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Prognostic Factors of Testicular Cancer: A Single Institution Retrospective Study

***Eman Ahmed Abd El-Aziz Mesha, Rasha Hamdy Hamed,**
Ibrahim Ali Mohamed Awad, Shimaa El-Metwaly Attia
Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Mansoura University, Egypt
***Corresponding author:** Eman Ahmed Abd El-Aziz Mesha, **Mobile:** (+20) 01141884884,
ORCID NO: 0009-0009-9322-1366, **E-Mail:** emanabdelaziz1993@gmail.com

ABSTRACT

Background: Testicular cancer (TC) is the most common cancer in young males, representing about ~1% of new cases of cancer in male patients around the world.

Objective: The study aims to assess prognostic factors of testicular cancer, overall survival and progression free survival.

Patients and Methods: Sixty patients with testicular cancer who had been attended to the Clinical Oncology and Nuclear Department at Mansoura University Hospitals between January 2006 and Desember2020 were included in this retrospective analysis.

Results: The median age of the patients was 43 years. The most common presentation was testicular mass (71.7%). Cryptorchidism was presented in 7 cases (11.7%). Most of our patients were germ cell tumors 51cases (85%) divided into seminoma 34 patients (56.7%), nonseminoma17 patients (28.3%), 7 patient (11.7 %) were nongerm cell tumors and 2 patients (3.3%) were miscellaneous tumors. Regarding tumor, node and metastasis (TNM) staging, 43 patients (71.7%) were stage I, and 14 patients (23.3%) were stage III. Regarding lymph node metastasis, 57 patients (95%) were N0. All patients underwent high inguinal orchiectomy, (80%) of patients received chemotherapy, and 7 patients (11.7%) received radiotherapy. The 5 years overall survival was (91.7%) while 5 years progression free survival was (88.3%).

Conclusion: Absence of cryptorchidism, germ cell tumors, node negative and stage I all are good prognostic factors.

Keywords: Prognostic factors of testicular cancer; Orchiectomy; Seminoma; Non-seminoma; Testicular cancer.

INTRODUCTION

Testicular cancer represents about ~1% of new cases of cancer in male patients around the world. In Western nations, it is the most prevalent cancer among people between the ages of 14 and 44. Globally, the incidence of testicular cancer differs from <1 affected individual per 100,000 males in large parts of Africa and Asia to 9.2 in Switzerland, 9.4 in Denmark and 9.9 in Norway. India has the lowest age-standardized incidence of 0.5/100,000 men [(1)]**.** Testicular cancer is the most prevalent solid tumor in young males. The incidence rate for testicular cancer is about 1.86/100,000 in Egypt[(2)].

Traditionally, testicular cancer appears as a solid, ache-free mass. Less frequently, patients with seminoma may exhibit mild testicular discomfort and swelling that could be epididymo-orchitis. Others may exhibit retroperitoneal lump, enlarged breast, thrombus formation, or emboli in pulmonary vessels in addition to supraclavicular or mediastinal lymph node[(3)] .

Ninety-five percent of testicular cancer cases are germ cell tumors (GCT), which are classified into seminoma (classic, anaplastic and spermatocytic variants) and non-seminomatous germ cell tumors (NSGCT), which include (embryonal carcinoma, teratocarcinoma, teratoma, choriocarcinoma and yolk sac tumors). Five percentage of testicular tumors are (sex cord stromal tumors, lymphoma). They may arise in other extragonadal locations including the retroperitoneum and the mediastinum[(4)].

The way testicular cancer is treated has improved. Testicular cancer treatment was revolutionized by the addition of cisplatin-based combination chemotherapy, radiotherapy, and retroperitoneal lymph node dissection (RPLND). Even in the presence of metastatic disease, patients diagnosed with testicular cancer have a good prognosis[(5)].

AIM OF WORK

This retrospective study aimed to determine the clinico-epidemiological characteristics and treatment outcome of patients with testicular cancer treated at Clinical Oncology and Nuclear Medicine Department at Mansoura University Hospital from January 2006 to December 2020, and also, to assess progression-free survival (PFS), and overall survival (OAS) for all the patients with different methods of treatment and evaluation of prognostic factors.

PATIENTS AND METHODS

This retrospective analytical study based on the hospital records of the testicular cancer patients who were admitted to Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospital from January 2006 to December 2020 inclusive. A rough anticipated number of reliable patient records was 60. The information was obtained using a standard form: age, medical history (risk factors like cryptorchidism, smoking, history of testicular trauma, clinical data (side, clinical symptoms as testicular mass, scrotal swelling, scrotal pain or asymptomatic), laboratory tests include tumor markers as (b-HCG, LDH, alpha-fetoprotein) and complete lab as (CBC, LFTs, KFTs), radiological assessment as testicular ultrasound, CT chest, abdomen and pelvis, MRI, PET

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CT for staging and follow up, pathology of tumor, TNM staging, site of failure, treatment details as surgery, chemotherapy ,and radiotherapy.

Overall survival (OAS), which is defined as the time from diagnosis till death (including deaths with or without recurrence) or lost follow up and progression free survival (PFS) were estimated in all patients from the begging of diagnosis of the disease to date of progression. They were assessed and correlated with the previous factors to study their prognostic significance.

Inclusion criteria:

- Pathologically proven testicular carcinoma.
- All stages.
- Age >18 year

Exclusion criteria:

- Other malignancies.

Ethical consent:

Study protocol was approved by Medical Research Ethical Committee, Faculty of Medicine, Mansoura University, code 9163767. An informed consent was taken from all patients. This study has been done in accordance with Helsinki Declaration.

Statistical analysis

The available data were categorized, organized, and examined. The appropriate statistical tests were run using SPSS version 25 (Statistical Package for the Social Sciences). Quantitative data were presented with median and range but qualitative data were presented as numbers and percent.

The difference between group medians will be made using the Mann Whitney U test (z test), and Kruskal-Wallis test while The Chi-square test will be used to compare percentages. The survival of patients was displayed by Kaplan-Meier survival curve. The differences were considered statistically significant for the analysis when p value was ≤ 0.05.

RESULTS

The median age of patients was 43 years with a range of (19-71) years. Trauma was detected in 2 cases (3.3%). Smoking was detected in 24 cases (40%). Cryptorchidism was recorded in 7 case (11.7%). At diagnosis 56 cases were symptomatic (93.2%). The most common symptom was testicular swelling or mass **(Table 1).**

Table (1): Patient characteristics

Characteristic	N	%
Age		
≤20 years	1	1.7
>20 years-≤30 years	4	6.7
≥31 years-≤40 years	20	33.3
≥41 years-≤50 years	18	30
≥51 years-≤60 years	8	13.3
≥61 years-≤70 years	7	11.7
>70 years	2	3.3
Trauma		
Yes	2	3.3
No	58	96.7
Smoking		
Yes	24	40
No	36	60
Cryptorchidism		
Yes	7	11.7
No	53	88.3
Clinical presentation		
Testicular mass or swelling	43	71.7
Scrotal heaviness	6	10
Scrotal pain	7	11.7
Asymptomatic	4	6.6

As regard tumor characteristics right side testicular cancer was detected in 35 cases (58.3%). According to histopathology, germ cell cancer was detected in 51 cases (85%): Seminoma was detected in 34 case (56.6%). Sex cord or gonadal stromal tumors were presented in 5 case (8.3%).

Regarding lymph node metastasis, 57 patients (95%) were N0. 13 patients (21.7) had lung metastasis. Stage I was the most frequent reported stage. Whole patients underwent surgery (100%), 48 cases (80%) were treated by systemic therapy, and 7 cases (11.7%) treated with radiotherapy. According to site of failure, paraaortic LN was the commonest site **(Table 2).**

Table (2) as regard tumor's characteristics:

Characteristic	Frequency	Percentage
Side of tumor		
Right	31	51.7
Left	29	48.3
Histopathological type		
Germ cell tumors		
Seminoma	34	56.7
Non-seminoma	17	28.3
Non-germ cell tumors		
Sex cord tumors	5	8.3
Mixed germ cell tumors	2	3.3
Miscellaneous tumor	2	3.3
LN metastasis		
N0	57	95
N1	2	3.3
N2	1	1.7
Metastatic site		
NO	47	78.3
Lung	8	13.4
Lung + Others	5	8.3
TNM staging		
I	43	717
II	3	5
III	14	23.3
Treatment modalities		
Surgery+ chemotherapy		
Surgery +radiotherapy	48	80
Surgery +surveillance	7	11.7
Surgery+chemotherapy	3	5
+radiotherapy	2	3.3
Site of failure		
NO	56	93.3
PALN	3	5
PALN+ mediastinum	1	1.7

LN: Lymph nod
N : Node
PALN: Para aortic lymph node

The survival figures:

Figure (1): Shows OAS of all cases. The 5-years OAS was 91.7%, The median OAS was 109.5 months with range (39 – 201).

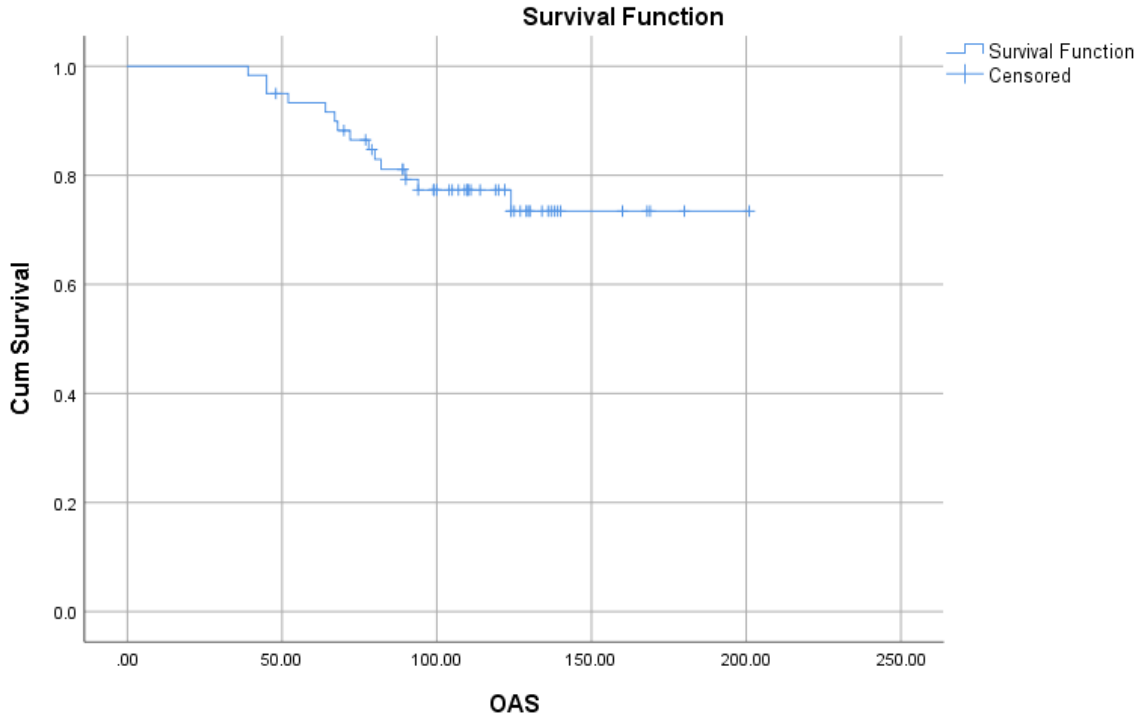

Figure (1): OAS curve of all cases

Figure (2): shows PFS curve for all cases. The 5-years PFS was 88.3%**.**

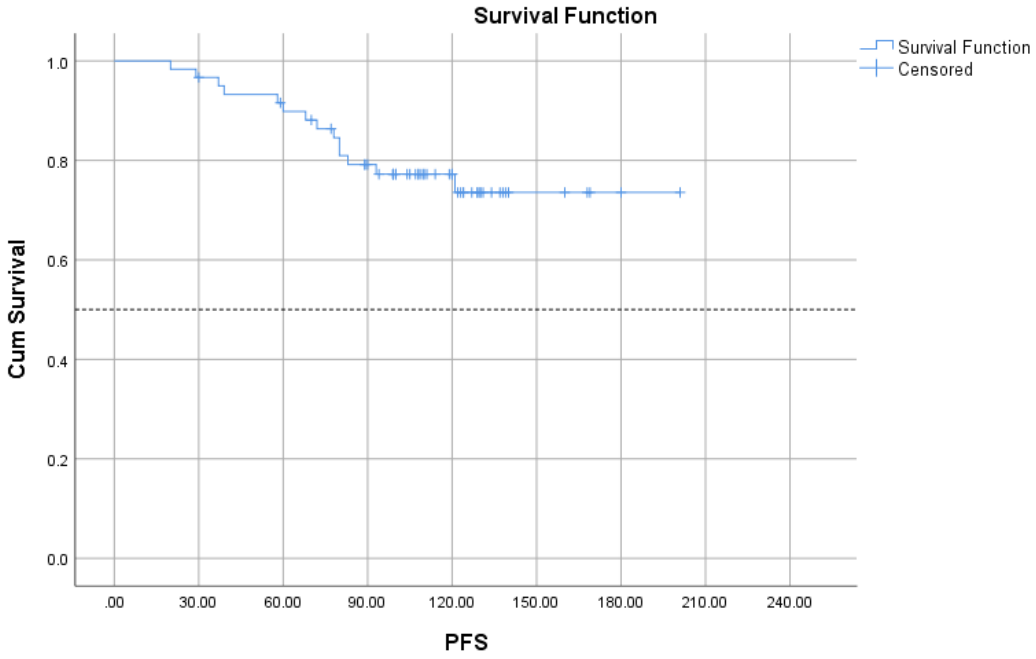

Figure (2): PFS curve for all cases included (n=60).

Prognostic factors affecting OAS are summarized in **table (3)**. Starting with univariate analysis, factors that were associated with good prognosis with a statistically significant correlation with OAS, were absence of history of cryptorchidism, histological type (germ cell tumor), negative lymph node, and early stage.

Prognostic factors affecting PFS are shown in **table (3).** Prognostic factors that had a statistically significant negative correlation with PFS in univariate analysis were negative lymph node, absence of metastasis, and stage I.

Table (3): Univariate analysis of OAS prognostic factors

Factor		5-years OAS %	95% Confidence index	P-value	5-years PFS %	95% Confidence index	P-value
Age	≤20 years	1.7	(0.412 – 0.432)	0.452	1.7	(0.24 – 0.257)	0.234
	<20- ≤30 years	5			5		
	≥31- ≤ 40 years	31.7			31.7		
	≥41- ≤ 50 years	28.3			26.7		
	≥51- ≤ 60 years	10			8.3		
	≥61- ≤ 70 years	11.7			11.7		
	>70 years	3.3			3.3		
Trauma	No	88.3	(1 -1)	0.665	85	(1 – 1)	0.601
	Yes	3.3			3.3		
Smoking	No	60	(0.633 – 0.652)	0.34	51.7	(0.685 – 0.703)	0.511
	Yes	40			36.7		
Cryptorchidism	No	88.3	(0.091 – 0.10)	**0.036****	85	(0.180 – 0.195)	0.139
	Yes	11.7			9.6		
Presenting symptoms	Mass or swelling	65	(0.739 – 0.756)	0.66	65	(0.430 – 0.450)	0.416
	Heaviness	8.3			8.3		
	Pain	11.7			8.3		
	Asymptomatic	6.7			6.7		
Side	RT	48.3	(0.659 – 0.677)	0.586	46.7	(0.694 – 0.712)	0.620
	LT	43.3			41.7		
Pathological subtypes	Germ cell tumors	85	(0.155 – 0.169)	**0.03****	83.4	(0.217 – 0.233)	0.086
	Non germ cell tumors	5			3.3		
	Miscellaneous tumor	1.7			1.7		
T	T1	55	(1 – 1)	0.906	55	(0.530 – 0.550)	0.459
	T2	33.3			30		
	T3	3.3			3.3		
N	N0	88.3	(0.087 – 0.098)	**0.003****	85	(0.124 – 0.137)	**0.019****
	N1	3.3			3.3		
	N2	0			0		
M	M0	76.7	(0.009 – 0.013)	**<0.001****	73.3	(0.026 – 0.032)	**0.008****
	M1						
	• Lung	10			10		
	• Other sites	1.7			1.7		
	• Lung and others	3.3			3.3		
Stage	I	70	(0.023 – 0.029)	**0.007****	68.3	(0.014 – 0.02)	**0.006****
	II	5			5		
	III	16.7			15		
Treatment	Surgery	5	(0.743 – 0.760)	0.714	5	(0.68 – 0.698)	0.576
	Surgery + Chemotherapy	71.7			68.3		
	Surgery + Radiotherapy	11.7			11.7		
	Surgery + RT + chemotherapy	3.3			3.3		

*P value ≤ 0.05 (significant), **P value < 0.001 (highly significant).

There was no detection of statistically significance in OAS or PFS in multivariate analysis presented in **table (4).**

Table (4): Multivariate analysis of OAS prognostic factors

	Hazard Ratio of OAS	95% Confidence index of OAS	P-value of OAS	Hazard Ratio of PFS	95% Confidence index of PFS	P-value of PFS
Cryptorchidism	2.89	0.628 – 13.372	0.173	-	-	-
Pathological subtypes	25916	0.000 – -	0.985	-	-	-
N	256.33	0.00 – 1.981	0.812	217	0.00 – 2.319	0.835
M	0.519	0.228 – 1.182	0.118	0.683	0.333 – 1.403	0.299
Stage	24860	0.000 – 2.500	0.733	209980	0.00 – 1.824	0.759

DISCUSION

The study's median age was 43 years, which ranged between (19-71) years. The age between 30-50 years represented 63.3% with no statistically significant prognostic value was found in univariate analysis. Our results is similar to results of **Dong *et al.***, study in which most common age group is 30-50 years with also no statistically significant prognostic value[6].

In our study 3.3% of the patients had history of trauma that was less than the results observed by **Stone *et al.*** in which trauma was present in 28 % of cases (P = 0.03) in their study[7]. The results of our study do not support the hypothesis that testicular trauma is an important risk factor for testicular cancer with no statistically significant prognostic value was found in univariate analysis. This may be due to difficulty in reporting trauma.

As regard smoking, about 40% were smoker, this is similar to **Bjerring *et al.*** that detected 41% of cases were smokers, with no statistically significance in both studies. Smoking has not been considered as a risk factor for testicular cancer as testicular cancer is mainly a disease of young men, period of smoking may be insufficient to induce testicular carcinogenesis [8].

One study suggested that cigarette smoking exerts an adverse factor on testicular cancer that is not mitigated by smoking cessation and not altered by age at initiation-n[9].

In our study cryptorchidism was detected in (11.7%) of patients, this reported result is similar to two studies having result of (10.7%) and (10%) respectively Its absence has OAS with significant p value (0.039). Cryptorchidism is the most common congenital genitourinary abnormality in males and is the most firmly established risk factor for testicular cancer [10,11].

Regarding clinical presentation, the most common was testicular swelling or mass in about 43 cases (71.7%), which is similar to another study [12].

According to side affected, the right side represented 31 cases (51.7%) and left side represented 29 cases (48.3%) with no statistically significant prognostic value was found in univariate analysis. These data differ from the study of **Zawam *et al* .,** in which left side was affected in 17 cases (53.1%) and right in 15 cases (46.9%)[2].

But our data were similar to one study [13]. There is no statistically significant difference in all three studies which include **Zawam *et al., Ashraf et al., and our study.***

According to histopathological type, most common pathological type was seminoma 34 cases (56.7%) followed by non-seminoma 28 cases (28.3%), sex cord or gonadal stromal tumors 5 cases (8.3%), mixed germ cell/sex cord stromal tumors 2 cases (3.3%), miscellaneous tumor 2 cases (3.3%). These data are similar to two studies[10,14].

As regard anatomical factors including TNM staging system in our study according to lymph node, metastatic site N0 (95%), MO (78.3%) were statistically significant with p value (p=0.003, p <0.001 respectively). These data were similar to one study [15], which had lymph node>> N0 (74.9%), metastatic site >>M0 (84%).

Stage I was the most common stage in our study that was present in (71.1%) with statistically significant p value (0.007), which is similar to one study [16] that has statistically significance with p value (<0.001).

According to type of treatment, all cases in our study underwent surgery then surveillance in (5%) or chemotherapy (80%) or radiotherapy (11.7%) or chemotherapy and radiotherapy (3.3%**).** Data differ from the results of **Dong *et al.*** in which chemotherapy was in (20.7%) or radiotherapy in (60.3%) or chemotherapy and radiotherapy in (19%). This may be attributed to different staging between the two studies as in our study stage I (71.7%), stage II (5%), stage III (23.3%) and in **Dong *et al***. stage I (29.3%), stage II (55.2%), stage III (15.5%), and so treatment was also different [6].

In **Coleman *et al.*** all of patients underwent orchiectomy and stages were stage I (76%), stage II (19.7), stage III (2.5%), stage IV (1.5%) followed by surveillance in (30%) or chemotherapy (10%) or radiotherapy (60%). So, this study depended mainly on radiotherapy or surveillance in treatment, but we mainly depended on chemotherapy in treatment. This may be

due to side effects that occurred after radiotherapy like secondary malignancies and other problems such as unavailability of radiotherapy machines in all centers[17].

According to site of relapse in our study, it was detected in PALN in 5% and in mediastinum in 1.7% , these data are similar to another study [18].

The median OAS was 109.5 months with range (39 – 201), while the median PFS was 108 months with range (20 – 201), these results are similar to another study[6].

CONCLUSION

The results of the current study suggested that there are many factors affecting prognosis of testicular cancer.

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- **Author contribution:** Authors contributed equally in the study.

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