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Research Article

# Classical Seminoma in Geriatric Patients

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## Abstract

**Objectives:** Advanced age is a well-known risk factor for cancer development. Although 12% of cancer is seen at the age of 65 and above worldwide, when the total cancer population is evaluated, 60% of them are age 65 and above. Our aim in our study is to share our follow-up and treatment experience with patients with very rare geriatric seminoma.

**Methods:** In our study, patients aged 65 and over who were diagnosed with seminoma between 07.09.1998-19.11.2018 in our center were evaluated retrospectively. Patient interview information, patient files and electronic system data were used for the study.

**Results:** The data of 32 patients who were diagnosed with seminoma above 65 years of age were evaluated retrospectively. The median age of the patients is 68 (range 65-85). 24 (75%) patients stage 1; 6 (18.8%) patients are stage 2 and 2 (6.3%) patients are stage 3. As a first-line approach, active monitoring for 10 (31.3%) patients; Chemotherapy was applied to 22 patients. No patient RT was applied. The follow-up period of the study is 43 (range 2-121) months. Median PFS is 37 (range 1-115) months. The 5-year PFS value is 80.5%. During the follow-up period, 4 (13.5%) of the patients were ex. The Median OS value is 42 (range 2-121) months, and the 5-year OS value is 88%. The relationship between the stage and the OS is meaningful.

**Conclusion:** According to the results of our study, elderly seminoma patients can be safely treated and cured. Since we encounter treatment-related mortality, modification may be needed in the treatment protocol and treatment doses according to the comorbidities of the patients.

**Keywords:** Geriatric patients, seminoma, testicular cancer

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Advanced age is a well-known risk factor for cancer development. Although 12% of cancer is seen at the age of 65 and above worldwide, when the total cancer population is evaluated, 60% of them are age 65 and above.[1-3]

In contrast to many other cancers, germ cell tumours (GCTs) are more common in younger people, especially those in their 2nd and 3rd decades. Patients with seminomas constitute 50–60% of all GCTs patients, but only 2% of patients with seminoma are 65 or older.[4-6]

As seminoma patients are very sensitive to radiotherapy and chemotherapy, a 90% cure rate can be achieved even in advanced-stage patients. However, the standard chemotherapy regimens applied according to the stage cannot be applied to geriatric seminoma patients due to age, performance and existing comorbidities. Inadequate application of treatment decreases the chances of success, but there is no standard approach to treatment of geriatric GCTs patients because the geriatric patient population is small and many clinical trials exclude these patients.

Our aim in our study is to share our follow-up and treatment experience with patients with very rare geriatric seminoma.

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## Methods

In our study, patients aged 65 and over who were diagnosed with testicular cancer between 07.09.1998-19.11.2018 in our center were evaluated retrospectively. Patient interview information, patient files and electronic system data were used for the study. Patients' demographic conditions, tumor localization, tumor size, stage and pathological parameters of the disease, treatment type, treatment response and final status were noted.

The primary endpoint is Overall survey (OS), Progression free survey (PFS). The diagnosis date has been accepted as the start date for OS and PFS. The last control date for patients experiencing endpoints for OS is the exitus date for those with ex. The first event date for recurrence and distant metastasis as the endpoint for PFS is the last control date for non-relapse patients. Patients over 65 years of age who were diagnosed with testicular cancer and whose information was fully available, according to AJCC 8, aged 1-3 are included in the study. Patients who received palliative treatment were excluded from the study. Patients with a missing file and follow-up information, under 65 years of age, and non-seminoma pathology were excluded from the study.

### Statistical Analysis

In our study, SPSS ver.26 was used. Conformity of variables to normal distribution was evaluated by visual and analysis methods and non-parametric tests were used since it was observed that it did not fit the normal distribution. The categorical demographic characteristics of the patients were calculated with Chi-square and Fisher's exact test. Spierman's rank correlation test was used for univariate correlation analysis. For statistical analysis of two independent groups, Mann-Whitney U test was performed with 3 or more independent group analyzes using Kruskall Wallis test and significance was evaluated by post hoc analysis after bonferoni correction. In the univariate survey analysis, Kaplan Meirer was used and compared with the log rank test. In multivariate analysis, Cox regression test was used. Statistical significance limit was accepted as 0.05 and below.

## Results

In the study, the data of 32 patients who were diagnosed between 07.09.1998-19.11.2018, who were diagnosed with stage 1-3, 1640 testicular cancer, and who were diagnosed with seminoma above 65 years of age, were evaluated retrospectively. The median age of the patients is 68 (range 65-85). All patients had seminoma pathology and all received orchiectomy. None of the patients received pelvic radiotherapy (RT), retroperitoneal lymph node dissection (RPLND), and metastasectomy. In addition, there was no need for second relapse, second salvage chemotherapy (CT) or autologous stem cell transfusion during the follow-up period. The mass is 14 (43.8%) right localized, 18 (56.3%) left localized. The median tumor size is 3 cm (range 1-8). Lymphovascular invasion (LVI) is present in 14 (43.8%) patients and not observed in 18 (56.3%) patients. Rete testicular invasion was present in 14 (43.8%) patients, but not in 18 (56.3%) patients. Two of the patients (6.3%) had solid organ metastasis (1 liver 1 lung); Six patients (20.1%) had paraaortic metastasis. No metastasis was observed in 24 (74.8%) patients. When staging at the moment of diagnosis, 24 (75%) patients were stage 1; 6 patients (18.8%) are stage 2 and 2 patients (6.3%) are stage 3. As a first-line approach, active monitoring for 10 (31.3%) patients; 1 cure carboplatin in 9 (28.1%) patients; 2 cycles of BEP (Bleomycin, Etoposide, Cisplatin) in 1 (3.1%) patient; 3 cycles of BEP for 3 (9.4%) patients; 4 cycles BEP for 2 (6.3%) patients; 4 cycles of VIP (Etoposide, Ifosfamide, Cisplatin) in 1 (3.1%) patient; RT was applied to 6 (18.7%) patients. The follow-up period of the study is 43 (range 2-121) months. Patient and treatment data are summarized in Table 1.

### Progression Free Survival Detailed Analysis:

The mean follow-up period of the patients was 43 (range 2-121) months. Recurrence/relapse was observed in 6 (18.8%) patients during this period. Recurrences were LN in 3 (50%) patients; Cerebral in 1 (16.7%) patient; Bone in 1 (16.7%) patient; In 1 (16.7%) patient, it is in the lung localization. Treatments for relapses are summarized in Table 1. Complete response (CR) was obtained in all patients and there was no need for second salvage CT. Median PFS is 37 (range 1-115) months (Fig. 1). The 3-year PFS value of the patients was 93.5%; The 5-year PFS value is 80.5%.

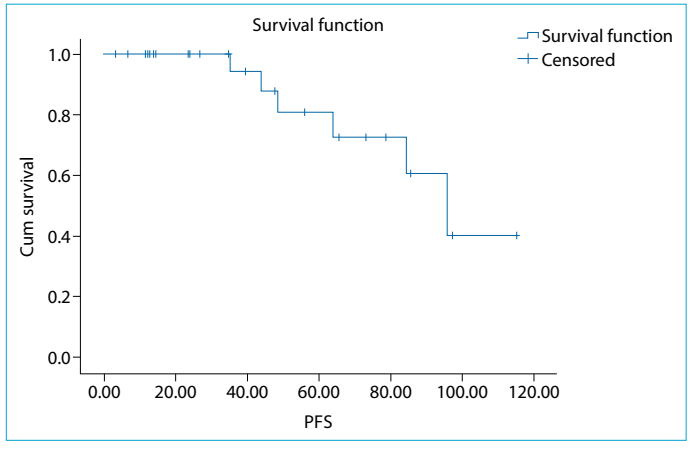


**Figure 1.** PFS analysis of patients.

**Table 1.** Patient demografics and treatment details

| | n (%) |
|---|---|
| Site | |
| Right | 14 (43.8) |
| Left | 18 (56.3) |
| LVI | |
| Presence | 14 (43.8) |
| Absence | 18 (56.3) |
| Rete testis invasion | |
| Presence | 14 (43.8) |
| Absence | 18 (56.3) |
| Metastasis | |
| Yes | 8 (25.2) |
| No | 24 (74.8) |
| Stage | |
| Stage 1 | 24 (74.8) |
| Stage 2 | 6 (18.8) |
| Stage 3 | 2 (6.4) |
| First Tx | |
| Observe | 10 (31.3) |
| RT | 6 (18.8) |
| CT | 16 (50) |
| Relapse | |
| Yes | 6 (20.7) |
| No | 26 (79.3) |
| Relapse site | |
| LN | 3 (50) |
| Brain | 1 (16.7) |
| Bone | 1 (16.7) |
| Lung | 1 (16.7) |
| Salvage CT prot | |
| 3cTIP | 1 (16.7) |
| 3cVIP | 1 (16.7) |
| 4cEP | 2 (33.3) |
| 4cVIP | 1 (16.7) |
| 2cTIP+RT | 1 (16.7) |
| Last status | |
| Ex | 4 (13.5) |
| Alive | 28 (86.5) |

The right side and the left side of the lesion did not significantly affect PFS (p=0.085) (Table 2). In addition, primary care (p=0.59); primary tumor size (p=0.40); LVI (p=0.52), rete testicular invasion (p=0.53), presence of metastasis at the time of diagnosis (p=0.12) were not significantly affected.

Although higher PFS is observed in stage 1, the difference is not significant (p=0.12) (Table 2).

## Overall Survival Detailed Analysis:

During the follow-up period, 4 (13.5%) of the patients were ex. Median OS value is 42 (range 2-121) months. The 3-year

**Table 2.** PFS-Localization and Stage relationship

| | PFS | p |
|---|---|---|
| Site | | |
| Left | 39 (6-115) | 0.085 |
| Rigt | 37 (1-97) | |
| Stage | | |
| Stage 1 | 37 (1-115) | 0.12 |
| Stage 2-3 | 36 (3-95) | |

**Table 3.** Recurrence and death relationship

| | Relapse | | p |
|---|---|---|---|
| | No | Yes | |
| Last status | | | |
| Alive | 23 (82.1%) | 5 (17.9%) | 0.58 |
| Ex | 3 (75%) | 1 (25%) | |

OS value of the patients is 94.1%; The 5-year OS value is 88% (Fig. 2).

The lesion side is right vs. left (p=0.69); LVI (p=0.32); rete testicular invasion (p=0.29); presence of metastasis at the time of diagnosis (p=0.33); stage (p=029), primary care (p=0.52); primary tumor size (p=0.31) was not significantly affected. In addition, salvage in patients with relapse was not significantly affected by the CT protocol (p=0.72).

The relationship between the stage and the OS is meaningful. Higher OS value was obtained in stage 1 patients.

When the relationship between relapse and deaths was evaluated, no significant relationship was detected (p=0.58) (Table 3), that is, deaths were not significantly associated with relapse, possibly due to comorbid diseases. Recurrence was not noted in 3 (75%) of 4 patients with ex.

When the side effects of the 22 patients were examined during chemotherapy and radiotherapy treatment, more than

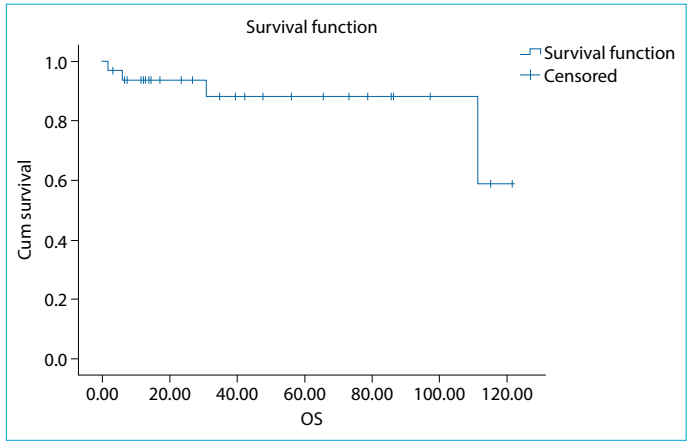


**Figure 2.** OS analysis of patients.

half (63.6%, n=14) of patients had leukopenia, almost all of the patients had anemia (86.3%, n=19) and the majority of the patients had thrombocytopenia (86.3%, n=19). Nearly all of patients (77.2%, n=17) had first- and second-degree nausea and vomiting. In addition, neurotoxicity was found in 68.1% (n=15) of the cases and 58.8% (n=10) was grade 2. Chemotherapy was continued with dose adjustment after side effects. Side effects management is provided easily. None of the patients died due to treatment-related side effects.

## Discussion

In the present study, we share our experience treating and following up with testicular seminoma patients aged 65 and over. Previous studies report that approximately 90% of patients who receive a GCT diagnosis are under 50 years old and only 2% of these patients are 65 years or older.[7,8] Although GCTs are most common in patients between the ages of 20 and 35, their incidence is increasing in older people. In a pathological review, Berney et al.[9] found that 82% of 50 patients with a median age of 67 were seminoma patients. In our study, testicular seminoma patients over the age of 65 made up 1.95% of all GCT patients.

In a study in which 60 patients over the age of 60 with testicular GCTs were evaluated retrospectively,[10] 77% of patients had stage 1 disease. Other retrospective studies conducted in elderly GCT patients observed that elderly patients with stage 1 disease were more common than younger patients.[8,11] When the patients in our study were evaluated by stage, we determine that stage 1, 2 and 3 patients were 75%, 18.8% and 6.3%, respectively. In addition, according to SEER data in geriatric testicular seminoma patients, the distribution of patients according to stage 1, 2 and 3 is 85.8%, 7.2%, and 5.5%, respectively.[8]

Systemic chemotherapy data applied to elderly patients diagnosed with GCTs is very limited, since elderly patients cannot be included in prospective studies and retrospective patient series are also limited.[10] In our study, 22 patients received chemotherapy. In retrospective studies, because of there is an increase in the frequency of side effects, comorbidities, organ dysfunctions and low tolerance of chemotherapy, causes dose decreases in clinicians' chemotherapy application.[12-14] In our study, only 18.8% of patients developed recurrence after first-line treatment, and a full response was obtained in all patients after one-step salvage treatment. The studies in the literature show that the rate of recurrence varies from 3.4% to 20% depending on the stage.[15]

The five-year relapse-free survival rate was reported to be 95% in the study conducted by Haugnes et al.[15] The relapse-free rate as reported to be 92.6% in the study conducted by Tandstad et al.[16] In our study, the three-year PFS value of the patients was 93.5%, and the five-year PFS value was 80.5%. All age groups are included in these results. Until now, the literature data could not be compared clearly since there were no data on progression-free survival results in elderly patients.

Darren et al.[17] observed the four-year cancer-specific survival rate to be 85.8% in studies involving patients aged 50 and over diagnosed with GCTs, supporting the results of this study and those of other previous studies in the literature.[18-20] In our study, the three-year OS value of the patients was 94.1%, and the 5-year OS value was 88%. Our results are consistent with the literature.

In our study, there was no patient loss due to treatment complications. The most common side effect was haematological, and other manageable side effects were observed.

The weak point of the study is that this is a retrospective study in a rare group of patients. In addition, the cause of death of two patients who died in the first and third months after diagnosis is unknown. When conducting oncological evaluations in the geriatric patient population, evaluating whether patients' comorbidity and deaths are related to oncological disease will contribute to better results. The strength of the study is that it was performed in a single patient group in a single centre. It is the first study in the literature in which geriatric testicular seminoma patients were evaluated alone.

The present study shows that when older patients with testicular seminoma are evaluated, their physiological fitness and chemotherapy tolerance are more important than their age. If the performance of the patients is fit, they can receive treatment like young patients. Other studies in the literature support these results.[21]

## Conclusion

According to the results of our study, elderly seminoma patients can be safely treated and cured. Since we encounter treatment-related mortality, modification may be needed in the treatment protocol and treatment doses according to the comorbidities of the patients. Prospective studies comparing old and young seminom patients are needed to correctly interpret the survival data we obtained in older patients.

### Disclosures

**Ethics Committee Approval:** The study was approved by the Ethics Committee of Gulhane Training Research Hospital 22.10.2019-19/354.

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

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – N.K., B.Y.; Design – N.K.; Supervision – N.K.; Materials – B.Y.; Data collection &/or processing – B.Y.; Analysis and/or interpretation – N.K., B.Y.; Literature search – B.Y.; Writing – N.K., B.Y.; Critical review – N.K.,B.Y.

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