



An Overview of Seminomatous and Non-Seminomatous Germ Cell Testicular Tumors: A Single-center Experience

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Abstract

Objective: Although germ cell tumors (GCT) are rare malignancies, they are the most common solid tumors in men aged 15-40 years. This study aimed to compare the demographic and clinical characteristics, treatment responses, and survival characteristics of patients with seminomatous GCTs (SGCT) and non-seminomatous GCTs (NSGCTs) followed in our center.

Materials and Methods: Patients with histologically confirmed testicular GCTs and followed up in our hospital between January 2005 and January 2021 were included in this retrospective study. This study was approved by the Institutional Ethics Committee of Ankara City Hospital.

Results: Of the 360 patients, 65.8% (n=123) had NSGCTs and 34.2% (n=237) had SGCTs. The median age at diagnosis of the SGCT group was 36 years and that of the NSGCT group was 28 years (p=0.000). Both the diagnostic and postoperative levels of β -human chorionic gonadotropin were significantly higher in the NSGCT group (p=0.000, p=0.000 respectively). Rates of retroperitoneal lymph node dissection (3.3% vs 9.3%; p=0.036), adjuvant radiotherapy (RT) (17.1% vs 3%; p=0.000), adjuvant chemotherapy (CT) (61.1% vs 40.4%; p=0.003), and metastatic first-line CT (22.8% vs 47.3%; p=0.000) were different between the two groups. The 10-year overall survival expectancy rate was 89% in the SGCT group and 83% in the NSGCT group.

Conclusion: This study drew attention to the characteristics and treatment responses of patients with NSGCTs and SGCTs. In this study, NSGCTs were diagnosed at an earlier age than SGCTs. The proportion of patients with stage 1 disease at diagnosis was higher in the SGCT group, while that of patients with stage 3 and metastasis at diagnosis were higher in the NSGCT group. In addition, the rates of adjuvant CT and adjuvant RT were higher in the SGCT group, while the metastatic first-line CT rate was higher in the NSGCT group.

Keywords: Testicular germ cell tumors, chemotherapy, radiotherapy, autologous stem-cell transplantation

Introduction

Although germ cell tumors (GCTs) are rare malignancies, they are the most common solid tumors in men aged 15-40 years (1). Testicular cancers constitute only 0.5% of all cancers in men. Even if its etiology is not yet fully clarified, risk factors include family history, cryptorchidism, contralateral testicular tumor, infertility, and testicular microlithiasis (2). Moreover, 95% of testicular cancers are GCTs and 5% are non-GCTs and various non-specific stromal tumors. Testicular GCTs is divided into two groups, namely, as seminoma and non-seminoma. Non-seminomatous GCTs (NSGCTs) are divided into five subtypes: embryonal carcinomas, yolk sac tumors, choriocarcinomas, teratomas, and mixed GCTs (MGCTs) (3).

The majority of the patients can be treated by orchiectomy and, if necessary, systemic or local treatments (4). Patients with GCTs have excellent survival rates because of advances in chemotherapy (CT), radiotherapy (RT), and surgery (5). A cure is expected in 95% of all patients with testicular cancer and approximately 80% of patients with metastatic disease (4).

In this study, we aimed to compare the demographic and clinical characteristics, treatment responses, and survival data of patients with seminomatous GCTs (SGCT) and NSGCTs followed in our center.

Materials and Methods

This study was approved by the Institutional Ethics Committee of Ankara City Hospital (decision no: EI-21-1661). Patients with

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histologically confirmed testicular GCTs and followed up in our hospital between January 2005 and January 2021 were included in this retrospective study. Clinicopathological characteristics of the patients and treatment modalities were recorded from the patient registration database of the hospital. β -human chorionic gonadotropin (BHCG), lactate dehydrogenase (LDH), and alpha fetoprotein (AFP) levels were measured upon diagnosis and 30 days after orchiectomy. Patients with a second cancer were excluded from the study.

Testicular cancer was staged using the Eighth Tumor, Node, Metastasis staging system developed jointly by the American Joint Committee on Cancer and the Union for International Cancer Control, which applies to both SGCT and NSGCTs (6).

According to the RECIST guidelines, responses were calculated using the following measurements: complete response (CR) (complete resolution of target lesions), partial response (PR) ($\geq 30\%$ decrease in the sum of the diameters of the target lesions compared with the baseline), progressive disease (PD) ($\geq 20\%$ increase in sum of the diameters of the target lesions compared with baseline or new metastatic lesions), and stable disease (SD; neither fitting in PR or PD categories). CR/PR, SD, and PD as per RECIST were independently analyzed (7).

The diagnosis of recurrent testicular GCTs was typically made based on an increase in serum tumor markers or evidence of disease progression on radiographic or physical examinations. Biopsy confirmation was also performed in cases where the recurrence symptom was atypical.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics version 24.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as median with the 25th percentile and 75th percentile. Categorical variables were presented as percentage. The normality of quantitative data has been analyzed by the Kolmogorov-Smirnov and Shapiro-Wilk tests. The Pearson chi-square test was used for the comparison of categorical variables between two groups, and independent sample t-test or Mann-Whitney U test was used for comparison of continuous variables between two groups. Survival analysis was calculated according to the Kaplan-Meier (Log rank, Breslow, and Tarone-Ware analyses) method. P-value < 0.05 was considered significant.

Results

Of the total 360 patients, 65.8% (n=237) had NSGCTs and 34.2% (n=123) had SGCTs. The median age at diagnosis of the SGCT group was 36 years and that of NSGCT group was 28 years (p=0.000). The tumor diameter measure by computed tomography was 4.5 cm in the SGCT group and 4 cm in the NSGCT group. No significant difference was found in the mean tumor diameter between the two groups. The median BHCG levels upon diagnosis and after surgery were significantly higher in the NSGCT group (p=0.000 and p=0.000, respectively). No difference was noted between the two groups in terms of LDH levels upon diagnosis and after surgery (Table 1).

Of the NSGCTs, 74% were MGCTs, 12.2% were embryonal carcinomas, 7.2% were teratomas, 5.1% were yolk sac tumors, and 0.8% was choriocarcinomas. Of the MGCTs, 80.1% were

embryonal carcinomas, 63.5% were teratomas, 49.7% were yolk sac tumors, 35.4% were seminomas, and 11.6% were choriocarcinomas (Table 2).

The proportion of patients with stage 1 disease at diagnosis was 73.9% in the SGCT group and 46.8% in the NSGCT group (p=0.000), while the proportion of patients with stage 3 disease at diagnosis was 9.2% in the SGCT group and 30.4% in the NSGCT group (p=0.000). The proportion of patients with stage 2 disease at diagnosis was comparable between the two groups. The proportions of patients with SGCTs and NSGCTs in the good-risk group were 93.4% and 59.5%, respectively (p=0.000). The proportion of the patients in the intermediate-risk group were 6.4% and 25.7%, respectively (p=0.000). The rates of patients with positive lymph nodes (LNs) at diagnosis were 27.8% and 52.3% in the SGCT and NSGCT groups, respectively. The proportions of patients with metastasis at diagnosis were 0.8% and 27% in the SGCT and NSGCT groups, respectively. Moreover, the proportions of patients with LN positivity and metastatic disease were significantly higher in the NSGCT group (p=0.006 and p=0.000, respectively) (Table 1).

The recurrence rate was 17.1% in the SGCT group and 18.6% in the NSGCT group. The proportion of patients with recurrence was not different between the two groups (p=0.727). The rate of patients who underwent retroperitoneal LN dissection (RPLND) was significantly higher in the NSGCT group (9.3%, n=22) than in the SGCT group (3.3%, n=4) (p=0.036). While one patient in the SGCT group had post-CT RPLND and three patients had primary RPLND, 16 patients with NSGCT had post-CT RPLND and six patients had primary RPLND. In patients with SGCT who underwent RPLND, seminoma was detected in one patient (stage 1 disease) and necrosis was detected in three patients (two and one patient has stage 2 and 1 disease, respectively). In patients with NSGCT who underwent RPLND, 27.3% of the patients had teratomas (four and one patient had stage 2 and 3 disease, respectively), 18.2% had necrosis (one, two, and one patient had stage 1, 2, and 3 disease, respectively), 31.8% had other non-seminomatous subtypes (two, three, and two patients had stage 1, 2, and 3 disease, respectively), 9.1% had seminomas (two patients had stage 3 disease), 9.1% had reactive LNs (one and one patient had stage 1 and stage 3 disease), and 4.5% were non-diagnostic (one patient had stage 2 disease) (Table 3).

The proportion of patients receiving adjuvant RT was significantly higher in the SGCT group (17.1%, n=21) than in the NSGCT group (3%, n=7) (p=0.000). In the SGCT group, only one patient received testicular RT, while 20 patients received RT for para-aortic \pm iliac LNs (n=11) or inguinal LNs (n=9). All patients with NSGCTs received RT to para-aortic \pm iliac LNs (n=5) or inguinal LNs (n=2) (Tables 3 and 4).

The proportion of patients receiving adjuvant CT was significantly higher in the SGCT group (61.1%, n=44) than in the NSGCT group (40.4%, n=76) (p=0.003). As adjuvant CT in the SGCT group, 31.8% of the patients received carboplatin and 15.9% received cisplatin, etoposide, bleomycin (BEP, bleomycin 30 U IV weekly on days 1, 8, and 15 + etoposide 100 mg/m² IV on days 1-5 + cisplatin 20 mg/m² IV on days 1-5/repeat every 21 days) + cisplatin, etoposide (EP, etoposide 100 mg/m² IV on days 1-5 + cisplatin 20 mg/m² IV on days 1-5/repeat every 21 days) and

	SGCT n=123 (34.2%)		NSGCT n=237 (65.8%)		p-value
	Median (minimum; maximum)	%	Median (minimum; maximum)	%	
Follow-up period (years)	7.75 (0.70; 33)		8.79 (0.68; 22.08)		
Age at diagnosis (years)	36 (17; 62)		28 (15; 67)		0.000
Tumor diameter (cm)	4.50 (0.50; 12)		4.00 (1; 10)		0.411
BHCG at diagnosis (IU/mL)	2 (0.1; 2891)		17 (0.1; 275486)		0.000
LDH at diagnosis (U/L)	284 (127; 4720)		261 (120; 5400)		0.651
AFP at diagnosis (ng/mL)			110 (1; 128000)		
Postoperative BHCG (IU/mL)	0.2 (0.1; 1907)		2 (0.1; 596000)		0.000
Postoperative LDH (U/L)	187 (90; 1799)		217 (91; 3577)		0.055
Postoperative AFP (ng/mL)			10 (0.1; 116000)		
Recurrence	Yes	17.1%	18.6%		0.727
	No	82.9%	81.4%		
Stage at diagnosis	Stage 1	73.9%	46.8%		0.000
	Stage 2	16.8%	22.8%		0.146
	Stage 3	9.2%	30.4%		0.000
Risk group	Good	93.4%	59.5%		0.000
	Intermediate	6.4%	25.7%		0.000
	Bad		14.8%		
Tumor	T1	61.1%	50.4%		0.233
	≥T2	38.9%	49.6%		
Node positivity	Negative	72.2%	47.7%		0.006
	Positive	27.8%	52.3%		
Metastasis at diagnosis	No	99.2%	73.0%		0.000
	Yes	0.8%	27.0%		

SGCT: Seminomatous germ cell tumors, NSGCT: Non-seminomatous germ cell tumors, BHCG: β -human chorionic gonadotropin, LDH: Lactate dehydrogenase, AFP: Alpha fetoprotein

	%		%	
Pathological subtype	MGCTs	74.7%	Teratoma	63.5%
			Embryonal carcinoma	80.1%
			Yolk sac tumor	49.7%
			Choriocarcinoma	11.6%
			Seminoma	35.4%
	Teratoma	7.2%		
	Yolk sac tumor	5.1%		
	Choriocarcinoma	0.8%		
Embryonal carcinoma	12.2%			

MGCT: Mixed germ cell tumors

52.2% received BEP. In the NSGCT group, 23.6% of the patients received BEP + EP, 73.6% received BEP, and 2.6% received EP. The proportion of patients receiving metastatic first-line CT was significantly higher in the NSGCT group than in the SGCT group (47.3% and 22.8%, respectively) ($p=0.000$). No difference was found between the two groups in terms of metastatic first-line

treatment responses, rates of metastatic second-line treatment responses, metastatic second-line treatment responses, or autologous stem cell transplantation (ASCT) rates. ASCT was performed in four patients in the SGCT group and in 10 patients in the NSGCT group. In the SGCT group, PD was attained in one patient and SD was attained in three patients. In the NSGCT group, two patients had CR, one had PR, three had PD, and four had SD (Table 3).

The 10-year overall survival (OS) expectancy rate was 89% in the SGCT group and 83% in the NSGCT group. In the survival analysis, OS did not reach the median in either group (Figure 1).

Discussion

NSGCTs are seen in men aged 20-30 years, while SGCTs typically occur between age 30-40 years (8). In this study, the median age of the patients diagnosed with SGCTs was 36 years, while those with NSGCTs was 28 years, and a significant difference was found between the two groups. No difference was found in tumor size between the two groups, and 34.2% of the patients had SGCTs and 65.8% had NSGCTs. In another study conducted in Turkey, the incidence of NSGCT was higher, reporting 77.6%, similar to our study (9). In a retrospective analysis conducted in

Table 3. Treatments and treatment responses of patients with germ cell testicular tumors

n (%)		SGCT	NSGCT	
		n (%)	p-value	
RPLND	Yes	4 (3.3%)	22 (9.3%)	0.036
	No	119 (96.7%)	215 (90.7%)	
Adjuvant RT	Yes	21 (17.1%)	7 (3%)	0.000
	No	102 (82.9%)	230 (97%)	
Adjuvant CT		44 (61.1%)	76 (40.4%)	0.003
Metastatic first-line CT	Yes	28 (22.8%)	112 (47.3%)	0.000
	No	95 (77.2%)	125 (52.7%)	
Metastatic first-line CT response	CR	6 (21.4%)	27 (24.1%)	0.191
	PR	13 (46.4%)	53 (47.3%)	0.093
	PD	5 (17.9%)	17 (15.2%)	0.586
	SD	4 (14.3%)	15 (13.4%)	0.503
Metastatic second-line CT	Yes	20 (16.3%)	41 (17.3%)	0.803
	No	103 (83.7%)	196 (82.7%)	
Metastatic second-line CT response	CR	6 (30%)	7 (17.1%)	0.247
	PR	8 (40%)	16 (39%)	0.942
	PD	3 (15%)	9 (22%)	0.525
	SD	3 (15%)	9 (22%)	0.525
ASCT	Yes	4 (3.3%)	10 (4.2%)	0.653
	No	119 (96.7)	227 (95.8%)	
ASCT response	CR	0 (0%)	2 (20%)	
	PR	0 (0%)	1 (10%)	
	PD	1 (25%)	3 (30%)	
	SD	3 (75%)	4 (40%)	

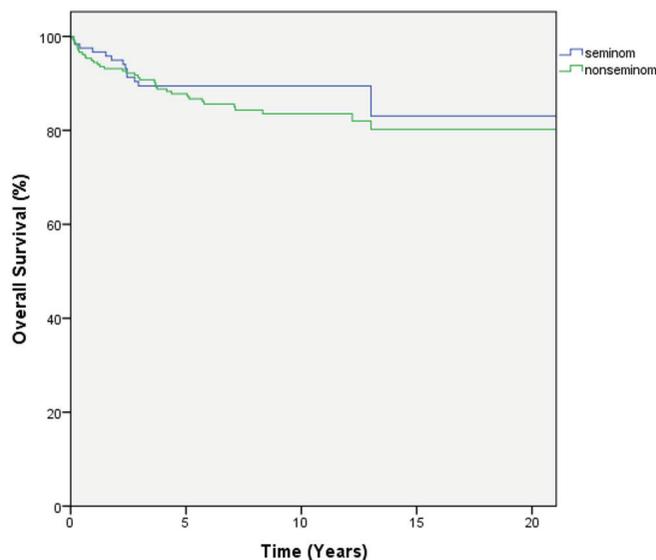
SGCT: Seminomatous germ cell tumors, NSGCT: Non-seminomatous germ cell tumors, RPLND: Retroperitoneal lymph node dissection, CT: Chemotherapy, RT: Radiotherapy, ASCT: Autologous stem cell transplantation, CR: Complete response, PR: Partial response, PD: Progressive disease, SD: Stable disease

Table 4. Adjuvant radiotherapy localization and adjuvant chemotherapy regimens

Adjuvant RT location	Para-aortic +iliac LN	11 (52.3%)	5 (71.3%)
	Testicular	1 (4.76%)	0 (0%)
	Inguinal LN	9 (42.8%)	2 (28.7%)
Adjuvant CT	Carboplatin (AUC 7)	14 (31.8%)	0 (0%)
	BEP+EP	7 (15.9%)	18 (23.6%)
	BEP	23 (52.2%)	56 (73.6%)
	EP	0 (0%)	2 (2.6%)

BEP: Bleomycin 30 U IV weekly on days 1, 8, and 15 + etoposide 100 mg/m² IV on days 1-5 + cisplatin 20 mg/m² IV on days 1-5/repeat every 21 days, EP: Etoposide 100 mg/m² IV on days 1-5 + cisplatin 20 mg/m² IV on days 1-5/repeat every 21 days, AUC: Area under the curve, LN: Lymph node

Germany, SGCTs constituted 64.5% of all testicular GCTs, while NSGCTs constituted 35.5% (10). In another study conducted in Japan, seminomas and non-seminomas were found in 46.7% and 53.3% of the patients, respectively (11). In another study conducted in Turkey (12), 46.4% of the patients with testicular tumors had seminomas and 53.6% had non-seminomas.

**Figure 1.** Overall survival curve of seminomatous and non-seminomatous germ cell tumors

In another study (13), these rates were 49.2% and 50.7%, respectively. Ethnic differences and environmental factors are possible reasons for the differences in the rates of testicular GCTs in different countries.

In the SGCT group, the rates of stage 1, 2, and 3 diseases were 73.9%, 16.8%, and 9.2%, respectively. In the NSGCT group, the corresponding rates were 46.8%, 22.8%, and 30.4%, respectively. The widespread use of ultrasonography and increased awareness of the public about testicular cancer and testicular self-examination are possible reasons for the higher rates of early-stage testicular tumors compared with metastatic tumors. In addition, testicular cancer may be more easily noticed as it manifests itself with painless scrotal swelling. The rates of stage 1 disease in the SGCT group and stage 3 diseases in the NSGCT group were significantly higher than in those of other stages. In another study, while the rates of stage 1, 2, and 3 diseases were 80.2%, 13.5%, and 6.3%, respectively, in the SGCT group, those in the NSGCT group were 53.3%, 27.1%, and 19.6%, respectively (1). Moreover, the proportion of patients with SGCT in the good-risk group was higher than that of patients in the NSGCT group. Patients with moderate risk were higher in the NSGCT group than in the SGCT group. In the present study, 74.7% of the NSGCTs were MGCT, 12.2% were embryonal carcinomas, 7.2% were teratomas, 5.1% were yolk sac tumor, and 0.8% was choriocarcinomas. The subcomponents of MGCTs were as follows: 80.1% were embryonal carcinomas, 63.5% were teratomas, 49.7% were yolk sac tumors, 35.4% were seminomas, and 11.6% were choriocarcinomas. In a study conducted in Turkey, 77.6% of the patients had MGCT histology and 82.2% of them contained histological components of embryonal carcinoma, 53.3% of teratomas, 49.6% of yolk sac tumors, 37.8% of seminomas, and 5.9% of choriocarcinoma (9). In another study, approximately 65.3% of NSGCTs were MGCT, 18.7% were embryonal carcinomas, 7.2% were yolk sac tumors, 4.5% were teratomas, and 1.6% was choriocarcinomas (13).

In the present study, BHCG levels measured at diagnosis and in the postoperative period were significantly higher in the NSGCT group than in the SGCT group, but no significant difference was found between the two groups in terms of LDH levels. In similar study, while HCG levels were higher in the non-seminoma group at diagnosis, no difference was found between the seminoma and non-seminoma groups in terms of LDH (1).

The American Urological Association (AUA) guidelines on testicular cancer and European Association of Urology (EAU) guidelines in testicular cancer recommend active surveillance after orchiectomy in stage 1 SGCTs and stage 1 NSGCTs (14,15). Adjuvant CT may be a good option in high-risk cases to reduce the risk of recurrence (16). If adjuvant CT will be given, one course of carboplatin (area under curve 7) CT for SGCT and one course of BEP CT for NSGCT can be considered (14,15). In this young patient group, in addition to recurrence, long-term side effects of the treatments, such as cardiovascular events and secondary malignancy, should not be ignored (17). The ratio of patients receiving adjuvant CT was higher in the SGCT group, while proportion of patients receiving metastatic first-line CT was higher in the NSGCT group. Metastatic second-line CT rates were comparable between the two groups. However, CT response rates in patients receiving first- and second-line CT were not different between the two groups. In this study, the recurrence rates after adjuvant therapy were comparable in both groups. In addition, 81% and 88.6% of the patients diagnosed with recurrent SGCTs and NSGCT, respectively, had relapsed within 3 years. Kollmannsberger et al. (18) reported that the recurrence rate was the highest in the first 3 years after adjuvant CT in these patients.

Post-CT resection of residual masses or RPLND is often associated with normalization of tumor markers and long-term survival (19). The EAU guideline recommends nerve-sparing RPLND to highly selected patients with stage 1B NSGCTs, i.e., those with contraindication to adjuvant CT and unwilling to accept surveillance (strong recommendation), and primary RPLND in men with post-pubertal teratomas with somatic malignant components (weak recommendation) (15).

According to the AUA guideline recommendation for patients with stage 1A NSGCTs, RPLND or one cycle of BEP CT is an effective and appropriate alternative treatment option for patients who does not accept surveillance or had incompatible status (14). The guideline offers surveillance, RPLND or one or two cycles of BEP CT based on shared decision-making for patients with stage 1B NSGCTs (14). The AUA guideline also stated that clinicians may offer RPLND as an alternative to CT in select patients with clinical stage 2B NSGCTs with normal post-orchiectomy serum AFP and beta-hCG. To date, little data are available on outcomes for men receiving RPLND as primary treatment for SGCTs (14). In a study using data from the Surveillance, Epidemiology, and Final Results program, the rates of RPLND were 1.3% in stage 1 disease and 10.6% in stage 2 disease in men diagnosed with testicular SGCTs between 1988 and 2013 in the United States (20). In this study, RPLND was performed in 3.3% of the patients with SGCTs and 9.3 of those with NSGCTs. In all patients who underwent RPLND, the viable

tumor, necrosis, and reactive LN and non-diagnostic LN rates were 57.6%, 30.7%, and 11.5%, respectively. In a single-center analysis of 504 patients with NSGCTs who underwent RPLND, 51% had fibrosis/necrosis, 37% had teratomas, and 15% had viable GCTs (21). Similar results were reported in another study (22). Seminomatous GCTs are extremely sensitive to RT, while NSGCTs are more radioresistant. In the present study, 17.1% of the patients with SGCTs and 3% with NSGCTs received adjuvant RT. In the SGCT group, only one patient received testicular RT, while 20 patients received RT for para-aortic \pm iliac LNs. All patients with NSGCTs received RT to para-aortic \pm iliac LNs.

In this study, a total of 14 patients had undergone ASCT. While 3 of 14 patients received high-dose CT + ASCT as third-line therapy, 11 patients received second-line therapy. Moreover, 2% of the 14 patients had CR, 1 had PR, 7 had SD, and 4 had PD. Randomized studies have reported no improvement in high-dose CT outcomes with ASCT (23,24). However, in non-randomized studies, better results have been reported when high-dose CT/ASCT was used as second-line CT, rather than third-line CT. In other studies, treatment-related mortality was <5%, and long-term disease-free survival was between 40% and 70% (24,25,26).

In the present study, the 10-year OS expectancy rate was 89% in the SGCT group and 83% in the NSGCT group. The median OS could not be reached. Although the incidence of testicular cancer has increased, related mortality decreased over time (27). In the 1970s, the application of cisplatin-based CTs decreased the mortality rate while increasing the life expectancy rate to 95% (28). In one study, the 10-year OS expectancy rate was 90.8% in patients with testicular cancer diagnosed at age <50 years, while the OS expectancy rate was 80.4% in those diagnosed at age >50 years. In another study, the 5-year OS expectancy rates were 93.8% and 87.9% in the SGCT and NSGCT groups, respectively (29).

Study Limitations

The retrospective study design was the most important limitation of this study. Thus, surgical techniques, RT doses, and number of CT cycles could not be found in patient records.

Conclusion

In this study, clinical and laboratory characteristics, treatment responses, and survival characteristics of patients with SGCTs and NSGCTs who were followed up in our center were examined. The aim was to draw attention to the similar and different characteristics and treatment responses between the two groups. Compared with SGCTs, NSGCTs were diagnosed at an earlier age. The proportion of patients with stage 1 disease at diagnosis was higher in the SGCT group, and those with stage 3 disease and metastasis at diagnosis were higher in the NSGCT group. In addition, the rates of adjuvant CT and adjuvant RT were higher in the SGCT group, while RPLND and metastatic first-line CT rates were higher in the NSGCT group. Evaluation of the clinical laboratory and survival data of 360 patients with GCTs was the strength of the study. However, studies involving a large patient population from different ethnic and geographical regions are warranted.

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Ethics

Ethics Committee Approval: This study was approved by the Institutional Ethics Committee of Ankara City Hospital (decision no: El-21-1661).

Informed Consent: Retrospective study.

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Authorship Contributions

Critical Review: Y.E., Y.A., G.U., E.A., Concept: Ö.B., Design: S.A.E., Ö.B., M.D., D.U., Data Collection or Processing: S.A.E., Ö.B., M.D., Ö.A.İ., Analysis or Interpretation: S.A.E., Y.E., Y.A., İ.E., Literature Search: S.A.E., G.U., Writing: S.A.E., İ.E.

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