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Demographics and Outcomes of Testicular Tumors in Patients Treated at King Faisal Specialist Hospital and Research Centre, Riyadh

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ABSTRACT

Testicular cancer is a relatively rare but significant malignancy, primarily affecting males between the ages of 15 and 35. The incidence and epidemiological patterns of testicular cancer vary across different geographic regions. This study aims to describe the demographics and outcomes of testicular tumors in patients treated in a tertiary setting at King Faisal Specialist Hospital and Research Centre in Riyadh. This retrospective cohort study was conducted at King Faisal Specialist Hospital and Research Centre (KFSHRC), focusing on patients across various regions in the kingdom from 2000 to 2017. The research offers a comprehensive retrospective analysis. The records of 125 males diagnosed and treated with testicular cancers with an age bracket of 14-35 years were examined. It was observed that males aged 26-35 showed the highest rate of incidence of testicular cancer. The primary differences between the progression of seminomas and nonseminomas are explored, with the latter comprising diverse subtypes such as yolk sac tumors, teratomas, embryonal carcinomas, and choriocarcinomas. This research studied patient demographics, clinical presentations, histopathological patterns, treatment modalities, and associated complications. Apart from stage 3 cases, the present research found consistency in survival outcomes, recurrence rates, and risk variables across locations. This retrospective cohort study challenges long-held beliefs and offers new insight into the treatment and prognosis of patients with testicular cancer at the KFSHRC. This study is significant because it has the potential to influence future methods of treating testicular cancer and advance knowledge of the subtleties and regional variations of the illness, which is beneficial for both patients and healthcare professionals.

INTRODUCTION

Testicular germ cell tumors are the most common types of testicular cancers and contribute to a total of 90% of testes cancer (Bahrami *et al.*, 2007). Testicular tumors account for only 1% of all cancers in men and around 5% of all urological cancers (Siegel *et al.*, 2018). Testicular cancers normally occur in patients with ages ranging from 15 years to 35 years.

The incidence and epidemiological patterns of testicular cancer vary across different geographic regions. American Cancer Society (ACS) has reported that 9910 newly diagnosed patients of testicular tumors in the year 2022, out of which 460 are residents of the USA (Alghamdi, 2023). The International Agency for Research on Cancer (IARC) has reported s that the age-standardized incident rate for testicular cancer in men in Saudi Arabia is around 0.8 cases per 100,000 people (S, 2007).

Nearly 440 deaths were predicted to occur due to testicular cancer in the USA, with a survival rate as high as 95% and five years of lifespan in the year 2017 (Gilligan *et al.*, 2019). The frequency of prevalence of testicular cancer is highly dependent on the geographic locations of susceptible cases (Huyghe *et al.*, 2003). European countries have shown the highest age-standardized incident rates, up to 6.3% (Shanmugalingam *et al.*, 2013). Notably, regions of the USA, such as North American countries, have also given significant age-standardized incident rates of about 5.1%, and Latin America and the Caribbean have incident rates of 4.4% (Nigam *et al.*, 2015). In comparison, Asian and African countries have the lowest age-standardized incident rates of 0.77% and 0.34% (Wang *et al.*, 2021).

The incidence of Germ Cell Tumors appears to be increasing worldwide. In the United States, the age-dependent prevalence frequency for puberty hitting boys and men 15 to 49 years old accelerated from 2.5 to 5.1 per 100000 people in the year 2004 (Bleyer, 2007). Meanwhile, the growth rate of seminomas was exponential concerning seminomas germ cell tumors.

The focused study aims to fulfill the research gap that proves that there is comparatively limited data available on the prevalence of testicular cancer in Saudi Arabia.

The present retrospective cohort study aimed to perform an extensive analysis of testicular tumors in residents of Saudi Arabia whom King Faisal Specialist Hospital and Research Centre have treated. The present research examined incidence rate, prevalence trends, patient management and its outcomes, and the progression-free survival of patients.

MATERIALS AND METHODS

Study Design and Setting

The study is a retrospective cohort study of pre-existing data. All participants of this study are patients who were diagnosed or had received treatment for a testicular tumor in the King Faisal Specialist Hospital & Research

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Center (KFSHRC). The retrospective cohort study covers multiple clinical aspects, including histological types of the tumor, the staging of the cancer, and the mode of treatments employed for those cases that were treated. The current study has also included radiographic imaging of the tumor and tumor markers. Case records that were incomplete or lacked essential data were excluded. Only those patients who were residents of Saudi Arabia and were diagnosed and treated at King Faisal Specialist Hospital & Research Center (KFSHRC) were included in the study.

Participants

The study included a total of 125 patients; all the patients underwent orchiectomy surgery as a treatment. The participants were categorized as one main group and had four sub-groups. The main group comprises residents of Riyadh and those living outside Riyadh.

Our study included 1 main group and 4 subgroups. The main group compared patients living in Riyadh with those residing outside Riyadh. The sub-groups are formed based on the recurrence of cancer, the pathology type of cancer, the progression or the risk factor of the tumors, and the stage of the tumors.

Data source and variables

The medical records of patients, including the demographic data and all the data regarding the pathological type of tumors, the rate of recurrence of the tumors, and the progression of the disease, were retrieved from the reported data of the Research Centre. The symptoms and their appearances, the treatment procedure and their impacts, and the progression-free survival rate were directly obtained from the clinical data present in the repository of the research center. The factors used to narrow down the data included the age of patients, who were classified into sub-groups; patients aged 25-65 were included. The demographic data was also categorized into subgroups of patients living in Riyadh and outside Riyadh. Data from patients across different kingdom regions with testicular cancer treated at King Faisal Specialist Hospital & Research Center (KFSHRC) were analyzed to study the pattern of testicular tumors and management outcomes in tertiary care hospitals in many regions of Saudi Arabia.

Data Analysis

The Kaplan-Meier method was applied to calculate survival curves, and the log-rank test was used to compare them. All the statistical data were studied using SPSS version 13.0 (SPSS Inc.Chicago, IL, US), and the standard deviation were calculated for the demographic characters of the population. The two-tailed unpaired or paired Student's t-test was used to determine the statistical variation between the sub-groups.

Statistical Considerations

The study's main goal was the rate of cancer-specific survival (CSS), calculated by the interval between the moment surgery is completed and the time of death or last follow-up. Another critical parameter of the research was recurrence-free survival (RFS), calculated by studying the interval between the surgery date and tumor recurrence. The third main parameter of the study, called Overall survival (OS), was calculated from the period of surgery to the time of mortality. The fourth parameter analyzed was the Thirty-day mortality. It represents any death that happened within 30 days after radical orchiectomy. The P values $P < 0.05$ for all tests were considered significant.

Ethical Considerations

Ethical approval was taken from the hospital's Institutional Review Board (IRB). Ensuring anonymity and secrecy is the top concern when discussing and publishing our results. Participants' private information is kept private, protecting their right to privacy and following the protocol according to ethical guidelines.

RESULTS AND DISCUSSIONS

Analysis of Survival Curve Analysis

The study used a chi-square homogeneity test to find the difference between the survival rate of patients living in Riyadh and those residing outside Riyadh. The relation between these variables was non-significant 1, $X2$ (1, $N = 125$) = 0.97, $p=0.32$, and the survival curve showed no difference in overall survival. Nonetheless, there was a difference in survival between seminoma and NSGT; the test was marginally significant at $X2$ (1, $N = 125$) = 3.14, $p=0.07$. Moreover, the overall survival between patients with undescended and normal testis showed no difference, and the test was not significant $X2$ (1, $N = 125$) = 0.25, $p=0.6$. Finally, survival rate by stage presentation showed no difference in the overall testicular cancer stage groups 1A-2C presentation except for group 3, which had the worst prognosis, and the test was marginally significant $X2$ (6, $N = 125$) = 11.68, $p=0.06$.

Patients Characteristics

The present research included a total of 125 patients who were diagnosed and treated at King Faisal Specialist Hospital & Research Center (KFSHRC) between 2010-2017. All these patients suffered from two different pathologies, including non-seminomatous germ cell tumors (NSGCT) and seminomatous germ cell tumors. Patient characteristics are shown in the figures below. The median age was 33 (range: 28–40 yr). Figure 1 shows that the highest ratio of patients affected by testicular cancer lies in the age bracket of 26-35 years. One reason behind this could be the presence of seminomatous germ cell tumors, which commonly affect men in their thirties and above. The second highest number of patients noted was 0-25 years old; these patients are more likely to be affected by non-seminomatous germ cell tumors. 9.60% of patients were 46-55, while patients in their late fifties and early sixties constituted only 4%. Patients in their late sixties were countable as they accounted for less than 1% of the whole selected population.

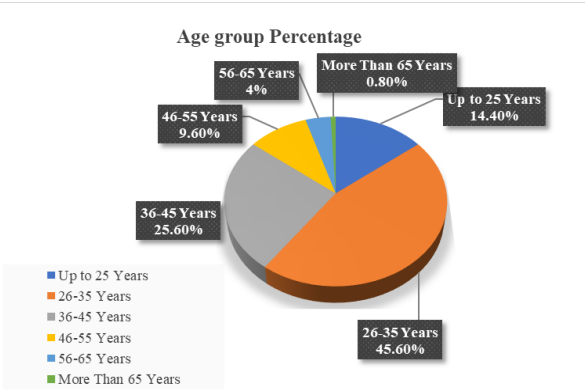

Figure 1: Age ratio of patients affected by testicular cancer.

Types of Pathologies

Seventy-three out of a total of 125 patients were affected by non-seminomatous germ cell tumors (NSGCT). Of those 73 patients, nearly 54 were affected by mixed germ cell tumors. It was also seen that almost 52 recorded cases were affected by seminomas. The line graph in Figure 3 shows the survival probability of patients affected by the non-seminomatous germ cell tumor (NSGCT) and seminomatous germ cell tumor. Seminoma survival rates are higher than other testicular germ cell tumor forms, as indicated by the curve representing this tumor type. The high survival rate for seminomas is because, compared to other forms of testicular germ cell tumors, seminomas usually show less aggressive behavior. The survival probability declines with time, as seen by the curves for each of the three groups. The decline in survival probability is because some cancer patients still pass away after receiving treatment. The degree of overall survival decreases over time. Figure 2 shows an examination of survival curves reveals a noteworthy distinction in overall survival between seminoma and other germ cell cancers.

Demographic characteristics

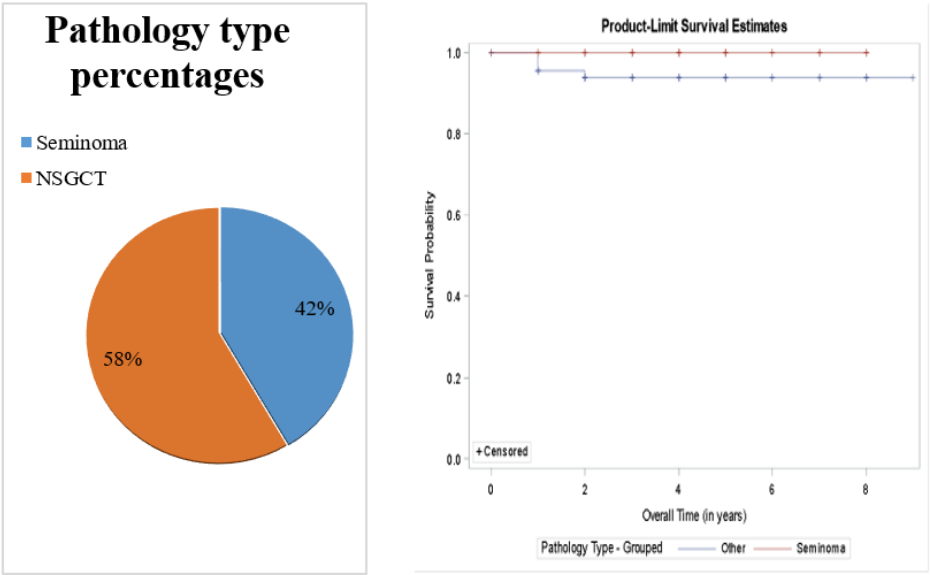

Figure 2: Survival curves between seminoma and other germ cell cancers.

Analysis of patients' demographic data showed that nearly 50% of included patients were residents of Riyadh. Almost 12% belonged to the northern province, while nearly 10% of the cases were reported from the eastern province. Jawf and Tabuk showed the lowest cases, i.e., only 0.8%. Figure 4 depicts a difference in survival between the two groups: the group living in Riyadh has a higher probability of survival than those living in other regions. This high survival probability could be due to several factors, such as healthcare access or lifestyle differences. The likelihood of survival is high in the first few years following surgery, but it then starts to decline. According to the survival curve study, figure 3 shows no overall survival difference between Riyadh and other places.

Most patients, i.e., 29.6% included patients, were diagnosed and treated at stage 1A, and 8.8% were diagnosed at stage. At stage 3, the worst progression was seen, and nearly 25.6% patients of total patients suffered through it. This worst progression can be due to the aggressive nature of non-seminomatous germ cell tumors (NSGCT). At the end of the study, 6(4.8%) patients had recurrence, 4(3.2%) passed away due to disease, and 115(92%) were in remission.

Risk Factor- cryptorchidism

In the case of patients with testicular cancer, undescended testis appeared to be a prominent risk factor. The graph in Figure 5 shows that the probability of survival is lower for people who have been affected by an undescended testis condition than for people who have not been exposed to any such risk factor. Patients with any history of undescended testis are likely to develop testicular cancer. Figure 5 shows no discernible difference in overall

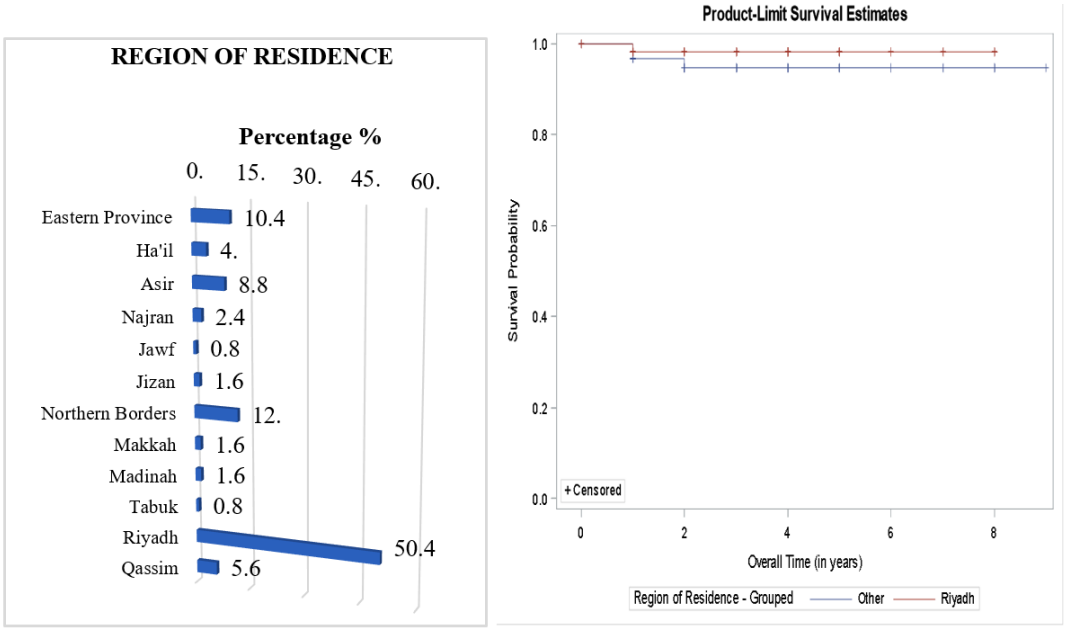

Figure 3: survival difference between Riyadh and other places

survival between patients with descending testicles and those without, according to survival curve analysis.

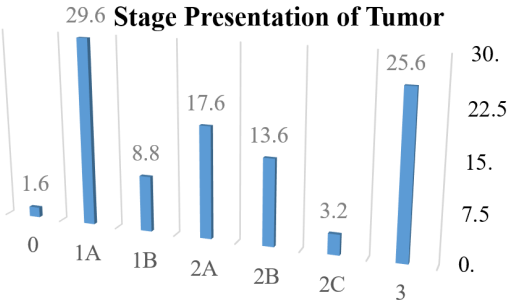

Figure 4: Stage Presentation of tumor

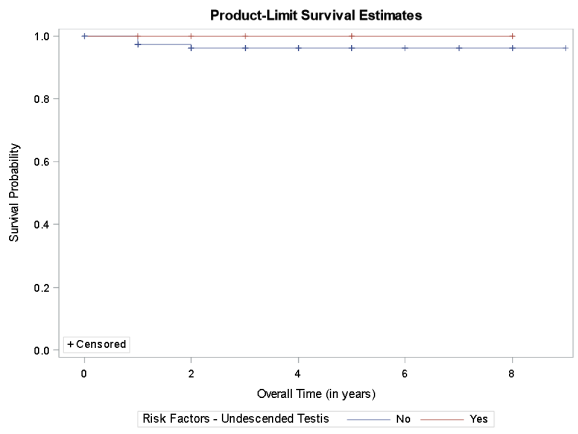

Figure 5: Survival curve analysis shows no significant difference in overall survival between patients with descending testicles and those without.

Discussion

Testicular cancer is a malignant tumor associated with the testicles, which are the primary components of the male genitals. Testicles are primarily responsible for the production of sperm; they also regulate hormonal balance as they are responsible for the release of testosterone. Testicular cancer usually occurs between the ages of 15 and 35. Testicular cancer is common in young men, and it can be easily diagnosed by self-examination of the testicles and the tumor can be cured by surgery if diagnosed early (Altunkurek, 2020). The degree of incidence of testicular cancer highly depends upon factors such as demographic locations, age, multiple types of pathology, and congenital disabilities such as cryptorchidism, which act as major risk factors (Yazici *et al.*, 2023).

The reported cases of testicular cancers globally are approximately 78400, making it the 20th most prevalent cancer (Safiri *et al.*, 2023). Testicular cancer showed an interesting trend in terms of demographic locations; it was seen that more than 62 nations worldwide were affected (Bray *et al.*, 2013), with the highest rate in West, North, and South Europe, Oceania, and North America. The continents that are less developed, such as Asia and Africa, showed the lowest rate (Giona, 2022). The rate of incidence of testicular cancer in Saudi Arabia has been accelerated in the last decades (Abomelha, 2017). As per the Saudi Cancer Registry (SCR), in 2017, the total reported cases reached the figure of 8850 new cases, and the death toll reached an approximate number of 410 (Baird *et al.*, 2018). In Europe, the survival rate shown by testicular cancer is 95% per person, which to date is the highest recorded survival rate for any cancer occurring in men (Znaor *et al.*, 2020).

There are many risk factors contributing to testicular cancer in men, such as smoking, undescended testis, family history, and infertility. The major risk posing factor is cryptorchidism, or the condition of having an undescended testicle. Patients with this condition are more likely to get testicular cancer compared to others (Ergül *et al.*, 2024). Patients having genetic conditions such as Klinefelter syndrome can raise a person's chance

of acquiring testicular cancer (Swerdlow *et al*., 2006). In case of genetic mutation such as those in the KITLG gene also increases the risk of developing testicular cancer (Pyle *et al*., 2024). It can relapse in men who have been affected previously by testicular cancer in either testicle. The study has shown that the age bracket mostly affected by testicular cancer ranges from 15-35, so men at this age are most prone (Franco *et al*., 2023). One of the main reasons why European and American nations have shown the highest rate of incidence for testicular cancer is the fact that white men are more prone to this cancer compared to other ethnicities (Ghazarian *et al*., 2015). Environmental factors also play a role in the prevalence of testicular cancer. Studies have shown that exposure to toxins such as endocrine-disrupting chemicals (EDCs) during pregnancy and the early stages of life increases the risk factor of acquiring testicular cancer (Cannarella *et al*., 2023).

Seminomas and nonseminomas (NSGCTs) are the primary germ cell tumors, accounting for most testicular malignancies. Because NSGCTs grow more quickly and are generally more aggressive, postoperative care is frequently needed (Siddiqui *et al*., 2020). Seminomas may not require further procedures since they grow more slowly and are less aggressive (Bray *et al*., 2006). To diagnose and treat both, the first step is usually orchiectomy (testicle removal). Orchiectomy is a surgical method and is known as the gold standard for treating testicular cancer. Post-orchiectomy treatment plans are tailored for the specific stage of the tumor identified after surgery (Stephenson *et al*., 2019).

Our study assessed the survival rate regarding disease recurrence, pathology type, patients with risk factors, and stage presentation between patients living in Riyadh, treated at KFSHRC, and patients from different kingdom regions. We retrospectively went through our patient's records from 2010-2017. Subsequently, our follow-up with the patients post-orchiectomy included radiological images and tumor markers (Chavarriaga *et al*., 2023). The study showed that the frequency of incidence of testicular cancer showed a significant relation with the age of the patients, as most of the studied patients were in the age group of 26-35 years.

Our retrospective cohort study found no statistically significant variations in overall survival between patients residing in and outside of Riyadh, indicating that geographic location may not be a relevant factor in the prognosis of seminoma and nonseminoma germ cell tumors (GCTs). Furthermore, the assessed risk factors affected neither the seminoma nor the NSGCT groups' overall survival. The results revealed that patients with pure seminomas had improved overall survival rates than those with pure NSGCTs, which suggests that nonseminoma variations were naturally more aggressive (Fero *et al*., 2021). Stage 3 presentations showed noticeably worse survival rates, underscoring the significance of early discovery and care, while Stage 1A–2C GCTs showed similar survival outcomes (Abdul-Muhsin *et al*., 2021).

One of the main reasons no significant difference was seen in patients living inside Riyadh and receiving the best treatment at King Faisal Specialist Hospital & Research Center (KFSHRC) and outside Riyadh is that patients across the kingdom were able to receive timely diagnosis and treatment. The lack of correlation between the risk factors under study and survival highlights the need for more research into more comprehensive risk profiles that affect the progression of tumors. Another explanation is that risk factors mentioned in the study are not associated with a worse prognosis. Therefore, neither the treatment regimen nor the follow-up should be changed for patients with testicular cancer and for patients who have risk factors. Furthermore, our findings converge with previous studies showing that seminoma had better survival overall than NSGCT. At the end of the study, out of 125 patients, 115(92%) were in remission, 4 passed away and 6 had recurrence. These findings show that testicular cancer has a good prognosis if treated properly (Cassell *et al*., 2020). Our finding that pure seminomas have a higher survival rate than NSGCTs corresponds with previous studies and highlights the intrinsic aggressiveness of nonseminoma variations. This knowledge can inform strategies for targeted treatment and risk stratification.

In our tumors staging sub-group, it was seen that group 2C had 4 patients only, making the results significant. Although our study was conducted at KFSHRC, we did not limit ourselves to the samples of patients treated at KFSHRC only; we included patients from other tertiary hospitals across the kingdom. The number of testicular cancer patients in the kingdom has been rising recently; during our study, we analyzed 125 cases from 2010 to 2017. Even though our sample size is small compared to the entire population, it can still serve as a starting point for more extensive research that can be carried out soon. As per our best knowledge and extensive research, we can surely state that there is not enough research conducted in Saudi Arabia on testicular cancer. We selected King Faisal Specialist Hospital & Research Center (KFSHRC) as our referral hospital because it is the primary national referral cancer center, receiving about 22% of all cancer cases nationwide. Our results provide new insight into the KFSHRC's strategy regarding the pattern of tumor progression and treatment outcomes for patients with testicular cancer. Furthermore, this will contribute to the body of knowledge regarding the management and surveillance of testicular cancer, namely GCTs, in Saudi Arabia.

Future Directions

Despite the sample size constraints, the study establishes the foundation for additional research on testicular cancer in Saudi Arabia. We must evaluate risk profiles more extensively, as the study indicates that some risk factors and survival are unrelated. Understanding the intrinsic aggressiveness of nonseminoma variants should be useful in developing strategies for focused treatment and risk classification. Research on tumor progression and

treatment outcomes is essential as the number of instances of testicular cancer in the kingdom rises. The correlations between various parameters reviewed in this retrospective provide light on trends and results at a national referral center, which helps with the care and surveillance of testicular cancer in Saudi Arabia, particularly germ cell tumors. Additional comprehensive study is necessary to enhance comprehension and direct advancements in diagnosis, therapy, and patient management.

CONCLUSION

This retrospective research challenges geographical assumptions regarding testicular cancer in Riyadh and surrounding areas. No significant differences in stage were found between Riyadh and residents living outside Riyadh. It also revealed that factors such as genetics, smoking, and family history did not affect survival in seminoma or nonseminoma germ cell tumors. Seminoma showed a higher overall survival, indicating differences in treatment response. It is important to detect testicular cancer early, as Stage 3 presentations correlated with the lowest survival. Although this study was conducted in Riyadh, future research should involve diverse tertiary care facilities nationwide. Finally, this study challenges geographical assumptions and opens avenues for improving testicular cancer treatment strategies.

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