EXPERIENCE OF TESTICULAR CANCER PATIENT LONG TERM FOLLOW-UP IN TERTIARY REFERRAL HOSPITAL

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ABSTRACT

Objective: *This study aims to determine the survivability testicular cancer patients at a tertiary hospital in Malang, Indonesia.* ***Material & Methods:*** *This is study conducted from January 2021 to January 2022 at Saiful Anwar General Hospital in Malang, East Java. Involving 32 testicular cancer patients. Data was obtained through medical record January 2017 – January 2022. Analysis was carried out to determine the survivability of the patient.* ***Results:*** *The results showed that the proportion of 1 to 5 year survival rate in testicular cancer patients was 96% and 21%. Kaplan Meier test showed significant difference of patient survival in the radiation therapy exposure (p=0.021), Karnofsky score (p=0.010), tumour type (p=0.019), and response of chemotherapy (p=0.015).* ***Conclusion:*** *The survival rate of testicular cancer patients are strongly influenced by the karnofsky score, radiation therapy exposure, tumour type, and chemotherapy response. Therefore early diagnosis and treatment plays an important role in improving survival rate of the patients.*

Keywords: *Testicular cancer, survival rate, seminoma, non seminoma.*

ABSTRAK

Tujuan: *Penelitian ini bertujuan untuk mengetahui tingkat ketahanan hidup pasien kanker testis di rumah sakit tersier di Malang, Indonesia.* ***Bahan & Cara:*** *Penelitian ini dilaksanakan pada Januari 2021 – Januari 2022 di Rumah Sakit Umum dr Saiful Anwar Malang, Jawa Timur dan melibatkan 32 pasien dengan kanker testis. Data diambil dari rekam medis dari Januari 2017 – Januari 2022. Dilakukan analisa data untuk menentukan tingkat ketahanan hidup pasien.* ***Hasil:*** *Hasil penelitian menunjukkan proporsi ketahanan hidup 1 dan 5 tahun pada pasien kanker testis ialah sebesar 96% dan 21%. Hasil uji Kaplan Meier menunjukkan bahwa adanya perbedaan yang signifikan pada ketahanan hidup pasien pada variabel skor Karnofsky (p=0.010), respon kemoterapi (p=0.015), dan kategori jenis tumour (p=0.019), paparan terapi radiasi (p=0.021).* ***Simpulan:*** *Proporsi ketahanan hidup pada pasien kanker testis sangat dipengaruhi oleh respon kemoterapi, paparan terapi radiasi, jenis tumor, karnofsky score. Maka dari itu deteksi dini dan penanganan secara cepat memiliki peranan penting dalam meningkatkan ketahanan hidup pasien.*

Kata Kunci: *Kanker testis, ketahanan hidup, seminoma, nonseminoma.*

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INTRODUCTION

Testicular cancer is one of the most prevalent malignancies found in young adult men with an ever-increasing incidence. Even so, the incidence of this cancer as a whole is quite rare, accounting for 1% of all cancers in men.[1]

Germ cell neoplasia in situ (GCNIS) as been described as a precursor lesion in malignant testicular germ cell tumours (TGCTs).[2] Males between the ages of 25 and 39 had the greatest incidence rate of testicular cancer overall. Factors that influence the incidence include ethnicity or race, with the highest rates being found in Scandinavians and Caucasians and lower rates in Africans and Asians. The 5-year survival rate for testicular cancer can reach 90% with the right current treatment.[3] Germ cell tumours arise from malignant transformation of the primordial germ cell pool. Under normal development circumstances, these cells will divide to become oocytes in females and spermatogenia in males.[4] Cryptorchidism, family history, and a prior diagnosis of testicular cancer are a few of the risk factors connected to testicular camcer. According to a meta-analysis, there is also a prenatal risk factors for testicular cancer that

includes inguinal hernia, gemelli, and bleeding during pregnancy.[2]

Testicular germ cell cancers are generally classified into 2 groups, namely seminomas and non-seminomas. Malignant cells in the seminoma group resemble primordial germ cells greatly and are distinguished by the malignant proliferation of clones of primordial germ cells. As for the nonseminone category, it includes several different subtypes and usually consists of a mixture of several cell types either with or without a seminose component. Seminoma tumours grow more slowly and have a better prognosis than the nonseminoma group, which is another distinction that can be made between the two groups. Seminomas are moreover extremely sensitive to radiation. In comparison to the seminoma group, the nonseminoma group exhibited greater levels of aggression and a faster pace of tumour growth. This contributes to the nonseminoma tumour incidence being higher in the age group of 25 to 29 years compared to the seminoma group in the age group of 35 to 39 years.[5] Data regarding the survival of testicular cancer patients and the factors that influence it are still very limited. Therefore, this study aims to determine the survival rate of testicular cancer patients, both seminomas and nonseminomas, at tertiary hospitals in Malang, East Java,

OBJECTIVE

The purpose of this retrospective study was to determine the survival rate of testicular cancer patients in both the seminoma and non-seminoma groups against factors that influenced, among others, age, Karnofsky score, stage, TNM staging, whether they received radiation or not, and response to chemotherapy.

MATERIAL & METHODS

This was a retrospective study carried out at the Dr. Saiful Anwar Malang Regional General Hospital in East Java between January and July 2022. From January 2017 to January 2022, patient data was obtained retrospectively from medical record databases. The inclusion criteria were met by a total of 32 patients, all of whom had testicular cancer, seminoma or non-seminoma. Every patient had an orchidectomy. Age, TNM stage, history of chemotherapy, and history of therapy were all collected data from medical records. then used SPSS version 26 for Windows to perform data analysis.

RESULTS

A total of 32 patients were reviewed, and 9 individuals dropped out for various reasons. So, 23 people took part in the survey by the time it was over.

Table 1. Event data for Testicular Cancer.

	Events	Censored	Total
Age			
<35 years old	9	4	13
≥35 years old	6	4	10
Karnofsky Score			
<80	7	1	8
≥80	8	7	15
Stadium			
IA	0	1	1
IIB	1	0	1
IIIB	5	2	7
IIC	1	1	2
IIIC	8	4	12
Radiation Exposure			
Positif	1	5	6
Negatif	14	3	17
Chemotherapy Response			
Complete	3	7	10
Partial	1	0	1
Stable disease	5	0	5
Progressive disease	6	1	7
Tumour Type			
Non Seminoma	12	1	13
Seminoma	3	7	10

The Kaplan Meier Curve illustrates how the survival rate declines over time in response to the time of observation and the likelihood of an event (patient death). The Kaplan Meier survival curve is used to determine the survival characteristics of testicular cancer patients based on factors that are thought to influence patient survival, including: age, Karnofsky score, cancer stage, radiation exposure, chemotherapy response, and tumour type category. With a survival percentage of 21% from 96% at the beginning of the observation, the time parameter employed is based on days beginning in January 2017 and ending in January 2022 (Figure 1).

As seen in Figure 2 of the graph, the red line is lower than the blue line, indicating that patients aged ≥ 35 have a higher death rate than patients <35 tahun. The median survival rate (50% of respondents died) at age <35 years was 928 days and at age ≥ 35 years was 178 days.

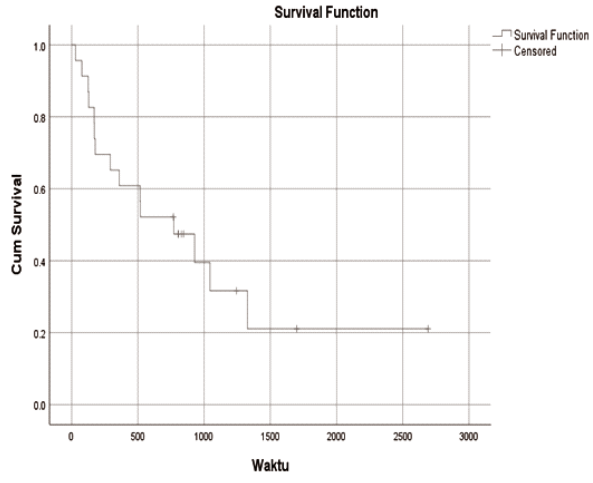

Figure 1. Survival proportion in testicular cancer patients

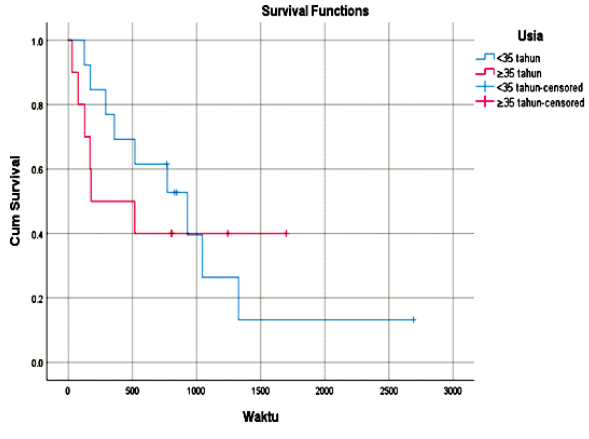

Figure 2. Survival proportion in testicular cancer patients based on age.

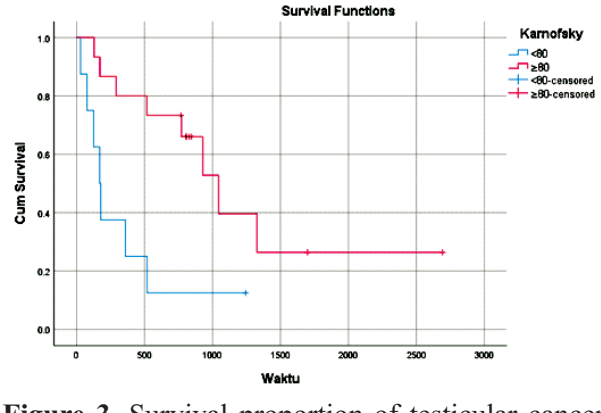

Figure 3. Survival proportion of testicular cancer patients based on the karnofsky score

Figure 3 of demonstrates that the blue line is below the red line, indicating that patients with a Karnofsky score below 80 have a higher mortality risk than patients with a Karnofsky score over 80, with median survival rate of 50% in respondents who passed away.

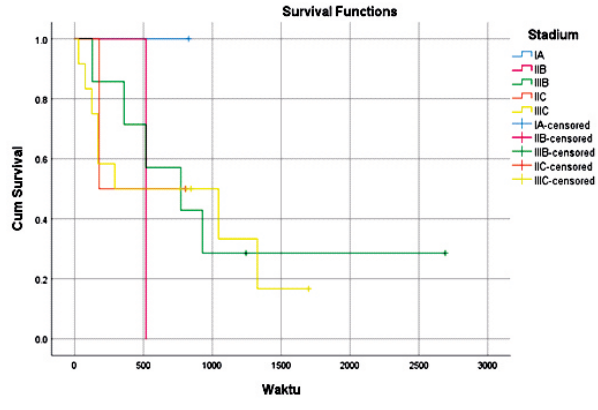

Figure 4. Survival proportion of testicular cancer patients based on cancer stage.

The yellow line is shown on the chart in Figure 4 to be lower than the other lines. This demonstrates that stage III C patients had a higher death rate than patients in other stages. It is assumed that there is no variation in the survival curve between the variable groups because the curves in Figure 4 appear to coincide or be near to one another. There was one patient with stage IA and one with censorship, and one with stage IIB and one with events (died). So that the median survival rate is not obtained. There were 7 patients in the stage IIIB group, including 2 censored patients and 5 event patients (patients who passed away). Patients with stage IIIB have a 928-day survival rate. There were 2 patients in the stage IIC group, 1 of whom passed away and 1 of whom was censored. Patients in stage IIIB have a 178-day survival rate. There were 12 stage IIIC patients in the cohort, including 4 censored patients and 8 event patients (patients who passed away). Patients with stage IIIC have a 1327-day survival rate.

The red line is below the blue line in Figure 5 of the graph, indicating that patients who do not receive radiation exposure die at a higher rate than those who do. The median survival time for individuals who did not receive radiation exposure was 359 days, with 50% of them passing away. The median survival rate for patients who experienced

events (died) was absent for respondents who had radiation exposure, with just 1 patient passing away at 517 days.

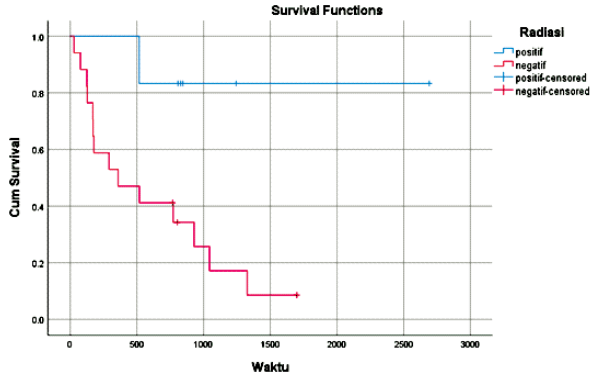

Figure 5. Survival proportion of testicular cancer patients based on radiation exposure.

The green line in Figure 6 of the graph is lower than the other lines, indicating that stable chemotherapy responses have a greater mortality rate than other chemotherapy responses. With regard to respondents who responded to partial therapy, stable therapy, and progressive therapy, the median survival rate (50 percent of respondents died) was 519 days, 170 days, and 359 days, respectively.

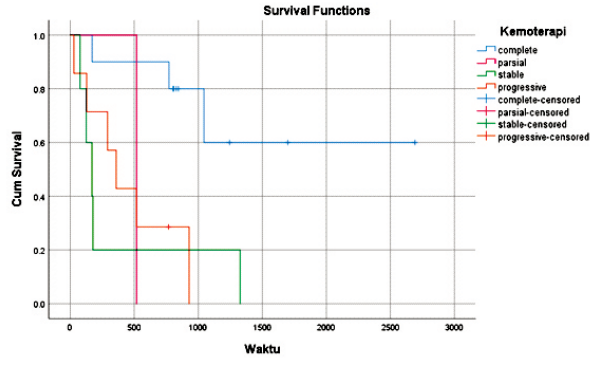

Figure 6. Survival proportion of testicular cancer patients based on chemotherapy response.

The blue line on the graph in Figure 7 is below the red line, indicating that the death rate of patients in the non-seminoma cancer group is higher than patients with seminoma cancer group. The median survival rate (50% of respondents died) in the non-seminoma group was 517 days.

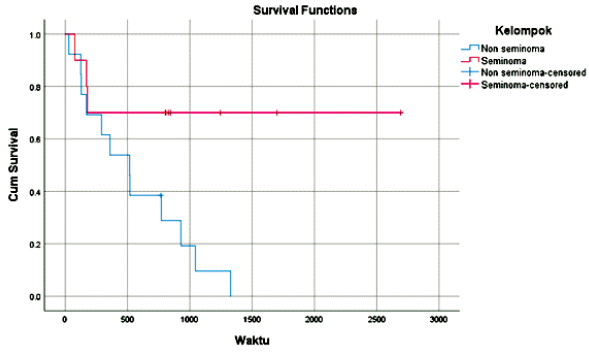

Figure 7. Survival proportion of testicular cancer patients by type of tumour.

Furthermore, to support the hypothesis on the Kaplan Meier Survival Rate curve that has been presented, it is necessary to carry out the Log Rank test. This test is used to determine whether there is a significant difference between the survival curves within the group on each factor variable. Table 2 presents the results of the Log Rank test based on the factors thought to influence testicular cancer patients.

Table 2. Log rank test.

Variables	Log Rank	Df	p-value
Age	0.098	1	0.755
Karnofsky Score	6.653	1	0.010*
Cancer Stage	1.059	4	0.901
Radiation Exposure	5.327	1	0.021*
Chemotherapy Response	10.495	3	0.015*
Tumour Type	5.525	1	0.019*

Note: * = statistically significant

The results of the Log Rank test (Table 4) show that the survival rate of patients with testicular cancer differs considerably depending on the Karnofsky score, radiation exposure, chemotherapy response, and tumour category because the p-values for these four variables are less than 0.05. Meanwhile, there were no significant differences in testicular cancer patient survival rates according to age or cancer stage (p>0.05).

DISCUSSION

Several studies have suggested that the survival of testicular cancer patients is quite high with a 5-year relative survival rate of more than 90%. However, it was also mentioned that there were

differences regarding the survival of men with different ethnicities.[6] According to Wei Dong et al., the seminoma testicular cancer survival rates at 3, 5, and 10 years were 94.8%, 86.2%, and 70.7%, respectively, indicating a comparatively good survival rate with proper therapy. appropriate. Orchiectomy is the primary therapy for testicular cancer.[3]

DeRouen et al suggested that the survival rate of younger patients was higher than that of patients diagnosed at an older age. At an early age, they have less comorbidities, which is a factor that could have an impact.[7] This is similar to this study, where the age group >35 years had lower survival rates than the group <35 years. According to earlier studies, older age groups were found to have lower relative testicular cancer survival rates than younger age groups. In contrast, aging beyond 40 dramatically increased testicular cancer mortality in research by Fossa et al. by up to two times. Several factors contributed to this, including suboptimal therapy, comorbidities, low tolerance to chemotherapy, tumour characteristics and biological behavior that different at older ages.[8]

Testicular cancer in stage I presents substantially more frequently than other stages, between 70 and 85%.[9] Due to the extremely limited number of patients participated in this study-stage I patients accounted for just one-variables related to patient survival by stage could not be assessed. The clinical stage of seminoma cancer does, however, have a significant impact on the prognosis. According to Daugaard et al, stage I nonseminoma testicular cancer patients who underwent orchidectomy and retroperitoneal lymph node dissection had survival rates of 99.3%, 99.3%, and 99.1% at 5, 10, and 15 years, respectively, with relapse rates of 1.6% in 5 years.[8] The patient's survival rate declines with increasing clinical stage. According to the report by Wei Dong et al., stage I had a 5-year survival rate of 94.15 percent, stage II of 87.5 percent, and stage III of 66.7 percent.[10]

As a result of improvements in this therapy, there have been numerous innovations in the treatment of testicular cancer.[3] Radiotherapy has become the standard therapy for seminoma testicular cancer, especially in stages I, IIA, and IIB. Recurrence risk is also decreased by postoperative radiotherapy.[9] These findings supported that in this trial, patients who did not receive radiation therapy had a greater mortality rate than those who did. With a suggested dose of 16-20 Gy, scrotal radiation therapy inhibited the progression of stem cell neoplasia. Leydig cell function can still be preserved with doses under 20 Gy, but the cure rate is reduced. It should be noted that radiation therapy also eliminates healthy stem cells.[11] In this study, patients who did not receive radiation therapy had a higher mortality rate. In addition to radiation therapy itself, another potential contributing factor is that only patients with stages I, IIA, and IIB are advised to receive radiation therapy.[12]

Depending on the risk group as determined by the IGCCCCG prognostic factor classification, the BEP regimen, a first-line combination regimen, is administered for 3 to 4 cycles. In this study, the group of patients with stable disease had the highest rates of survival when compared to other patient groups. A number of trials have shown that changing some of the drug's active ingredients or increasing the dosage of ifosfamide and etoposide can improve overall survival by 50-60%.[13] BEP cycles of at least 2 cycles also provide a recurrence rate that is lower than 4%, so giving BEP can be the right strategy to prevent recurrences.[10] Regimen of cisplatin or carboplatin as a neo adjuvant can reduce the risk of bilateral tumours and relapse.[7]

Additionally, it was discovered in this study that patients with a Karnofsky score ≥ 80 had a greater likelihood of survival. The Karnofsky score is a global assessment to evaluate the patient's performance status in carrying out daily functions. The major survival rate for cancer patients and the Karnofsky score are known to be correlated.[14] The Karnofsky score is a predictor of survival which is directly proportional with the survival rate. The higher the Karnofsky score (≥ 50%), the longer the median survival time.[13] Reports regarding the effect of the Karnofsky score on survival rates are still very limited, but the results in this study are similar to previous studies demonstrating that the Karnofsky score significantly affects the survival rate of patients with cancer.[14]

Seminomas typically have a better outlook prognosis, metastasis less frequently, and can typically be treated with just surgery. However, because of their increased susceptibility for metastases, the nonseminone group needs more intensive care. The nonseminoma group also experienced a higher rate of relapse.[9] The results of this study are also in accordance with a study by Robinson from 2007 in which seminoma-positive patients had a better prognosis than non-seminoma-positive individuals.[15] To assess the risk of a relapse

in 5-10 years, testicular cancer patients need to be monitored.[5]

There are several limitations in this study, this study has a number of limitations, including the relatively small sample size, the omission of other variables that could be confounding factors, such as the patient's socioeconomic status, which can influence patient's life style and nutritional status, and the occurrence of the COVID-19 pandemic through 2020 and 2021.

CONCLUSION

Testicular cancer survival rates continue to increase as therapy evolves. Testicular cancer survival rates continue to increase as therapy evolves. Several factors related to survival rates in testicular cancer patients in this study were the Karnofsky score, radiation therapy, chemotherapy response, and tumor type, seminoma or nonseminoma. Therefore, early detection and management have a very important role to increase theare crucial for improving the survival rate of patients with testicular cancer.

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