed consent was obtained from all patients.

Survival and follow-up data were analyzed, as of September 2025. Patients who did not undergo an FSS were excluded from the study. FSS was defined as the preservation of at least one ovary and uterus. The decision for FSS was based on patient preference and tumor extent. Data collected from hospital records included age, marital status, menstrual patterns, medical history, surgical details, histopathological subtype, chemotherapy administration, obstetric outcome, and status of recurrence and survival.

The decision to use adjuvant chemotherapy depended on tumor stage and histopathology and was made by the gynecologic oncology tumor board following current guidelines. Regimens for SCSTs included three courses of bleomycin (20 mg/m^2, on days 1, 8, and 15), etoposide (120 mg/m^2, from days 1 through 5), and cisplatin (20 mg/m^2, from days 1 through 5) [Bleomycin + Etoposide + Cisplatin (BEP)] or 3 to 6 courses of paclitaxel (175 mg/m^2, every 3 weeks) and carboplatin (area under curve =5, every 3 weeks). After the completion of adjuvant chemotherapy, a thoracoabdominal computed tomography scan was conducted.

After confirmation of no recurrence or any residual disease, the patients were taken into a routine follow-up program. The follow-up protocol for these patient groups was planned for every 3-4 months for two years, biannually between the 3 to 5 years of follow-up, and annually thereafter until the detection of any progression or disease recurrence. Follow-up included a gynecologic examination, pelvic ultrasound (US), testing of disease-related serum tumor markers (alpha-fetoprotein, human chorionic gonadotropin, cancer antigen 125, etc.), and thoracoabdominal computed tomography scans every six months during the first two years. If pregnancy occurred during follow-up, a transvaginal US was added to routine obstetric visits.

Disease-free survival (DFS) was defined as the interval between surgery and disease recurrence. Overall survival (OS) was defined as the time between the surgery and the time of death related to the disease. Obstetric outcomes were evaluated by collecting data up until the patient's last follow-up visit from the hospital records and patient files.

The statistical analyses were performed using IBM SPSS for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). The data are expressed as the median and range for continuous variables. Binary variables are reported as numbers and percentages. The Kaplan-Meier test was used to identify differences between the curves for DFS and OS. Multivariate analysis was performed using the Cox regression test. p-values <0.05 were considered statistically significant.

Results

A total of 35 patients were included in the study. Median (range) age of the patients was 29.0 (12-44) years. The median follow-up duration was 141.0 (41-268) months. Patient characteristics are detailed in Table 1.

A total of 6 (17.1%) recurrences were observed during follow-up. Disease-related deaths were observed in 3 (8.6%) patients. The 5-year DFS and OS were 85.7% and 97.1%, respectively. Five-year DFS rates for stages IA, IC1, and II were 81.0%, 91.7%, and 100%, respectively (p=0.855). Five-year OS rates for stages IA, IC1, and II were 100.0%, 91.7%, and 100.0%, respectively (p=0.938). No factors significantly affected DFS in univariate analysis. Kaplan-Meier survival curves comparing histological subtypes for DFS and OS are shown in Figures 1 and 2. The need for adjuvant treatment was the only prognostic factor for OS in univariate analysis (p=0.015). However, multivariate analysis revealed no significant prognostic factors for OS. Detailed univariate and multivariate analyses for factors affecting DFS and OS are given in Tables 2 and 3.

All patients (100.0%) maintained regular menstrual cycles after treatment. To date, 25 of the 35 patients were married or partnered. Post-treatment, 12 pregnancies occurred in 9 patients (36.0%), resulting in 6 live births (50.0%). Among these pregnancies, 6 (50.0%) occurred in patients with granulosa cell tumors, while the remaining occurred in patients with Sertoli-Leydig cell tumors. Adjuvant chemotherapy and age >35 years did not significantly affect conception or live birth rates (for adjuvant chemotherapy p=0.691 and p=0.615; and for age >35 years p=1.000 and p=1.000; respectively). A flowchart illustrating obstetric outcomes is provided in Figure 1.

Table 1. Demographic and clinical outcomes of the patients

	Median (range)		
Age	29.0 years (12-44)		
	n (%)		
Histologic types		**Median age (range)**	
Granulosa cell	23 (65.7)	31.0 (15.42)	
Adult type	19 (54.3)		**p**
Juvenile	4 (11.4)		
Sertoli-leydig	8 (22.9)	20.5 (12-33)	0.167
Retiform	8 (22.9)		
Sex-cord stromal tm	4 (11.4)	27.0 (15-44)	
Unclassified	4 (11.4)		
Histologic types	**n (%)**	**Cyst size (mean, cm) (range)**	**p**
Granulosa cell	23 (65.7)	9.67 (2-29)	
Sertoli-leydig	8 (22.9)	9.75 (3-17)	0.373
Sex-cord stromal tumor	4 (11.4)	4.85 (1-9)	
Endometriosis			
Yes	3 (8.6)		
No	32 (91.4)		
Surgical Intervention			
USO +/- staging	29 (82.9)		
Cystectomy +/- staging	6 (17.1)		
Stage			
IA	21 (60.0)		
IC1	12 (34.3)		
II	2 (5.7)		
Site			
Right	21 (60.0)		
Left	14 (40.0)		
Adjuvant treatment			
BEP	4 (11.4)		
P/C	8 (22.9)		
None	23 (65.7)		

USO: Unilateral salpingooophorectomy, BEP: Bleomycin + Etoposide + Cisplatin, P/C: Paclitaxel + Carboplatin

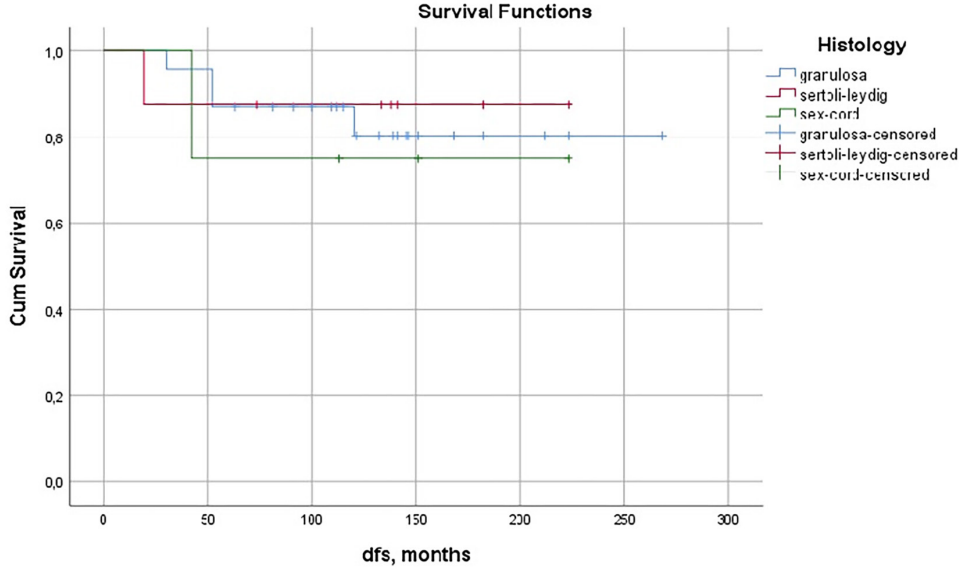

Figure 1. Disease-free survival plot of histologic subtypes (p=0.855)
DFS: Disease-free survival

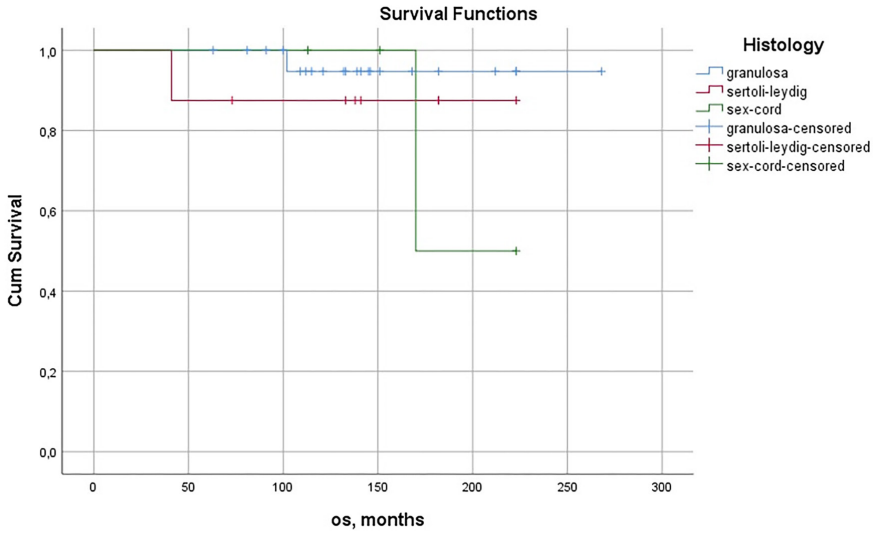

Figure 2. Overall survival plot of histologic subtypes (p=0.530)
OS: Overall survival

Table 2. Univariate and multivariate analysis of disease-free survival

	Univariate analysis			Multivariate analysis		
	N (%)	**5-year DFS (%)**	**p**	**HR**	**95% CI**	**p**
Endometriosis history						
Yes	3 (8.6)	100.0	0.457			
No	32 (91.4)	84.4				
Surgery						
USO	29 (82.9)	82.8	0.232			
Cystectomy	6 (17.1)	100.0				
Lymphadenectomy						
Yes	28 (80.0)	89.3	0.434			
No	7 (20.0)	71.4				
Chemo						
Yes	12 (34.3)	75.0	0.057			
No	23 (65.7)	91.3				
Site						
Right	21 (60.0)	90.5	0.585			
Left	14 (40.0)	78.6				
Tumor size						
<10 cm	21 (60.0)	94.4	0.311			
≥10 cm	14 (40.0)	91.7				
Histology						
Granulosa cell	23 (65.7)	87.0	0.855			
Sertoli-leydig	8 (22.9)	87.5				
Mixed sex-cord stromal tumor	4 (11.4)	75.0				
Histology						
Granulosa cell	23 (65.7)	87.0	0.996			
Others	12 (34.3)	83.3				
FIGO stage						
IA	21 (60.0)	81.0	0.497			
IC1	12 (34.3)	91.7				
II	2 (5.7)	100.0				
Post-treatment pregnancy						
Yes	9 (25.7)	100.0	0.114			
No	26 (74.3)	80.8				

USO: Unilateral salpingooophorectomy, BEP: Bleomycin + Etoposide + Cisplatin, HR: Hazard ratio, CI: Confidence interval, DFS: Disease-free survival

Table 3. Univariate and multivariate analysis of overall survival

	Univariate analysis			Multivariate analysis		
	n	**5-year OS (%)**	**p**	**HR**	**CI 95%**	**p**
Endometriosis history						
Yes	3 (8.6)	100.0	0.682			
No	32 (91.4)	96.9				
Surgery						
USO	29 (82.9)	96.6	0.406			
Cystectomy	6 (17.1)	100.0				
Lymphadenectomy						
Yes	28 (80.0)	96.4	0.115	1.861		0.200
No	7 (20.0)	100.0				
Adjuvant treatment						
Yes	12 (34.3)	91.7	**0.015**	445.864		0.947
No	23 (65.7)	100.0				
Site						
Right	21 (60.0)	95.2	0.834			
Left	14 (40.0)	100.0				
Tumor size						
<10 cm	21 (60.0)	100.0	0.886			
≥10 cm	14 (40.0)	91.7				
Histology						
Granulosa cell	23 (65.7)	100.0	0.530			
Sertoli-leydig	8 (22.9)	87.5				
Sex-cord stromal tm	4 (11.4)	100.0				
Histology						
Granulosa cell	23 (65.7)	100.0	0.305			
Others	12 (34.3)	91.7				
FIGO stage						
IA	21 (60.0)	100.0				
IC1	12 (34.3)	91.7	0.938			
Locoregional	2 (5.7)	100.0				
Post-treatment pregnancy						
Yes	9 (25.7)	100.0	0.256	320.274		0.951
No	26 (74.3)	96.2				

HR: Hazard ratio, OS: Overall survival, CI: Confidence interval, USO: Unilateral salpingooophorectomy

Discussion

Granulosa cell tumors were the most common histological subtype in our cohort (65.7%). Most of the patients were diagnosed at stage I (94.3%). Five-year DFS and OS rates were 85.7% and 97.1%, respectively. In univariate analysis, the need for adjuvant treatment was the only prognostic factor for OS, although it lost significance in multivariate analysis. Regarding reproductive outcomes after completion of treatment, nine patients conceived with 12 pregnancies. Resulting in six livebirths (50.0%).

The 5-year DFS of 85.7% compares favorably with other studies, such as Bergamini et al. (8), who reported 75% DFS in FSS subgroups. The similarity of DFS in patients undergoing radical surgery (87.0%) suggests that fertility-preserving approaches do not significantly compromise oncologic outcomes (8). The 5-year OS rate was 97.1% and was consistent with other series, including the MITO-9 study, which reported 100.0% survival for both radical surgery and FSS subgroups (8).

Interestingly, patients who received adjuvant chemotherapy exhibited shorter OS in univariate analysis but no prognostic factors emerged in multivariate analysis, likely due to the limited sample size. The decision to use chemotherapy in patients with SCSTs is based on both tumor histology and stage, and worse survival would be related to worse tumor behavior and the limited effect of chemotherapy administration for SCSTs. It has been reported that DFS was similar in stage IC patients who received or did not receive chemotherapy (9).

Six patients (17.1%) underwent cystectomy in this study, and 5-year DFS was 100.0% for this group. In a recent review,

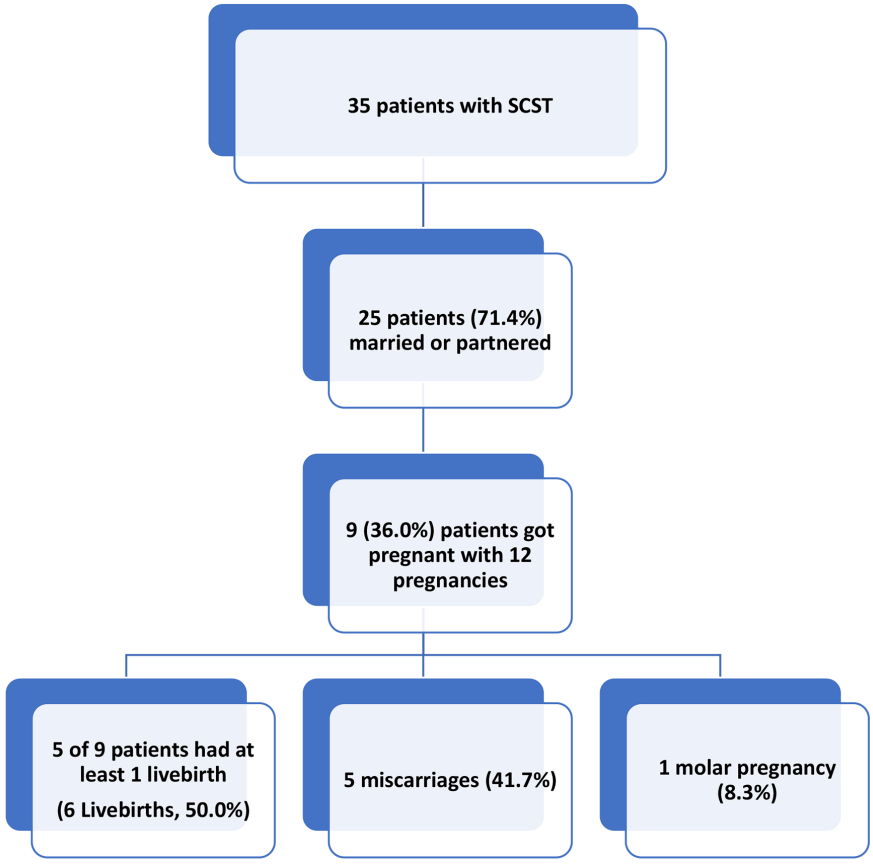

Table 4. Flowchart of obstetric outcomes
SCST: Sex-cord stromal tumor

it was reported that cystectomy was related to markedly worse recurrence outcomes (10). The MITO-9 study also reported worse DFS outcomes in patients who underwent cystectomy (8). The absence of upstaging in our cohort may relate to careful surgical excision.

Menstrual function remained normal after treatment in all cases. While the pregnancy rate was 36.0%, the live birth rate was 50.0%, considerably lower than a recent report of 95.0% (11). A recent review also reported a live birth rate ranging from 65% to 95% (10). We examined factors that could influence pregnancy, such as age >35 years and chemotherapy, but found no significant effects. Furthermore, a Gynecologic Oncology Study Group study reported 87.3% regular menstrual cycles after platinum-based chemotherapy (11). Although it is known that platinum-based regimens may be cytotoxic to the gonads, there appears to be little effect on menstrual regularity (12). Our relatively lower live birth rate suggests the need for further study, possibly related to treatment details or individual patient characteristics. The study's strengths include long median follow-up (almost 12 years), and comprehensive obstetric and oncological data (13). An expert histopathologist's review adds to the reliability of our findings.

Study limitations

Limitations include the retrospective design, which restricts data on subsequent pregnancies and long-term outcomes, and the single-center setting, which limited both sample size and generalizability.

Conclusion

In conclusion, ovarian SCSTs generally have a favorable prognosis, mostly diagnosed at early stages. FSS appears to be a safe and appropriate option, with excellent oncological and obstetric outcomes in selected patients. Larger, prospective, multicentric studies are required to establish definitive guidelines for fertility-preserving management in this patient population.

Ethic

Ethics Committee Approval: *This study was approved by the Başkent University Medical and Health Sciences Research Board (approval number: KA25/336, date: 18.09.2025).*

Informed Consent: *Retrospective study.*

Footnotes

Author Contributions: *Surgical and Medical Practices: A.A., E.K., H.A., N.H., A.H., Concept: M.T., N.Ö., G.Ö., Design: M.T., E.K., Data Collection or Processing: M.T., H.A., G.Ö., Analysis or Interpretation: M.T., N.Ö., G.Ö., Literature Search: M.T., A.A., H.A., Writing: M.T., H.A.*

Conflict of Interest: *No conflict of interest is declared by the authors.*

Financial Disclosure: *The authors declared that this study received no financial support.*

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