

## Research Article

# Survival Analysis of Our Patients Diagnosed with Testicular Cancer

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### Abstract

**Objectives:** The aim of our study is to determine the relationship between clinicopathological parameters and survival in our patients with testicular cancer who were followed up and treated in our centers.

**Methods:** Patients who were followed up and treated with the diagnosis of testicular cancer in Antalya Training and Research Hospital and Sanko University Hospital Medical Oncology Clinics were evaluated retrospectively.

**Results:** 164 patients with a mean age of  $32.8 \pm 10.8$  (range 15.6-67) years were included in the study. Seminoma was detected in 68 (41.5%) patients, non-seminomatous germ cell tumor (NSGCT) was detected in 91 (55.5%) patients, and non-germ cell testicular carcinoma was detected in 5 (3%) patients. A statistically significant difference was found between histological type and age ( $p < 0.001$ ). Mean age was  $37.4 \pm 10.1$  (range 20-67) years in seminoma patients,  $28.4 \pm 8.6$  (range 15.6-52.14) years in NSGCT patients,  $53.6 \pm 9.6$  (range 41.2-62.8) years in non-germ cell testicular cancers.

A statistically significant difference was found between histological subtype and stage ( $p = 0.003$ ). Of the patients diagnosed with seminoma, 54 (85.7%) patients were stage I, 6 (9.5%) patients were stage II, and 3 (4.8%) patients were stage III. In the NSGCT group, 47 (54.7%) patients were stage I, 17 (19.8%) patients were stage II, 22 (25.6%) patients were stage III. Stage I disease was detected in all patients diagnosed with non-germ cell testicular tumor.

**Conclusion:** Testicular cancer is the most common solid tumor seen in men aged 20-34 years. NSGCTs are diagnosed at a more advanced stage compared to seminomas.

**Keywords:** Testicular cancer, histological subtype, survival

**Cite This Article:** Sever ON, Solakhan M, Yerlikaya T, Enki S, Yildiz M, Yildirim M. Survival Analysis of Our Patients Diagnosed with Testicular Cancer. EJMI 2022;6(2):176-179.

Although testicular cancer accounts for only 1 percent of all cancers in men, it is the most common solid organ malignancy affecting men between the ages of 15 and 35.<sup>[1]</sup> Testicular cancer is also one of the best treatable solid malignancies, with a five-year survival rate of approximately 95 percent.<sup>[1,2]</sup>

Germ cell tumors (GCTs) account for 95 percent of testicular cancers. They may consist of a single dominant histological pattern or represent a mixture of multiple histological

types. In terms of treatment planning, testicular tumor is divided into 2 main categories: pure seminoma (no non-seminomatous element) and non-seminomatous germ cell tumors (NSGCTs). In most series, the ratio of seminoma to NSGCT is approximately one. Other testicular malignancies include sex cord-stromal tumors including Leydig cell and Sertoli cell tumors, gonadoblastoma and tumors of other cell types found in the testicles such as lymphoma, carcinoma tumors, and metastatic carcinoma.

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**Submitted Date:** February 02, 2022 **Accepted Date:** March 16, 2022 **Available Online Date:** March 25, 2022

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In our study, we aimed to determine the relationship between clinicopathological parameters and survival of our patients who were diagnosed with testicular cancer and followed up and treated in our centers.

## Methods

Patients who were followed up and treated with the diagnosis of testicular cancer in Antalya Training and Research Hospital and Sanko University Hospital Medical Oncology Clinics between January 2010 and December 2021 were evaluated retrospectively. Patient files and hospital automation records were examined by examining age, concomitant disease, date of operation, date of pathological diagnosis, testicular cancer histological subtype, stage at diagnosis, alpha fetoprotein (AFP), beta human chorionic gonadotropin ( $\beta$ -hCG) and lactate dehydrogenase (LDH) levels, before and after orchiectomy, chemotherapy protocol and dates, number of cures, relapse-recurrence date, second-line treatment protocol, patient's final status and follow-up period were obtained. The time from the date of diagnosis to relapse-recurrence was evaluated as progression-free survival (PFS), and the time from the date of diagnosis to death was evaluated as overall survival (OS).

The t-test or ANOVA was used to compare independent groups. Categorical measurements were analyzed with the chi-square test. The relationship between histological groups and age was investigated with the Kruskal-Wallis test and the relationship between the stage with the Chi-square test due to the abnormal distribution of the age variable. The Kaplan-Meier method was used to estimate the mean-median OS and PFS ratios. The log-rank test was used to compare the survival distributions between groups. Cox proportional regression model was used to estimate hazard ratios (HR). Results were reported as mean $\pm$ SD, median, number (n), and percent (%). A p value of <0.05 was considered significant in all tests. Data were expressed as mean $\pm$ SD for continuous variables and as numbers (n) and percentage (%) for categorical variables. Analyses were performed using the statistical package SPSS v15.0.

## Results

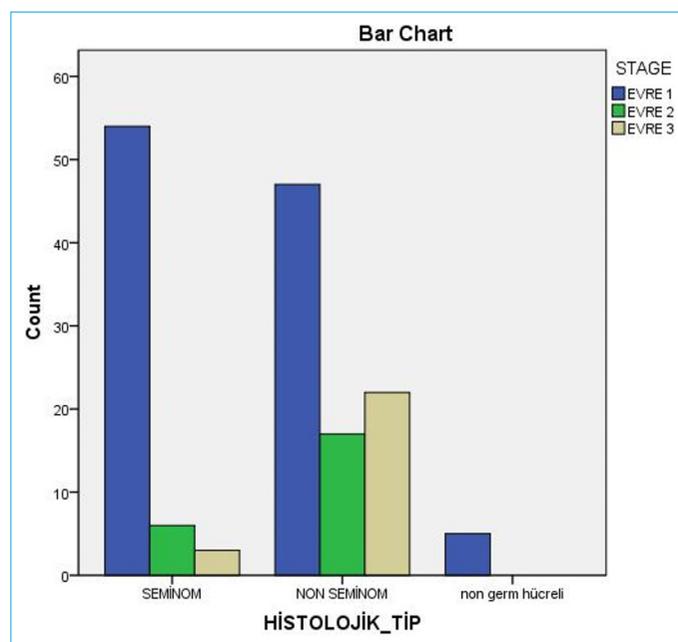
164 patients with a mean age of 32.8 $\pm$ 10.8 (Range 15.6-67) years were included in the study. Seminoma was detected in 68 (41.5%) patients, non-seminomatous germ cell tumor (NSGCT) was detected in 91 (55.5%) patients, and non-germ cell tumors were detected in 5 (3%) patients. There was a significant age difference between the histological groups (p<0.001). Mean age is 37.4 $\pm$ 10.1 (Range 20-67) years in seminoma patients, 28.4 $\pm$ 8.6 (Range 15-52) years in NSGCT patients, 53.6 $\pm$ 9.6 (Range 41-62) years

in non-germ cell testicular cancers. There was a significant difference between the histological groups in terms of pre-treatment AFP and  $\beta$  hCG levels (p<0.001 and p<0.001, respectively). Baseline AFP levels were 2.7 $\pm$ 1.6 (Range 0.9-9.3) ng/mL in seminoma patients, 1098 $\pm$ 4146 (Range 0.9-31466) ng/mL in NSGCTs, 14.6 $\pm$ 23.5 (Range 1.7-50) ng/mL in non-germ cell testicular cancers. Initial  $\beta$  hCG levels were 30.9 $\pm$ 84.1 (Range 0-497) mIU/mL in patients with seminoma, 9759.8 $\pm$ 40180 (Range 0-271080) mIU/mL in patients with NSGCTs, 0.2 $\pm$ 0.2 (Range 0-0.6) mIU/mL in non-germ cell testicular cancers. There was no significant difference between the histological groups in terms of pre-treatment LDH levels (p=0.065).

When 91 patients with NSGCTs were evaluated according to histological subtype, 71 (78%) had mixed germ cell tumor, 11 (12.1%) had embryonal carcinoma, 6 (6.6%) had teratoma, 2 (2.2%) had Yolk sac tumor and 1 (1.1%) had choriocarcinoma. Sertoli-leyding cell tumors were found in 3 of 5 patients with non-germ cell histology, and leiomyosarcoma and liposarcoma in one patient.

When the histological groups were evaluated in terms of stage, a statistically significant difference was found (p=0.003, Figure 1). Of the patients diagnosed with seminoma, 54 (85.7%) were stage I, 6 (9.5%) were stage II, and 3 (4.8%) were stage III. In the NSGCT group, 47 (54.7%) patients had stage I disease, 17 (19.8%) stage II disease, and 22 (25.6%) stage III disease. Stage I disease was detected in all patients with non-germ cell tumors.

The mean follow-up was 37.3 months (Range 0.33-157). When survival variance evaluated by histological types, sta-



**Figure 1.** Distribution of Stages by Histological Subgroups.

tistical significance was found between them ( $p=0.05$ , Figure 2). Median survival could not be reached in seminoma and non-germ cell tumors. The median survival in patients with NSGCTs was 157 months (Fig. 3).

## Discussion

Germ cell tumors predominantly affect young men aged 15 to 40 years, with an estimated 74500 new cases globally in 2020.<sup>[3]</sup> The incidence of testicular cancer shows geographical differences. While the highest incidence rates were observed in Denmark (10.2 per 100,000) and Norway (11.5 per 100,000), the incidence rates were low in Belarus and Ukraine (2.3 and 2.2 per 100,000, respectively) in 2010.<sup>[4]</sup> While testicular cancer is not among the top 10 most

common cancers in men of all age groups in our country, it is the most common cancer in men aged 15-24 with a rate of 26.1%. This rate decreases to 8.3% in men aged 25-49, and it is seen that it falls to the 4th rank among the most common cancers.<sup>[5]</sup> In our study, the mean age at diagnosis was  $37.4 \pm 10.1$  (range: 20-67) years in the seminoma group and  $28.4 \pm 8.6$  (range: 15-52) years in the NSGCT group.

Germ cell testicular cancers are generally associated with cryptorchidism, hypospadias, and testicular dysgenesis syndrome.<sup>[6]</sup> It has been shown that in utero exposure to some endocrine damaging chemicals such as organochlorine insecticides increases the risk of germ cell tumors.<sup>[7]</sup> In addition, it has been reported that germ cell tumors are more common in some families.<sup>[8]</sup> When the family history of the patients included in our study was questioned, there was no family history in any of the patients.

Contralateral testicular germ cell tumor is diagnosed in approximately 5% of patients, suggesting a genetic predisposition.<sup>[9]</sup> In our study, in one patient with a diagnosis of NSGCT, a simultaneous germ cell testicular tumor was detected in the other testis.

Approximately 55-60% of germ cell tumors are pure seminomas and 40-45% are non-seminomatous germ cell tumors.<sup>[7]</sup> In our study, while the rate of patients with seminoma was 41.5%, the rate of patients with non-seminomatous germ cell tumors was 55.5%. Probably due to slower progression, approximately 85% of seminomas are diagnosed as clinical stage I disease, compared to 60% for NSGCTs. In our study, in accordance with the literature, 85.7% of patients with seminoma were stage I, and 54.7% of patients with non-seminomatous germ cell tumors were stage I.

Approximately 95% of germ cell tumors arise in the testicles, while 5% develop outside the gonads (extragonadal). Extragonadal germ cell tumors are usually located in the midline of the body such as the retroperitoneum, mediastinum or cerebrum; this sometimes creates diagnostic difficulties.<sup>[10]</sup> There was no extragonadal location in any of the patients included in the study.

In conclusion, testicular cancer is the most common solid tumor seen in men aged 20-34 years. Non seminomatous germ cell testicular cancers are diagnosed at a more advanced stage compared to seminomas.

## Disclosures

**Ethics Committee Approval:** Ethics committee approval was not obtained in this study because retrospective data analysis was performed. Archive permission document was obtained on 07 August 2021.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

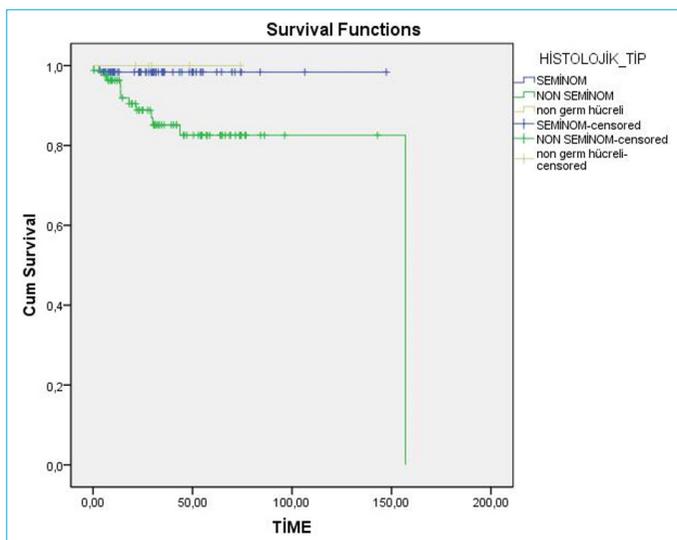


Figure 2. Survival by Histological Subgroups.

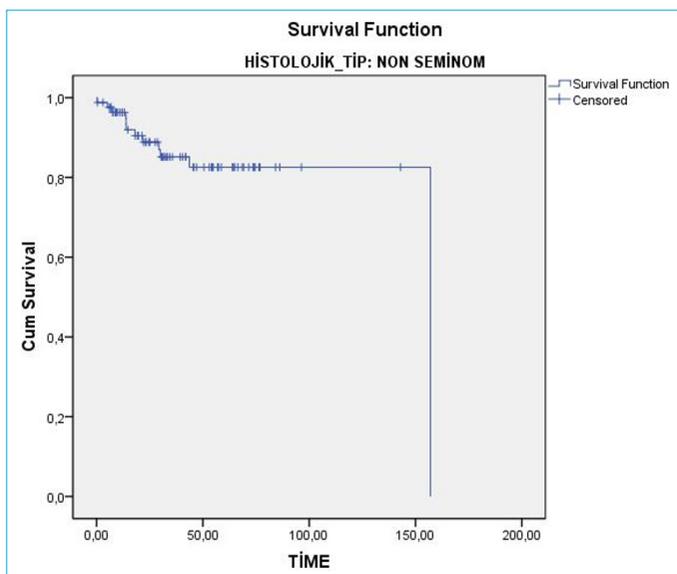


Figure 3. Survival in Patients with Nonseminomatous Germ Cell Testicular Tumor.

**Authorship Contributions:** Concept – O.N.S., M.S., M.Y.; Design – O.N.S., M.Y.; Supervision – M.Y., M. Yıldız; Materials – O.N.S., M. S., S.E., T.Y., M.Y.; Data collection/&processing – O.N.S., M.S., M.Y., S.E., T.Y., M. Yıldız.; Analysis and/or interpretation – O.N.S., M.Y.; Literature Search – O.N.S.; Writing – O.N.S.; Critical Review – M.Y., M.S., M. Yıldız.

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