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THE EFFECT OF HISTOPATHOLOGICAL CHARACTERISTICS OF TESTICULAR TUMORS ON OVERALL SURVIVAL IN IMMIGRANTS

GÖÇMENLERDE TESTİS TÜMÖRLERİNİN HİSTOPATOLOJİK ÖZELLİKLERİNİN GENEL HAYATTA KALMA ÜZERİNE ETKİSİ

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SUMMARY

Introduction: *Testicular cancer is a rare condition and incidence peaks in 2-3 decades. The incidence and oncological outcomes vary in patients with different race/ethnicity. In this study, we aimed to provide a description of racial difference in testicular cancer.*

Material and Method: *Between 2016 and 2020, A total 52 patients underwent radical orchiectomy due to testicular cancer. All patients with histologically proven testicular germ cell tumors were included the study. Patients with other urological or systemic cancers, and lack of data were excluded from study.*

Results: *The seminoma pathology was found in 27 patients. The median tumor size, and rete testis invasion were similar between groups (p=0.410, and p=0.487, respectively). The tumor stage was significantly higher in Immigrants (stage 2A and 3A, p<0.001) and overall survival was significantly lower in Immigrants (p<0.001). A total of 25 patients had non-seminoma pathology. The lymphovascular invasion, and tumor stage was also similar between groups (p=0.532, and p=0.781, respectively). However, overall survival was significantly lower in Immigrants (p=0.003).*

Conclusion: *Testicular cancer is a rare but significant disease for young patients. Race/ethnicity effects oncological outcomes of testicular cancer.*

ÖZ

Giriş: *Testis kanseri nadir görülen bir durumdur ve insidansı 2-3 dekatta pik yapar. Farklı ırk/etnik kökene sahip hastalarda görülme sıklığı ve onkolojik sonuçlar farklılık gösterir. Bu çalışmada testis kanserinde ırksal farklılığın tanımını vermeyi amaçladık.*

Gereç ve Yöntem: *2016-2020 yılları arasında toplam 52 hastaya testis kanseri nedeniyle radikal orşiektomi uygulandı. Histolojik olarak kanıtlanmış testiküler germ hücreli tümörü olan tüm hastalar çalışmaya dahil edildi. Diğer ürolojik veya sistemik kanserleri olan ve veri eksikliği olan hastalar çalışma dışı bırakıldı.*

Bulgular: *27 hastada seminom patolojisi saptandı. Medyan tümör boyutu ve rete testis invazyonu gruplar arasında benzerdi (sırasıyla p=0.410 ve p=0.487). Tümör evresi Göçmenlerde anlamlı olarak daha yüksekti (evre 2A ve 3A, p<0.001) ve genel sağkalım Göçmenlerde anlamlı olarak daha düşüktü (p<0.001). Toplam 25 hastada*

seminom dışı patoloji mevcuttu. Lenfovasküler invazyon ve tümör evresi de gruplar arasında benzerdi (sırasıyla p=0,532 ve p=0,781). Ancak, genel sağkalım Göçmenlerde anlamlı olarak daha düşüktü (p=0,003).

***Sonuç:** Testis kanseri genç hastalar için nadir fakat önemli bir hastalıktır. Irk/etnik köken, testis kanserinin onkolojik sonuçlarını etkiler.*

INTRODUCTION

Testicular cancer (TC) incidence peaks is 2-3 decades and with novel treatment modalities the mortality rates decreased low (1). The majority of TC are germ cell tumors (1,2). TC incidence has varies across European countries, and has increased at rates ranging from 2.3% in Sweden to 5.2% in Germany (3). There are some well establish risk factors defined including undescended testis, infertility, testicular dysgenesis, history of testicular cancer, age and ethnicity (4). TC causing unpleasant social and psychological problems in young ages. Disease management based on the risk adapted treatment which depends on histological type, tumor size, rete testis invasion for seminomas and lenfovascular invasion for non-seminoma tumors after orchiectomy (1). The overall survival rate is above %95 (5). The prognosis of TC after diagnosis depends on stage and therapeutic approach. The management options include active surveillance, radiotherapy, or chemotherapy.

Novel studies paid attention to race/ethnicity difference in TC (6). The Early studies showed that incidence of TC cancer varies in patients with different race/ethnicity (7) and additionally, publish data showed that Hispanics, and American Natives have the high rates of TC (1). Additionally, nonwhite patients also associated with poor prognosis when compared to other races (8).

In this study, we aimed to provide a description of racial difference, especially including patients' clinic pathological features and oncological outcomes in testicular cancer.

MATERIAL AND METHOD

Between 2016 and 2020, A total 52 patients underwent radical orchiectomy due to testicular cancer. All patients with histologically proven testicular germ cell tumors were included the study. Patients with other urological or systemic cancers, and lack of data were excluded from study. The study was approved by local ethic committee and the demographic data and postoperative follows up collected from one center database. The data including age at diagnosis, race, date of diagnosis, date of last follow-up, relapse status, as well as histopathological findings and size of the primary tumor, tumor stage, and survival status at last follow-up were collected. The patients were managed with according to oncologic guidelines, which usually included combination cisplatin-based chemotherapy and pelvic RT. The data was divided into two groups: group 1= Locals, and group 2= Immigrants. The data was assessed depending on histopathological groups into seminoma and non-seminoma.

Categorical variables such as presence of lymphovascular invasion or rete testis invasion were summarized with counts and percentages. The Shapiro Wilk test was used to determine normality and continuous variables such as age, tumor size, and follow-up were summarized with medians and interquartile ranges (IQR). The Kaplan–Meier analysis was used to generate overall survival rates. Mann Whitney U test was used for comparing continuous variables and Chi-square test was used for comparing the categorical variables. Statistical Package for the Social Sciences (SPSS) version 25 for MacOS was used to perform all statistical analyses. p value < 0.05 was accepted as statistical significance.

RESULTS

A total 52 patients were assessed, and the pathological findings was seminoma in 27 patients. The median age was similar between groups (group 1 =34 (27-41) and group 2 =28 (26-29), p=0.279, respectively). Table 1 shows comparison of patients with seminoma pathology according to their race. The median tumor size,

and rete testis invasion were similar between groups (p=0.410, and p=0.487, respectively). The tumor stage was significantly higher in group 2 (stage 2A and 3A, p<0.001). The Kaplan Meier analysis showed that overall survival was significantly lower in group 2 (p<0.001).

A total of 25 patients had non-seminoma pathology. The median age, side and median tumor size was similar between groups (p=0.642, p=0.542, and p=0.642, respectively). Table 2 shows comparison of patients with non-seminoma pathology according to their race. Additionally, lymphovascular invasion, and tumor stage was also similar between groups (p=0.532, and p=0.781, respectively). However, Kaplan Meier analysis showed that overall survival was significantly lower in group 2 (p=0.003).

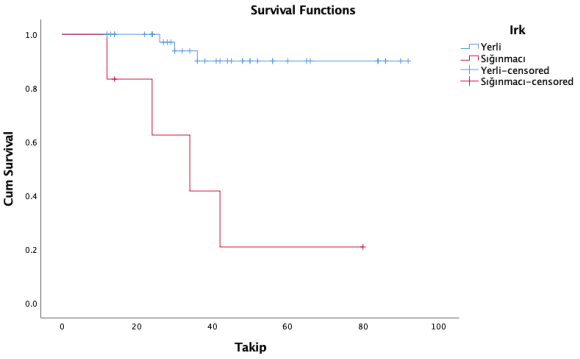

Figure 1. Kaplan-Meier survival analysis.

Table 1. Comparison of patients with seminoma pathology according to their race.

		Seminoma		
		Locals	Immigrants	*p*
Age [a] (year)		34 (27-41)	28 (26-29)	0.279
Side [b]	Right	13 (%52.0)	1 (%50.0)	0.741
	Left	12 (%48.0)	1 (%50.0)	
Focality [b]	Unifocal	24 (%96.0)	1 (%50.0)	0.145
	Multifocal	1 (%4.0)	1 (%50.0)	
Tumor size [a] (mm)		4 (2-8)	7 (4-11)	0.410
ITGHN [b]	Absent	13 (%52.0)	1 (%50.0)	0.741
	Present	12 (%48.0)	1 (%50.0)	
Tunica albuginea invasion [b]	Absent	18 (%72.0)	2 (%100.0)	0.541
	Present	7 (%28.0)	0	
Rete testis invasion [b]	Absent	17 (%68.0)	2 (%100.0)	0.487
	Present	8 (%32.0)	0	
Epididymis invasion [b]	Absent	19 (%76.0)	2 (%100.0)	0.598
	Present	6 (%24.0)	0	
LVI [b]	Absent	14 (%56.0)	2 (%100.0)	0.342
	Present	11 (%44.0)	0	
Lymph node on CT scan [b]	Absent	21 (%84.0)	1 (%50.0)	0.280
	Present	4 (%16.0)	1 (%50.0)	
Lymph node size (mm) [a]		24 (10-45)	35 (35-35)	****
Pathological stage [b]	Stage 1A	14 (%54.2)	0	<0.001#
	Stage 1B	7 (%29.2)	0	
	Stage 2A	3 (%12.5)	1 (%50.0)	
	Stage 2B	1 (%4.1)	0	
	Stage 3A	0	1 (%50.0)	
Adjuvant chemo [b]	Absent	17 (%68.0)	1 (%50.0)	0.564
	Present	8 (%32.0)	1 (%50.0)	
Follow up [b] (month)		38 (24-56)	46 (12-80)	0.889
Status [b]	Death	0	1 (%50.0)	<0.001^
	Alive	25 (%100.0)	1 (%50.0)	

[a] Data was expressed as median and interquartile range.
[b] Data was expressed as count and percentile.
İTGHN: Intratesticular germ cell neoplasia, LVİ: Lenfovascular invasion, Chemo: Chemotherapy.
 # Chi-square test was used. & Variables are constant
^Kaplan Meier survival analysis was used

Table 2. Comparison of patients with non-seminoma pathology according to their race

		Non-Seminoma		
		Locals	Immigrants	*p*
Age [a] (year)		28 (22-29)	28 (25-36)	0.642
Side [b]	Right	13 (%61.9)	3 (%25.0)	0.542
	Left	8 (%38.1)	1 (%25.0)	
Focality [b]	Unifocal	21 (%100.0)	4 (%100.0)	&
	Multifocal	0 (%0.0)	0 (%0.0)	
Tumor size [a] (mm)		4 (2-5)	6 (2-12)	0.642
ITGHN [b]	Absent	16 (%52.0)	3 (%75.0)	0.694
	Present	5 (%48.0)	1 (%25.0)	
Tunica albuginea invasion [b]	Absent	15 (%71.4)	1 (%25.0)	0.116
	Present	6 (%28.6)	3 (%75.0)	
Rete testis invasion [b]	Absent	16 (%76.2)	1 (%25.0)	0.081
	Present	5 (%23.8)	3 (%75.0)	
Epididymis invasion [b]	Absent	17 (%81.0)	2 (%50.0)	0.234
	Present	4 (%19.0)	2 (%50.0)	
LVI [b]	Absent	13 (%61.9)	2 (%50.0)	0.532
	Present	8 (%38.1)	2 (%50.0)	
Lymph node on CT scan [b]	Absent	14 (%66.6)	2 (%50.0)	0.382
	Present	7 (%28.4)	2 (%50.0)	
Lymph node size (mm) [a]		14 (10-17)	20 (15-25)	0.381
Pathological stage [b]	Stage 1A	12 (%51.2)	2 (%50.0)	0.781#
	Stage 1B	2 (%9.5)	0 (%0.0)	
	Stage 2A	5 (%23.8)	1 (%25.0)	
	Stage 2B	0 (%0.0)	0 (%0.0)	
	Stage 3A	2 (%9.5)	1 (%25.0)	
Adjuvant Chemo [b]	Absent	11 (%52.4)	1 (%25.0)	0.328
	Present	10 (%47.6)	3 (%75.0)	
Follow up [b] (month)		38 (24-56)	46 (12-80)	0.183
Status [b]	Death	3 (%14.3)	3 (%75.0)	0.003^
	Alive	18 (%85.7)	1 (%25.0)	

[a] Data was expressed as median and interquartile range.
[b] Data was expressed as count and percentile.
İTGHN: Intratesticular germ cell neoplasia, LVİ: Lenfovascular invasion, Chemo: Chemotherapy.
 # Chi-square test was used. & Variables are constant
^Kaplan Meier survival analysis was used

DISCUSSION

Testicular cancer is the most common solid cancer among patients age between 15-35 years old (1,4). Our study demonstrated that the Immigrants has poor oncological outcomes when compared the locals.

Testicular cancer has high cure rates with novel treatment modalities. Testicular cancer has a favorable prognosis, the low mortality overall and this situation may have made it difficult to identify real risk factors. The publish literature demonstrated racial differences among other cancer patients, such as melanoma, bladder cancer (9,10). Novel research pointed effect of the race/ethnicity to testicular cancer (6). Chia et al study assessed Cancer incidence in Asian, European, Americas, and Oceania and they showed that TC incidence is highest in European, and lowest in Asian and Africans (11). Hispanic

men are highest risk for testicular cancer; additionally, locals have higher incidence rates based on that alone. Hispanics comprise 15.4% of the population, while 72.3% are designated as non- Hispanic. Additionally, a novel study included 896 individuals who diagnosed with testicular cancer from 2000-2015 in New Mexico, showed that testicular cancer incidence rates were the higher in Mexicans when compared with the SEER18 data (12). And the authors also commented that their results significantly higher proportion of distant cancer at diagnosis but the survival rates in New Mexico were did not differ significantly from SEER18 data. Controversially, publish literature also pointed that Nonwhite patients with TC have been reported to have lower survival rates compared with other races, based on SEER program results (8). Early study by Bridges et al. a14 years review of 215 patients (Whites, African Americans, and Hispanics) demonstrated that African Americans had the lowest survival rates but the tumor type or stage did not differ between groups (13). Similar to these results, our study demonstrated that the incidence of TC is common in Local people, but the tumor stage was higher in Immigrants.

It remains unclear that why the incidence varies between races and the possible explanation is the differences in genetic factors, lifestyle, environmental factors, and especially, variability in hormone exposures. However, a previous study also found that there was a relationship with delayed of diagnosis in non-Caucasian compared with Caucasian. The authors commented that there is a the convergence of survival rates between racial groups and this is a results of increased awareness and/or improved health care access among non-Caucasian groups (14). We think that there are some problems in reaching the health care and sometimes crossing the border. Therefore, there may be a delay in the diagnosis. In addition, we suggested that self-testicular examination, which is frequently emphasized to men, contributes to the diagnosis of local people.

There are some limitations in our study. The retrospective nature of study is most important limitation. Another limitation is small number of populations, and it is not possible to fully distinguish the racial origin of our patient population. Additionally, it is not possible to say exactly how long patients have had testicular mass or delayed diagnosis especially in Immigrants.

CONCLUSION

Testicular cancer is a rare but significant disease for young patients. Similar to other cancer, race/ethnicity effects oncological outcomes of testicular cancer. Immigrants have poor outcomes when compared to Locals due to problems reaching healthcare. Therefore, self-testicular examination is important and needs to be emphasized to immigrants as well.

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