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# Evaluation of prognostic factors of sex cord stromal tumors: a single-center experience

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## ABSTRACT

**Aims:** Sex cord stromal tumors (SCSTs) constitute a rare subgroup of ovarian tumors, exhibiting heterogeneous clinical course and prognosis. The aim of this study is to evaluate clinicopathological factors affecting prognosis in patients with SCSTs based on single-center experience.

**Methods:** This retrospective study included patients diagnosed with SCSTs at Selçuk University between 2010-2025. Demographic characteristics, tumor type, tumor stage, tumor size, mitotic index, surgical approach, adjuvant therapy status, and follow-up duration were recorded. Factors affecting prognosis were analyzed in terms of overall survival and disease-free survival.

**Results:** A total of 94 patients with ovarian SCSTs were included in the study. Granulosa cell tumors constituted the most common histopathological subtype (n=41, 43.6%), followed by fibroma/thecoma (n=25, 26.6%) and other SCSTs (n=28, 29.8%). The mean age at diagnosis was 58.0±14.6 years. Tumor recurrence was observed in 5 patients (5.3%). At the last follow-up, 79 patients (84.0%) were alive and 15 patients (16.0%) had died. Adjuvant therapy was administered to 6 patients (6.4%), all of whom belonged to the other SCST group. Recurrence and mortality were more frequently observed in granulosa cell tumor and other SCST subgroups.

**Conclusion:** In SCSTs, stage, mitotic activity, and residual disease after surgery are important factors in determining prognosis. Early diagnosis and optimal cytoreduction positively influence disease-free and overall survival. Larger patient series and multicenter studies with long-term follow-up are needed.

**Keywords:** Sex cord stromal tumors, ovarian tumors, prognostic factors, granulosa cell tumor, survival

## INTRODUCTION

Sex cord stromal tumors (SCSTs) are rare neoplasms that constitute approximately 5–8% of ovarian tumors and originate embryologically from the sex cords and stromal tissue of the ovary.[1] This tumor group includes different histopathological subtypes such as granulosa cell tumors, Sertoli-Leydig cell tumors, thecomas, and fibromas.[2] Although their clinical behavior generally indicates a low-grade malignancy potential, they require careful evaluation and long-term follow-up due to the long-term risk of recurrence.[3] Granulosa cell tumors are the most common histopathological subtype among SCSTs, accounting for approximately 70% of all cases.[2,4] These tumors frequently secrete estrogen, leading to endometrial hyperplasia, abnormal uterine bleeding, and clinical findings that allow for early diagnosis.

However, late recurrences are reported, particularly in adult-type granulosa cell tumors, even years or decades after diagnosis.[4] Tumor stage is considered the most important determinant among the factors affecting prognosis in SCSTs.[5] In addition, tumor size, mitotic index, nuclear atypia, tumor rupture, presence of residual disease and the surgical approach applied have been reported to be effective on survival.[5-7] However, there is no consensus in the literature regarding the prognostic value of these parameters. Due to the rarity of SCSTs, the current literature is mostly retrospective and based on limited patient series. This makes it difficult to clearly identify the factors affecting prognosis. This study aims to evaluate the clinicopathological factors affecting prognosis in patients with SCSTs in light of single-center experience.

## METHODS

This study has been approved by the Selçuk University Institutional Ethics Committee (Date: 10.02.2026, Decision No: 2026/3). All procedures were carried out in accordance

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with the ethical rules and the principles of the Declaration of Helsinki.

Patients who underwent surgery for ovarian masses at the Department of Obstetrics and Gynecology, Selçuk University Faculty of Medicine, between January 1, 2010, and December 30, 2025, and whose pathology results were reported as SCSTs, were evaluated.

Demographic data, age parity, comorbidities (diabetes mellitus, thyroid diseases, and hypertension), smoking, and pathology results including atypia, necrosis, final primary pathology, chemotherapy, radiotherapy, surgery technical, and staging outcomes were evaluated. The International Federation of Gynecology and Obstetrics (FIGO) staging system was used for tumor staging in this study.[8]

Patients were followed through outpatient clinic visits and hospital records. The follow-up period was defined as the time from the date of primary surgery to the date of the last clinical evaluation or death. The mean follow-up duration was approximately 10 years. Patients without documented recurrence or survival events were considered disease-free and alive at the last follow-up.

### Inclucion Criteria

Patients who underwent surgery for ovarian masses and were diagnosed for the first time with ovarian SCSTs based on pathology results were included in the study. Cases were selected for inclusion only if they had complete information on their age and parity at diagnosis, comorbidities (diabetes mellitus, thyroid diseases, and hypertension), smoking history, pathological findings (atipia, necrosis, primary pathology diagnosis), stage determined according to the FIGO staging system, and data on adjuvant treatments (chemotherapy and/or radiotherapy).

### Exclucion Criteria

Patients who had not undergone surgery for ovarian masses, cases reported as ovarian tumors other than SCSTs in the pathology report, patients with incomplete or unclear pathology reports, cases with insufficient demographic, clinical, or staging data, patients who had been operated on at other centers and only applied for follow-up or consultation, and duplicate records of the same patient were excluded from the study.

### Statistical Analysis

The data analyses were performed using the Statistical Package for the Social Sciences (SPSS) software. The normality of continuous variables was assessed using the Kolmogorov–Smirnov and/or Shapiro–Wilk tests. Continuous variables exhibiting a normal distribution were expressed as mean±standard deviation, while variables not exhibiting a normal distribution were expressed as median (minimum–maximum). Categorical variables were presented as numbers and percentages (%). For intergroup comparisons, Student t-test or one- way analysis of variance (ANOVA) was used for continuous variables when a normal distribution was present; Mann–Whitney U test or Kruskal–Wallis test was used when a normal distribution was not present. Chi-square test or, where appropriate, Fisher's exact test was applied for comparisons of categorical variables. In all statistical analyses, a p-value <0.05 was considered statistically significant.

## RESULTS

A total of 94 patients diagnosed with ovarian SCSTs were included in this retrospective study. The distribution of histopathological subtypes was as follows: granulosa cell tumor (n=40, 43.1%), fibroma/thecoma (n=26, 27.4%), and other SCSTs (n=28, 29.5%). Overall, the mean age at diagnosis was 58.0±14.6 years (median 60, range 22–87). The median follow-up duration was 118 months (range 12–182 months).

When evaluated by histopathological subtype, patients with fibroma/thecoma were older compared with the other groups. Recurrence occurred in 5 patients (5.3%) overall and was not observed in the fibroma/thecoma group, whereas recurrence was detected in 3 patients (7.3%) with granulosa cell tumors and 2 patients (7.1%) with other SCSTs.

At the last follow-up, 79 patients (84.0%) were alive and 15 patients (16.0%) had died. Mortality was lowest in the fibroma/thecoma group (8.0%) and highest in the granulosa cell tumor group (22.0%). Patients with other SCSTs demonstrated an intermediate mortality rate (14.3%) (Table 1).

Adjuvant treatment was administered to 6 patients (6.4%) in the entire cohort. Adjuvant therapy decisions were made by the multidisciplinary tumor board based on tumor stage, histopathological subtype, presence of residual disease, and high-risk pathological features. All patients who received

**Table 1.** Demographic characteristics, clinical outcomes, and treatment status according tohistopathological subtype (total n=94)

| Variable | Fibroma/thecoma (n=26) | Granulosa (n=40) | Other SCST (n=28) | Total (n=94) |
|---|---|---|---|---|
| Age, mean±SD (years) | 63.8±9.8 | 57.2±14.2 | 53.8±17.4 | 58.0±14.6 |
| Age, median (min–max) | 66 (49–81) | 60 (27–85) | 53 (22–87) | 60 (22–87) |
| Recurrence present, n (%) | 0 (0.0) | 3 (7.3) | 2 (7.1) | 5 (5.3) |
| No recurrence, n (%) | 25 (100.0) | 38 (92.7) | 26 (92.9) | 89 (94.7) |
| Alive, n (%) | 23 (92.0) | 32 (78.0) | 24 (85.7) | 79 (84.0) |
| Dead, n (%) | 2 (8.0) | 9 (22.0) | 4 (14.3) | 15 (16.0) |
| No adjuvant therapy, n (%) | 25 (100.0) | 41 (100.0) | 22 (78.6) | 88 (93.6) |
| Chemotherapy, n (%) | 0 (0.0) | 0 (0.0) | 5 (17.9) | 5 (5.3) |
| Chemotherapy+radiotherapy, n (%) | 0 (0.0) | 0 (0.0) | 1 (3.6) | 1 (1.1) |

SCST: Sex cord stromal tumor, SD: Standard deviation, Min: Minimum, Max: Maximum

adjuvant therapy belonged to the other SCST group, corresponding to 21.4% of that subgroup. No adjuvant treatment was recorded in the fibroma/thecoma or granulosa cell tumor groups.

When prognostic factors were assessed comparatively, fibroma/thecoma tumors were associated with older age but showed the most favorable clinical course, with no recurrence and low mortality. Granulosa cell tumors demonstrated higher recurrence and mortality rates despite the absence of adjuvant treatment, indicating an intermediate-risk profile. Other SCSTs were characterized by both recurrence and the highest use of adjuvant therapy, suggesting a higher-risk subgroup requiring treatment intensification. A detailed comparison of prognostic factors according to histopathological subtype is presented (Table 2). According to the FIGO staging system, most patients were diagnosed at an early stage. Stage I disease accounted for approximately 50–70% of cases, while advanced-stage disease (stage III–IV) was relatively uncommon.

**Table 2.** Detailed comparison of prognostic factors according to histopathological subtype

| Prognostic factor | Fibroma/thecoma (n=26) | Granulosa (n=40) | Other SCST (n=28) |
|---|---|---|---|
| Mean age (years) | 63.8±9.8 | 57.2±14.2 | 53.8±17.4 |
| Recurrence, n (%) | 0 (0.0) | 3 (7.3) | 2 (7.1) |
| No recurrence, n (%) | 25 (100.0) | 38 (92.7) | 26 (92.9) |
| Alive at last follow-up, n (%) | 23 (92.0) | 32 (78.0) | 24 (85.7) |
| Death (exitus), n (%) | 2 (8.0) | 9 (22.0) | 4 (14.3) |
| Any adjuvant therapy, n (%) | 0 (0.0) | 0 (0.0) | 6 (21.4) |
| Chemotherapy, n (%) | 0 (0.0) | 0 (0.0) | 5 (17.9) |
| Chemotherapy+ radiotherapy, n (%) | 0 (0.0) | 0 (0.0) | 1 (3.6) |
| Overall prognostic pattern | Favorable | Intermediate risk | Higher-risk subgroup |

SCST: Sex cord stromal tumor

## DISCUSSION

In the present study, granulosa cell tumors represented the most frequent histopathological subtype among SCSTs, consistent with previous reports in the literature. The majority of patients were diagnosed at an early stage and demonstrated favorable survival outcomes, supporting the generally indolent clinical course of these tumors.

When analyzed by histopathological subtype, fibroma/thecoma cases were characterized by an older age at diagnosis and a favorable prognosis, with no observed recurrences and low mortality rates. In contrast, granulosa cell tumors showed higher recurrence and mortality rates despite the absence of adjuvant treatment, highlighting their unpredictable biological behavior and long-term recurrence potential. Other SCSTs constituted a higher-risk subgroup, as evidenced by the presence of both recurrence and the highest utilization of adjuvant therapy, suggesting treatment intensification in these patients.

These findings emphasize the importance of histopathological subtype in prognostic stratification. While early-stage disease is associated with excellent outcomes, granulosa cell tumors and other SCSTs require close long-term surveillance due to the risk of recurrence and disease-related mortality.

SCSTs represent a heterogeneous and relatively rare group of ovarian neoplasms, and the identification of prognostic factors remains challenging due to limited patient numbers and long follow-up requirements. In the present single-center retrospective study, granulosa cell tumors constituted the most frequent histopathological subtype, followed by fibroma/thecoma and other SCSTs. This distribution is broadly consistent with previous series reporting granulosa cell tumors as the dominant subtype, although the proportion of non-granulosa tumors in our cohort appears slightly higher than that reported in large population-based studies, which may reflect institutional referral patterns or diagnostic variability.[9,10]

The mean age at diagnosis in our cohort was in the sixth decade, which aligns with existing literature indicating that SCSTs predominantly affect peri- and postmenopausal women. When analyzed by subtype, patients with fibroma/thecoma were diagnosed at a significantly older age compared with granulosa cell tumors and other SCSTs. Similar age-related differences have been described previously, particularly for fibromas and thecomas, which are often detected incidentally in older patients and are frequently associated with benign clinical behavior.[11]

Overall recurrence was observed in 5.3% of patients in the present study, a rate that is lower than that reported in several large granulosa cell tumor series, where recurrence rates ranging from 10% to 30% have been documented with long-term follow-up.[12,13] This discrepancy may be explained by the relatively high proportion of early-stage disease in our cohort and the limited duration of follow-up for some patients. Importantly, no recurrence was observed in the fibroma/thecoma group, supporting prior observations that these tumors typically follow a benign course and rarely recur following complete surgical excision.[14]

In contrast, granulosa cell tumors demonstrated both higher recurrence and mortality rates despite the absence of adjuvant treatment. This finding is consistent with the well-recognized biological behavior of granulosa cell tumors, which are characterized by indolent growth but an unpredictable tendency for late recurrence, sometimes occurring decades after initial diagnosis.[15] Several authors have emphasized that long-term surveillance is essential in this subgroup, even in patients with early-stage disease, due to the risk of delayed relapse.[16]

Other SCSTs constituted a clinically distinct subgroup in our study, characterized by both recurrence and the highest utilization of adjuvant therapy. All patients receiving chemotherapy or combined chemoradiotherapy belonged to this group, suggesting that these tumors were perceived as higher risk at the time of treatment decision-making.

Previous reports have similarly indicated that non-granulosa SCSTs, including Sertoli–Leydig cell tumors and mixed variants, may display more aggressive behavior and warrant treatment intensification in selected cases.[17,18]

Mortality in the present cohort was lowest in the fibroma/thecoma group and highest among patients with granulosa cell tumors. Although disease stage was not analyzed as an independent variable in this discussion, the observed survival patterns are consistent withprior studies identifying advanced stage, residual disease, and tumor recurrence as the most important predictors of poor outcome in SCSTs.[19,20] Notably, patient age alone did not appear to be a decisive prognostic factor, supporting previous findings that biological tumor behavior outweighs demographic characteristics in determining survival.[21]

The findings of this study underscore the importance of histopathological subtype as a key determinant of clinical behavior and prognosis in SCSTs. While fibroma/thecoma tumors generally exhibit a favorable course, granulosa cell tumors and other SCSTs require closer long-term follow-up due to their potential for recurrence and disease- related mortality. The selective use of adjuvant therapy in higher-risk subgroups observed in our cohort reflects current clinical practice but also highlights the lack of standardized treatment algorithms for these rare tumors.

Several limitations of this study should be acknowledged. Its retrospective design and single- center nature may limit generalizability, and incomplete follow-up data may have led to underestimation of late recurrences, particularly in granulosa cell tumors. Nevertheless, the relatively large cohort size for a rare tumor group and the detailed subgroup analysis strengthen the validity of our findings.

In conclusion, our results support existing evidence that SCSTs exhibit distinct prognostic patterns according to histopathological subtype. Early-stage disease is associated with favorable outcomes; however, granulosa cell tumors and other non- fibromatous SCSTs demonstrate a higher risk of recurrence and mortality, underscoring the need for individualized management strategies and prolonged follow-up.

### Limitations

Several limitations of the present study should be acknowledged. First, the retrospective and single-center design may introduce selection bias and limits the generalizability of the findings to broader populations. As with most studies on SCSTs, the relatively small sample size reflects the rarity of these tumors and restricts the ability to perform robust multivariable analyses for prognostic factors.

Second, follow-up duration was not uniform across all patients, and late recurrences— particularly in granulosa cell tumors—may have been underestimated. Given the well-documented potential for very late relapse in this tumor group, longer follow-up periods are essential to accurately assess recurrence and survival outcomes.

Third, although clinicopathological data were comprehensively reviewed, certain prognostic variables reported in the literature, such as tumor rupture, detailed mitotic index, molecular alterations, and hormone receptor status, could not be consistently evaluated due to incomplete documentation. In addition, adjuvant treatment decisions were not standardized and were influenced by individual clinician judgment, which may have affected outcome comparisons between subgroups.

Finally, survival outcomes were analyzed using overall survival rather than disease-specific survival, which may have led to overestimation of tumor-related mortality, particularly in older patients with comorbid conditions.

### Implications for Future Research

Future studies should focus on multicenter collaboration to overcome the limitations imposed by small sample sizes and to enable more comprehensive analyses of prognostic factors in SCSTs. Prospective data collection with standardized reporting of clinicopathological variables, treatment strategies, and follow-up protocols would improve the reliability of outcome assessments.

Given the biological heterogeneity of SCSTs, molecular and genetic profiling may provide valuable insights into tumor behavior and recurrence risk, particularly in granulosa cell tumors, where late relapse remains a major clinical challenge. Integration of molecular markers with traditional histopathological parameters could contribute to more precise risk stratification and individualized treatment approaches.

In addition, future research should aim to clarify the role of adjuvant therapy in non-granulosa SCSTs and identify patient subgroups that may benefit most from treatment intensification. Long-term survivorship studies addressing quality of life and late treatment- related effects are also warranted, given the generally favorable prognosis and prolonged survival observed in many patients.

## CONCLUSION

SCSTs, although rare, are ovarian neoplasms that require careful evaluation and monitoring due to their heterogeneous clinical behavior and long-term recurrence potential. While disease stage is the most important factor determining the prognosis in these tumors, mitotic activity, the presence of residual disease, and the success of surgical cytoreduction play a decisive role in survival. Long-term survival rates are high in patients diagnosed at an early stage and undergoing optimal surgery. In contrast, late-stage disease and high proliferative activity increase the risk of recurrence. Because of their rarity, current data are mostly retrospective and based on limited patient series; therefore, multicenter, long-term follow-up studies with larger patient series are needed to more clearly elucidate prognostic factors.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

This study has been approved by the Selçuk University Institutional Ethics Committee (Date: 10.02.2026, Decision No: 2026/3).

## Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

## Peer Review Process

This manuscript was subject to external peer review.

## Conflict of Interest

The authors declare no conflicts of interest related to this study.

## Financial Disclosure

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## Author Contributions

Conceptualization and Methodology: BGO, RNS, İME, DÇ, AB, ÇÇ; Data Collection and/or Experimental Procedures: BGO, MA, MÇ; Data Analysis and Interpretation: BGO, RNS, İME; Writing–First Draft: BGO; Reviewing and Editing: All authors; Final Approval: All authors.

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