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Reproductive and oncologic outcomes in women with non-epithelial ovarian cancer: Single center experience over 25 years

Non-epitelyal over kanserli kadınlarda reprodüktif ve onkolojik sonuçlar: 25 yıllık tek merkez deneyimi

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Abstract

Objective: This study aimed to present our single-center clinical experience regarding tumor clinicopathologic features, treatment modalities, and reproductive and oncologic outcomes in patients with non-epithelial ovarian cancer (NEOC) over 25 years.

Materials and Methods: A total of 100 patients with clinicopathological diagnosis of NEOC who were treated at our tertiary care center between 1996 and 2022 were included in this retrospective cohort analysis study. Data on demographic, clinical and obstetric characteristics of patients at the time of initial diagnosis as well as tumor clinicopathologic features, treatment modalities, and oncological and reproductive outcomes were recorded.

Results: NEOCs involved germ cell tumors (GCTs) in 46 (46%) patients and sex cordstromal tumors (SCSTs) in 54 (54%) patients. Thirty patients with GCTs and thirty-four patients with SCSTs possessed histological subtypes with malignant features. Most patients with GCTs (37%) and SCSTs (55.6%) had FIGO Stage 1 disease at the time of initial diagnosis. Overall, 76.6% of patients in the GCT group (n=23) underwent fertility-sparing surgery (FSS), while 76.5% of the patients in the SCST group (n=26) were treated with non-fertility-sparing surgical procedures. All patients who underwent FSS and had a recurrence in their follow-up (n=4) was stage 3 patients. Seven out of 10 patients (2 patients at stage 3 and 5 patients at stage 1) who desired pregnancy delivered between 38 and 40 gestational weeks without any congenital anomaly. The prognosis was excellent in both groups, with 5-year overall survival (OS) rates of 93.5% in GCTs and 96.3% in SCST groups. The 5-year disease-free survival was 89.1% in GCTs and 94.4% in SCSTs. FSS was not associated with worse oncologic outcomes.

Conclusion: NEOCs usually have a good prognosis because they are detected at an early stage. FSS may be indicated for women of reproductive age with early-stage NEOCs.

Keywords: Disease-free survival, fertility, non-epithelial ovarian tumor, prognosis

Öz

Amaç: Bu çalışma, non-epitelyal over kanserli (NEOC) hastalarda, tümörün klinikopatolojik özellikleri, tedavi modaliteleri ve reprodüktif ve onkolojik sonuçlarına ilişkin merkezimizin 25 yıllık klinik deneyinimi sunmayı amaçlamıştır.

Gereç ve Yöntemler: Bu retrospektif kohort analizi çalışmasına, non-epitelyal over tümörü klinikopatolojik tanısı ile 1996 ile 2022 yılları arasında üçüncü basamak bir merkezde tedavi edilen 100 hasta dahil edildi. Hastaların ilk tanı anındaki demografik, klinik ve obstetric özellikleri ile tümörün klinikopatolojik özellikleri, tedavi yöntemleri, onkolojik ve reprodüktif sonuçları kaydedildi.

Bulgular: Non-epitelyal over tümörü hastalarının 46'sında germ hücreli tümör (GHT) ve 54'ünde ise sees kord-stromal tümörü (SKST) mevcuttu. GHT'lerde otus ve SKST'lerde otuz dört hasta, malign özelliklere sahip histolojik alt tipler sahipti. GHT (%37) ve SCST (%55,6) hastalarının çoğu ilk tanı anında FIGO ever 1 hastalığa sahipti. GHT hastalarının %76,6'sına (n=23) fertility koruyucu tümör rezeksiyonu (FSS) ve SKST'li hastaların yaklaşık %76,4'üne (n=26) fertility koruyucu olmayan cerrahi işlemler uygulandı. FSS uygulanan ve takiplerinde nüks gelişen hastaların tamamı (n=4) ever 3'teki hastalardı. Gebelik elde etmek isteyen 10 hastadan 7'si (2 hasta ever 3 ve 5 hasta ever 1) 38-40 hafta arasında doğum yaptı, konjenital anomali saptanmadı. Her iki grupta da

PRECIS: We aimed to report a single-center experience in non-epithelial malignant ovarian tumors by presenting different clinical and pathological characteristics, management, and reproductive and oncologic outcomes.

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prognoz mükemmel olup, 5 yıllık genel sağkalım GHT'de %93,5 ve SKST'de %96,3 idi. Beş yıllık hastalıksız sağkalım ise GHT'lerde %89,1 ve SKST'lerde %94,4 idi. FSS daha kötü onkolojik sonuçlarla ilişkili değildi.

Sonuç: NEOC, genellikle erken evrede tespit edildikleri için iyi bir prognoza sahiptir. Erken evre non-epitelyal over tümörleri plan fertil yaştaki kadınlarda FSS yapılabilir.

Anahtar Kelimeler: Hastalıksız sağkalım, fertilite, non-epitelyal over tümörü, prognoz

Introduction

Ovarian cancer is considered the gynecologic cancer with the highest associated mortality because most patients are already at an advanced disease stage at diagnosis[1]. Epithelial ovarian cancers are the most common type, while non-epithelial primary tumors are very rare entities accounting for 10% of all ovarian malignancies (0.25/100.000)[2,3]. Non-epithelial ovarian cancers (NEOCs) include germ cell tumors (GCTs), sex cord-stromal tumors (SCSTs), sarcomas, and small cell carcinoma of hypercalcemic type[4]. Malignant GCTs represent 5% of all ovarian cancers and SCST account for approximately 3-5% of ovarian malignancies with endocrine manifestations[5]. Both GCTs and SCSTs include a wide variety of sub-histological types along with similarities in their presentation, evaluation, management, and prognosis[6]. For GCTs, dysgerminomas and immature teratomas are the most common histological subtypes (70%), while the rarer subtypes include yolk sac tumor, embryonal carcinomas, non-gestational choriocarcinomas, and mixed germ cell tumors[4]. For SCSTs, subtypes include granulosa cell tumors (juvenile and adult type), Sertoli cell tumors and Sertoli Leydig cell tumors, fibromas, and thecomas[4]. Although each histological subtype has its own characteristics, they may resemble each other in terms of initial clinical presentation, radiological findings, and tumor markers. While SCSTs are a heterogeneous group presenting over various ages, GCTs are primarily diagnosed in adolescents and younger women[5]. Given that these tumors occur mostly in young women, maintenance of fertility is an important consideration and each patient should be evaluated individually.

NEOCs have a better prognosis than epithelial ovarian tumors because approximately 60-70% of both SCSTs and GCTs are diagnosed at a localized stage[2]. Surgery for young patients with GCTs and early-stage SCSTs should consider a fertility-sparing approach (unilateral salpingo-oophorectomy with preservation of the contralateral ovary and the uterus) without compromising the oncological management[5]. GCTs are very sensitive to platinum-based regimens, which makes patients with GCTs to be considered as proper candidates for fertility-sparing surgery (FSS) even at the advanced stage. However, the value of adjuvant chemotherapy in the setting of SCSTs remains inconclusive due to the lack of randomized trials and definitive prognostic factors[2]. Unilateral salpingo-oophorectomy can be performed in patients with stage 1 disease-deserving of fertility. Hysterectomy and bilateral salpingo-oophorectomy should be performed in postmenopausal women and in patients with advanced-stage disease[5].

Little is known about the management of women with NEOCs, possibly due to the infrequent presentation of these cancers. Some proposed treatment policies are not widely accepted[5]. Treatment should be performed depending on the patients age and histopathological type. For Stage Ia pure dysgerminoma, surgery is recommended because of the relatively low recurrence rate in these patients (15-25%)[7]. Moreover, some studies revealed that close surveillance after FSS can be used in the management of all grades of immature teratoma and all stage I dysgerminomas with reserving chemotherapy only for the relapsed cases[7,8]. All patients with stage I yolk sac tumors are treated with adjuvant treatment after surgery[9], while publications suggest close and active surveillance after the surgery[8]. The most commonly used regimen in patients with NEOCs is the bleomycin/etoposide/cisplatin (BEP) combination[10]. Stage Ia granulosa cell tumors do not require adjuvant therapy[5]. Adjuvant therapy has been administered to stage 1c patients in some studies, but its benefit remains controversial[11]. Debulking surgery followed by adjuvant chemotherapy is the most effective treatment for advanced-stage SCSTs[5].

This study aimed to evaluate clinical characteristics, tumor clinicopathological features, treatment modalities, and oncological and reproductive outcomes in NEOC patients according to histological subtypes.

Materials and Methods

A total of 100 patients with clinicopathological diagnosis of NEOC who were treated at our tertiary care center (Department of Gynecological Oncology, Akdeniz University Faculty of Medicine, Antalya, Turkey) between 1996 and 2022 were included in this retrospective cohort analysis study.

The study was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by the institutional ethics committee (Akdeniz University Clinical Research Ethics Committee - KAEK-657; date: 09.11.2022). Informed consent was obtained from each subject or their first-degree relatives (for the deceased ones).

Demographic, clinical and obstetric characteristics of patients at the time of initial diagnosis and tumor clinicopathologic features were retrieved from paper- and electronic medical records. Data on age, body mass index (BMI), clinical manifestations at the time of diagnosis, reproductive history, presence of pregnancy at the time of diagnosis, menopausal status, tumor characteristics (histopathological subtype and stage according to the International Federation of Gynecology and Obstetrics (FIGO 2014) staging classification[12], tumor size

and histological grade, serum tumor markers when available, treatment characteristics regarding the primary treatment modality, type of surgical interventions, chemotherapy (regimen, setting and the number of cycles), treatment protocols in case of recurrence, oncological outcome recurrence status, overall survival (OS), disease-free survival (DFS), reproductive outcome, congenital anomaly of offspring, and secondary malignancy were recorded. Tumors were classified according to the World Health Organization (WHO 2014) classification. Information that could not be accessed through medical reports (i.e., obstetric results and menstrual pattern) was obtained by a phone call. Patients with sarcoma and small cell carcinoma of hypercalcemic type, those with insufficient data or lack of attendance to follow-up, and those with ovarian metastasis originating from non-gynecologic primary sites were excluded from the study.

Follow-up visits for recurrence assessment were performed at 3-month intervals and 6-month intervals for the first 2 years and following years. Data on symptoms, tumor markers, and pelvic examination findings were recorded at each visit. Imaging modalities used in relapse detection were chest X-ray, pelvic ultrasound, and computed tomography (CT) or positron emission tomography CT (PET/CT). OS was defined as the time from initial diagnosis to death. DFS was defined as the interval between the date of remission and the date of the first recurrence detected. FSS was defined as the preservation of the uterus and at least part of one ovary.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows version 23.0 (IBM Corp., Armonk, NY). For descriptive statistics, the mean, standard deviation, median, minimum-maximum values, and frequencies were used, depending on the normality of the data. Data were expressed as mean ± standard deviation (SD), median and n (%) where appropriate. Survival analysis was performed via Kaplan-Meier analysis.

Results

Overall, GCTs and SCSTs were noted in 46 (46%) and 54 (54%) patients with NEOC, respectively. Baseline demographic, clinical, and obstetric characteristics and tumor clinicopathologic features of patients are shown in Tables 1 and 2.

The mean age at diagnosis was 31.7 years (range, 11 to 63 years) in patients with GCT, while it was 52.8 years (range, 13 to 77 years) in those with SCST. Thirty patients in the GCT group and 34 patients in the SCST group possessed histological subtypes with malignant features. The most common subtypes of GCTs were mature teratoma (32.6%) and dysgerminoma (23.9%). Among SCSTs, the most common subtype was adult granulosa cell tumor (53.7%), followed by fibroma (27.8%). Acute abdominal pain was the key clinical presentation in 65.2% of patients with GCTs and in 40.7% of patients with SCSTs. The majority of patients with GCTs were premenopausal (78.3%), while the majority of patients with SCSTs were postmenopausal (66.7%). Most patients with GCTs (37%) and SCSTs (55.6%) had FIGO Stage 1 disease at the time of initial diagnosis. None of the patients presented with FIGO Stage 4 disease. The mean value of Ca-125 was 95.6 IU/mL in GCT patients (n=37) and 57.6 IU/mL in SCST patients (n=43).

Treatment modalities and oncological outcome in patients with malignant NEOCs are demonstrated in Table 3. Overall, 76.6% of patients in the GCT group (n=23) underwent fertility-sparing tumor resection (FSS), while 76.5% of the patients in the SCST group (n=26) were treated with non-fertility-sparing

Table 1. Baseline demographic, clinical and obstetric characteristics and tumor clinicopathologic features in patients with germ cell tumor (n=46)

	Germ cell tumors (n=46)
Age (years), mean ± SD	31.7±14.6
BMI (kg/m²), mean ± SD	24.2±5.9
Gravidity/Parity, mean	1.1/0.9
Menopausal status, n (%)	
Premenopausal	36 (78.3)
Postmenopausal	10 (21.7)
Initial complaint (abdominal pain), n (%)	30 (65.2)
Tumor type, n (%)	
Malignant	30 (65.3)
Benign	16 (34.7)
Histology subtype, n (%)	
Dysgerminoma	11 (23.9)
Immature teratoma	6 (13)
Yolk sac tumor	2 (4.3)
Mixed GTCs	3 (6.5)
Mature teratoma	15 (32.6)
Somatic-type tumors associated with teratoma*	4 (8.7)
Monodermal, teratoma**	3 (6.5)
Gonadoblastoma	2 (4.3)
FIGO stage, n (%)	
I	17 (37)
II	2 (4.4)
III	11 (23.9)
IV	0 (0)

*Somatic-type tumors associated with teratoma include three cases of squamous-cell carcinoma arising from mature cystic teratoma, one case of carcinoid tumor. **Monodermal teratomas included two cases of PNET and one cases of benign struma ovary, SD: Standard deviation, BMI: Body mass index, GTC: Germ cell tumor

Table 2. Baseline demographic, clinical and obstetric characteristics and tumor clinicopathologic features in patients with sex cord stromal tumor (n=54)

	Sex cord-stromal tumors (n=54)
Age (years), mean ± SD	52.8±13.9
BMI (kg/m²), mean ± SD	27.2±6.2
Gravidity/Parity, mean	3.9/2.7
Menopausal status, n (%)	
Premenopausal	18 (33.3)
Postmenopausal	36 (66.7)
Initial complaint (abdominal pain), n (%)	22 (40.7)
Tumor type, n (%)	
Malignant	34 (62.9)
Benign	20 (37.1)
Histology subtype, n (%)	
Adult granulosa cell tumor	29 (53.7)
Juvenile granulosa cell tumor	1 (1.8)
Sertoli-Leydig cell tumors	3 (5.6)
Sex cord tumor with annular tubules (SCTAT)	1 (1.9)
Fibroma	15 (27.8)
Thecoma	5 (9.3)
FIGO stage	
I	30 (55.6)
II	2 (3.7)
III	2 (3.7)
IV	0 (0)

SD: Standard deviation, BMI: Body mass index

surgical procedures. FSS was applied in 29 (45.3%) patients overall, including unilateral salpingo-ovariectomy in 25 (39%) patients, cystectomy in 2 (3.1%) patients, and bilateral salpingo-ovariectomy in 2 (3.1%) patients. Adjuvant therapy was indicated in 8 patients with SCST and 24 patients with GCT. Most patients in the GCT group received bleomycin, etoposide, and cisplatin (BEP) combination chemotherapy for median 2.7 cycle. Other rarely administered chemotherapeutics were paclitaxel, carboplatin, vincristine, doxorubicin and cyclophosphamide, followed by ifosfamide and etoposide, 5-FU and prednisolone.

The median duration of follow-up was 90 months (range, 3 to 324 months) and 83.5 months (range, 8 to 252 months) for malignant GCTs and SCSTs, respectively. Overall, 11 of 64 (17.1%) patients with malignant NEOC developed recurrence, including 6 cases with GCTs and 5 cases with SCSTs. Most of the recurrences were detected in the abdomen (8 of 11 patients)

Table 3. Treatment modalities and oncological outcome in patients with malignant non-epithelial ovarian cancers

	Germ cell tumors	Sex cord-stromal tumors
Surgery type, n (%)		
Fertility-sparing	23 (76.6)	8 (23.5)
Non-fertility-sparing	7 (23.4)	26 (76.5)
Adjuvant chemotherapy		
BEP regimen, n (%)	19 (41.3)	2 (3.7)
Other regimens, n (%)	5 (10.9)	6 (11.2)
Number of cycles, median	2.7	1
Recurrence treatment, n (%)		
Exclusive surgery	2	0
Exclusive chemotherapy	1	0
Surgery and chemotherapy	1	1
Median follow-up (months)	90	83.5
Oncological outcome		
Recurrence, n (%)	6 (20)	5 (14.7)
5-year DFS rate (%)	89.1	94.4
5-year OS rate (%)	93.5	96.5

BEP: Bleomycin-etoposide-cisplatin, DFS: Disease-free survival, OS: Overall survival

and most patients underwent a second surgery followed by chemotherapy (7 of 11 patients). GCT was the diagnosis in three out of five patients with mortality. The 5-year OS rates were 93.5% and 96.3% in the GCTs and SCSTs groups, respectively (Figure 1). The 5-year DFS rate was 89.1% in patients with GCTs and 94.4% in those with SCSTs (Figure 2).

There were thirty-one patients younger than 40 years who had a final pathology result reported as malignant. Of these 31 patients, 17 were nulliparous, 18 were married, and 13 were single. The chemotherapy regimens included BEP in 16 patients, VIP (etoposide, ifosfamide, cisplatin) in 2 patients, and a combination of cyclophosphamide, 5-FU, and prednisolone in one patient with a Sertoli-Leydig cell tumor, while 12 patients did not receive any chemotherapy as they were diagnosed at stage 1. FSS was not performed only for 2 patients in this group because they did not have a desire for pregnancy. All patients who underwent FSS and had a recurrence in their follow-up (n=4) were stage 3b or 3c, and unfortunately one of them died due to disseminated disease. Seven out of 10 patients (two patients at stage 3 and five patients at stage 1) who desired pregnancy delivered full-term babies (n=9) between 38 and 40 gestational weeks with no congenital anomalies. The pregnancy rate was 70%, and none of the pregnancies were with assisted reproductive technology (ART) (Table 4). The median interval between surgery and delivery was 24 months (range, 9 to 156 months). No recurrence occurred in these patients. None of the

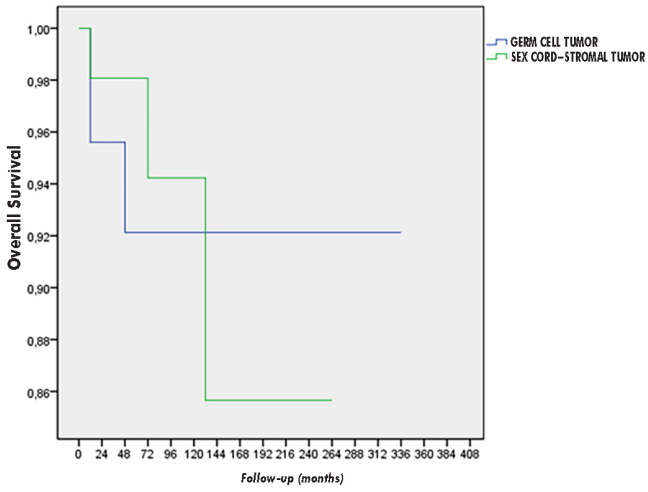

Figure 1. Kaplan-Meier curves for five-year overall survival (OS) in women with GCTs and SCSTs

GCTs: Germ cell tumors, SCSTs: Sex cordstromal tumors

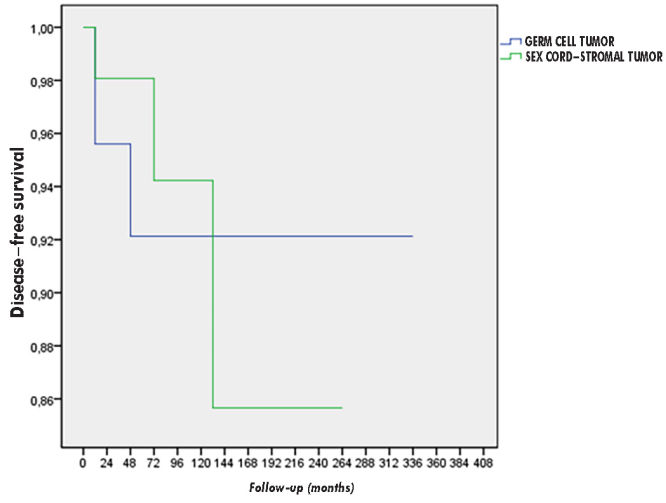

Figure 2. Kaplan-Meier curves for five-year disease-free survival (DFS) in women with GCTs and SCSTs

GCTs: Germ cell tumors, SCSTs: Sex cordstromal tumors

patients had undergone completion surgery after childbearing. Twenty patients did not try to get pregnant after fertility-preserving procedures.

Three women were pregnant at the time of diagnosis; the histological types in these patients were Sertoli-Leydig cell tumor (stage 1a), dysgerminoma (stage 1c2), and immature teratoma (stage 1c1). Fertility-preserving surgery including unilateral salpingo-oophorectomy and complete surgical staging was performed for treating these patients.

Discussion

NEOCs are considered to be diagnosed at an early age and to have a good prognosis in relation to the excellent chemotherapy response[13]. NEOCs include ovarian GCTs and SCSTs, and both groups have benign and malignant forms[13]. In this study, clinical and treatment characteristics and oncological and reproductive outcomes of GCTs and SCSTs were assessed in our series of NEOC patients. Moreover, the oncologic outcomes were also evaluated specifically among women undergoing FSS, which has been addressed only by a few studies to date[14-27].

NEOCs are relatively rare forms of ovarian cancer that occur mostly in women of childbearing age, except for granulosa cell tumors, which have a wide age spectrum including both premenopausal and postmenopausal women. Our findings support the data from previous studies with NEOC patients indicating overall good obstetric and survival outcomes along with no recurrences in women undergoing FSS even at the advanced stage[28]. Studies on fertility preservation surgery are mainly conducted in the setting of GCTs[13]. FSS did not adversely affect recurrence rates in all reviewed studies, and therefore, it is recommended as the gold standard surgical management of patients with early-stage GCTs[29]. Johansen et al.[15] indicated that the ability to conceive was preserved by using FSS since all conceptions were natural and all deliveries occurred at full term in their study. The pregnancy rate varies from 50% to 93%, and the live birth rate ranges from 65% to 95%[19,20,25,30-35].

The pregnancy rate (70%) in our study was similar to that in previous studies. Literature data on FSS outcomes in women

Table 4. Pregnancies achieved after fertility-sparing operation according to the tumor type

Patient no	Type of tumor	Stage	CT	Time to pregnancy (month)	Mode of delivery	Gestational week	Congenital anomaly	Recurrence
1	Dysgerminoma	1a	BEP	50	NVD	40	None	No
2	Dysgerminoma	3a1	BEP	71	CS	40	None	No
3	Granulosa cell tumor	1c1	None	11	NVD	40	None	No
4	Sertoli-Leydig	1a	None	9	CS	40	None	No
5	Dysgerminoma	1c2	BEP	24	CS	39	None	No
6	Immature teratoma	3c	BEP	156	CS	39	None	No
7	Dysgerminoma	1c2	BEP	23	CS	38	None	No

BEP: Bleomycin-etoposide-cisplatin, NVD: Normal vaginal delivery, CS: Cesarean section, CT: Chemotherapy

with SCSTs are scarce and mainly based on case reports or short series[36-40]. In a systematic review by Bercow et al.[14], FSS was considered not to be associated with worse DFS or OS compared to conventional surgery. There is a scarce amount of data regarding the fertility and pregnancy outcomes of granulosa cell tumors because these tumors are very rare and their peak incidence is in the perimenopausal period. In a review of a few retrospective studies on fertility-sparing management and pregnancy in patients with granulosa cell tumor by Iavazzo et al.[38], the authors recommended FSS to be performed only in well-selected patients after their informed consent. Some authors also reported no significant difference between FSS and radical surgery in terms of survival outcome[41]. In our study, most of the women who delivered were in the GCTs group, in accordance with consideration of GCTs rather than SCSTs to be more common in the reproductive age. Notably, chemotherapy was not considered to have a negative effect on fertility in NEOC patients[42]. Various combined regimens including vincristine, dactinomycin, cyclophosphamide, bleomycin, etoposide, cisplatin, doxorubicin, and vinblastine have been used after FSS, revealing satisfactory results on conception and pregnancy rates after chemotherapy exposure[18,35,42-49]. Most of our patients who delivered also received chemotherapy. Meanwhile, pregnancy or even delivery after completing chemotherapy may not affect recurrence or mortality[34].

Supporting the previously reported series, the survival outcome in our study confirms the overall good prognosis of ovarian non-epithelial tumors. Park et al.[30] found the 5-year DFS and OS rates for GCTs to be 86% and 97%, respectively. Malignant SCSTs carry a favorable prognosis with a 5-year OS of 97.2%[34]. Due to related high rates of recurrence and mortality, OS of advanced-stage disease, especially in SCSTs, is poor[34].

The type of surgery, patient age at the time of investigation, patient desire to conceive, fear of recurrence, and tumor histologic subtype are considered amongst the factors with considerable impact on fertility rates. Bilateral salpingo-oophorectomy and uterine conservation enable pregnancy by egg donation for women with gonadoblastoma. However since the oocyte donation is illegal in our country, preservation of the uterus does not increase fertility rates. Unfortunately, two patients with gonadoblastoma in our series could not have children due to this restriction, despite their desire for pregnancy.

Nonetheless, the conception rate may increase in the longer term. Some patients in our series did not try to conceive despite having FSS, possibly due to reasons such as prediction of good outcomes after fertility preservation and high chemotherapy response in case of recurrence[13]. Although these reasons appear to be highly acceptable for GCTs, they should be discussed in detail with patients have SCSTs.

Patients of reproductive age with NEOC should have access to professional family planning and infertility counseling to discuss fertility outcomes and treatment options[50]. Although the exact numbers of our patients who received presurgical family planning counseling and visited a reproductive medicine specialist are unknown, obstetric outcomes may be better if adequate counseling is given to these patients[13].

To reduce the risk of recurrence, completion surgery should be discussed with women who no longer intend to conceive. However, due to high curability rates, completion surgery after childbearing may not be necessary for GCTs. The use of completion surgery after childbearing remains debatable in SCSTs[51]. This decision may be personalized because there are still uncertainties regarding the long-term outcomes after this type of surgery[50]. The patients must be fully informed about oncological and obstetrical outcomes.

Study Limitations

The major limitations of this study seem to be retrospective single center design and small sample size of the cohort in relation to the rarity of these tumors, which prevented the conduction of reliable subgroup analyses with respect to different tumor histological subtypes. Also, our results regarding the obstetric outcomes after FSS should be interpreted with caution given the likelihood of a large sample to provide more reliable results. Furthermore, reproductive potential, which is a multifactorial phenomenon with considerable interindividual differences, was not detailed in our study.

Conclusion

In conclusion, FSS seems to be a potentially favorable surgical modality in the setting of NEOC for young women who intend to conceive. It can be offered to patients even at advanced disease stages, particularly in those with GCTs, depending on tumor histopathology and prognostic factors. Recurrence is considered to be rare in general, while it develops more frequently at advanced disease stages. Adjuvant chemotherapy does not seem to affect fertility outcomes. Larger prospective studies are needed to better evaluate long-term oncologic and reproductive outcomes in women with ovarian cancer undergoing FSS.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by the institutional ethics committee (Akdeniz University Clinical Research Ethics Committee - KAEK-657; date: 09.11.2022).

Informed Consent: Informed consent was obtained from each subject or their first-degree relatives (for the deceased ones).

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.S., C.K., H.A.T., S.D., T.Ş., Concept: S.S., C.K., H.A.T., S.D., T.Ş., Design: S.S., C.K., H.A.T., S.D., T.Ş., Data Collection or Processing: S.S., C.K., H.A.T., S.D., T.Ş., Analysis or Interpretation: S.S., C.K., H.A.T.,

S.D., T.Ş., Literature Search: S.S., C.K., H.A.T., S.D., T.Ş., Writing: S.S., C.K., H.A.T., S.D., T.Ş.

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