Survival Patterns of Hormone Refractory Prostate Cancer in Sulaymaniyah, Iraqi Kurdistan

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Abstract

As the most common solid tumor diagnosed among men, prostate cancer is responsible for the death of a remarkable number of men worldwide every year. The present study was carried out in order to figure out the survival patterns and the effective variables in patients with hormone refractory prostate cancer. Using a retrospective cohort design with a nested case-control study approach, the present study was carried out on 150 patients with prostate cancer at Hiwa Cancer Hospital located in Sulaimania, the Iraqi Kurdistan in 2014. The patients were assigned into a case group (who developed resistance to androgen deprivation therapy) and a control group (who did not develop resistance to androgen deprivation therapy within the first three years of prostate cancer treatment). The required data were collected through a researcher-designed questionnaire and using the patients' hospital records. Most of the patients aged between 65 to 80 years. According to the results, the highest survival probability belonged to the age group 60-80, while the lowest was related to those aged less than 60 years, and there was no significant relationship between age groups and overall survival ($p>0.05$). Prostate cancer is more likely to develop in males aged 65 to 80 year. They patients' overall survival is not correlated with their age, while there is a correlation between the stage of their tumors and their overall survival. The patients' their progression-free survival was found to be significantly affected by their age and histopathology, while the stage of their tumors was not in a significant correlation with their progression-free survival.

Keywords: *Prostate cancer, survival patterns, adenocarcinoma.*

Introduction

Although prostate cancer (PC) has been referred to as the most common solid tumor among men in developed countries and less common in underdeveloped countries, its etiology is still not well-known[1]. PC has been introduced as the fifth leading cause of mortality in males worldwide[2]. The most significant risk factor for PC is being an elderly male, such that it is the most commonly detected cancer among elderly men [1]. In addition to age and male gender, other effective factors in incidence of prostate cancer have been introduced as family history, race, diet, obesity, smoking, and alcohol[3].

Statistics has shown that 20 to 30% of the diagnosed patients have diagnosed or metastatic disease, out of whom 25% die within 2 years 4. As shown by the statistics published by GLOBOCAN 2018, the age-standardized incidence and mortality rate of PC in Iraq

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have been reported to be respectively 6.6 and 2.0 per 100,000 [5]. Moreover, the incidence rate of PC among the population living in Sulaimani, the Kurdistan Region of Iraq was 36, 67, and 41 cases respectively in 2008, 2012, and 2013[6].

PC incidence and survival rates vary widely in different regions of the world; however, little variation has been reported in mortality rate [7]. It has been reported that the risk of death is more common in men with a Gleason grade of 8-10 tumor, advanced clinical stage, or prostate-specific antigen (PSA) of greater than 20 nanograms per milliliter (ng/mL).In addition poor survival rates have been reported in patients with castration-resistant prostate cancer (CRPC) which is an advanced form of PC [8].

The 5-year survival rate is defined as the percentage of patients who live a minimum of 5 years after their cancer is diagnosed. Research has indicated improvement in the 5-year survival rate for patients with prostate cancer [9] which has largely been attributed to the fact that there has been in increase in utilizing the PSA test for PC diagnosis. Survival rate can be influenced by many factors including the patient's age, overall health status, the treatment received, and how well the cancer responds to the treatment. According to the reports by the American Cancer Society, over the last 25 years, there has been an increase from 68% to 100% in the 5-year relative survival rate for all stages of prostate cancer [10]. It has also been reported that 5-year relative survival rate is slightly lower in men under the age of 50 years [11].

Given what was mentioned above and the fact that no study has focused on survival patterns of and effective factors in patients with prostate cancer in the Kurdistan Region of Iraq, the present study was carried out in order to figure out the parameters involved with survival patterns and rates of PC patients.

Method

Study Design and Patients: This study was carried out using a retrospective cohort design with a nested case-control study approach on a number of patients suffering from prostate cancer at Hiwa Cancer Hospital located in Sulaimania, the Kurdistan Region of Iraq in 2014. The participating patients were chosen from among the total number of the patients (n=257) who were diagnosed to have prostate cancer through laboratory investigations (biopsy and elevated PSA) at Hiwa Cancer Hospital from July 1, 2009 to July 1, 2014. Of those 257 patients, 150 cases were selected as the study sample in the present study (75 with castration resistant prostate cancer, 75 with non-castration resistant prostate cancer). Using Statsdirect statistical software and based on the assumption of an event rate of 0.2 in the control group, the sample size was determined to be 150 17. After the patients were chosen, they were divided into two groups, such that those with resistance to androgen deprivation therapy were considered as the case group and those without resistance to androgen deprivation therapy within the first three years of prostate cancer treatment were regarded as the control group.

Data Collection: A researcher-administered questionnaire was utilized to collect the required data through structured interviews with the patients either on phone or face-to-face at their homes. The questionnaire aimed to collect data on the patients' socio-demographics, medical history of chronic diseases, PC-related risk factors, and anthropometric measurements. Moreover, the patients' hospital records were reviewed under the supervision of the managing physicians in order to collect required clinical data. It should be noteworthy that no examination was carried out in the present study to obtain required data.

Statistical Analysis: After the collected data were revised and coded, they were analyzed through SPSS (version 20). In so doing, descriptive statistics was utilized, and the results were expressed as means (±standard deviation). In addition, Pearson's Chi-square test, Mann Whitney test, independent samples t-test, and one-sample Kolmogorov-Smirnov test were run to check if the difference between the groups was significant or not. The level of statistical significance was set at $p<0.05$ for all statistical tests. Survival analysis was conducted using Cox prorportional hazards model. A Kaplan-Meier curve was constructed.

Ethical Considerations: The ethical considerations were taken into account by receiving approval for the study protocol from the research ethics committee of the High Institute of Public Health (HIPH) - Alexandria University, Egypt. Furthermore, necessary approval was retrieved from the Ministry of Health, the Kurdistan Region of Iraq and Directorate of Health Sulaimaniyah. Finally, informed consent was obtained from the participants, and necessary measures were taken in order to keep their information strictly confidential.

Results

Based on the findings, the proportion of castration resistance was 63.03%. Distribution of PC cases and the controls according to age and family history has been shown in table 1.

Table 1. Distribution of PC cases and the controls according to age and family history

Sociodemographic characteristics	Group				*X2* (P-value)	OR (95% CI)
	Controls		Cases			
	No	%	No	%		
Age in years						
▪ 50-	11	14.7	8	10.7	0.43 (0.511)	1
▪ 65-80	44	58.7	45	60.0		1.4 (0.51-3.4)
▪ 80+	20	26.7	22	29.3		1.5 (0.51-4.5)
Family history						
▪ No	64	85.3	66	88.0	0.23 (0.631)	1
▪ Yes	11	14.7	9	12.0		0.79 (0.31-2.1)

Regarding the clinical characteristics, the results revealed that in terms of their disease stage, 40%, 28%, 17.3%, and 14.7% of the cases were respectively in stages II, IV, III, and I, while 45.3%, 24.7%, 16%, and 4% of the controls were respectively in stages II, I, III, and IV, and the two groups were significantly different in this regard (p=0.001) (See Table 2).

Table 2. Comparison between the CRPC and non-CRPC patients regarding their clinical characteristics

Clinical characteristics	Group				*X2* (P-value)	OR (95% CI)
	Controls		Cases			
	No	%	No	%		
Histopathology						
▪ Adenocarcinoma	71	94.7	75	100.0	0.043*!	9.5 (1.2-179.1)*
▪ Sarcoma	4	5.3	0	0.0		1
Stage						
▪ Stage I	26	34.7	11	14.7	17.9 (0.001)*#	1
▪ Stage II	34	45.3	30	40.0		2.1 (0.88-4.9)
▪ Stage III	12	16.0	13	17.3		2.6 (1.0-7.3)*
▪ Stage IV	3	4.0	21	28.0		16.5 (4.1-67.1)*

The mean overall survival time among the PC patients according to their age has been shown in table 3.

Table 3. The mean overall survival time among the PC patients according to their age

Age	Mean		P-value
	Estimate	Std. Error	
<60	4.18	0.297	0.982
60-80	4.47	0.107	
80+	4.36	0.168	
Overall	4.46	0.091	

Regarding the patients' OS according to the stage of their tumor, as expected, the Kaplan-Meier curves indicated that the highest probability of survival belonged to tumors of stage I, followed by those patients with tumors of stages II and II, and the lowest OS belonged to patients with tumors of stage IV (See Figure 1). with a statistically significant difference between the groups(p<0.001).

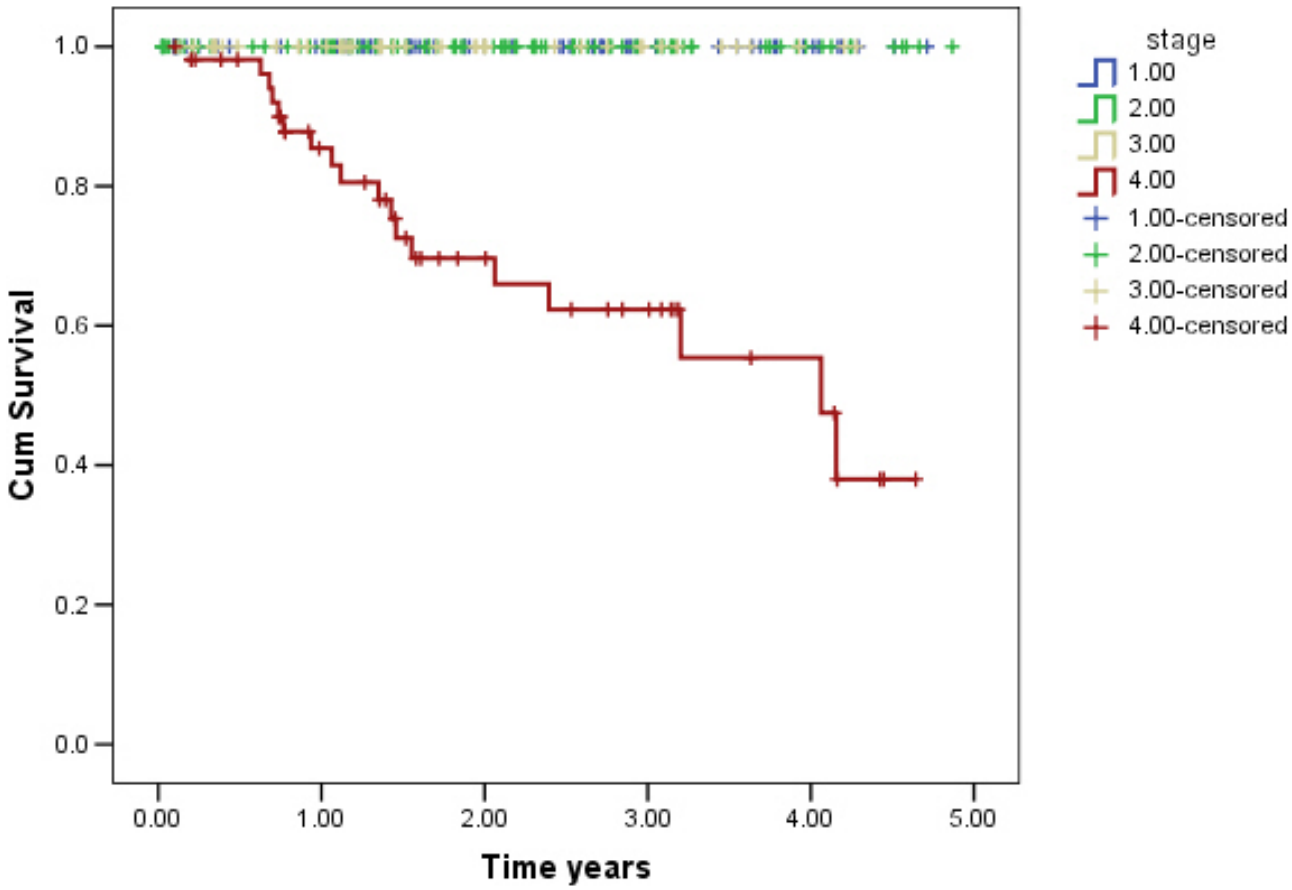

Fig. 1. Kaplan-Meier survival curve of patients with prostate cancer according to stage of tumor

Regarding the patients' progression-free survival (PFS), the results showed that the mean and median PFS were respectively 2.469 (±0.116) and 2.712 (±0.155) years (See Table 4).

Table 4. The mean and median progression-free survival in the PC patients

Mean				Median			
Estimate	Std. Error	95% CI		Estimate	Std. Error	95% CI	
		Lower Bound	Upper Bound			Lower Bound	Upper Bound
2.469	.116	2.241	2.696	2.712	.155	2.408	3.017

The results also showed that there was a significant difference between different age groups in terms of their progression-free survival (p=0.025), such that patients aged 60-80 years had the longest PFS and those over 80 years the shortest PFS. Also, regarding the patients' histopathology, the results revealed a significant difference between patients with adenocarcinoma and sarcoma in terms of their PFS (p=0.006), such that patients with adenocarcinoma had a remarkably longer PFS. (See Table 5).

Table 5. Comparison between different age groups, stages, and histopathology regarding their PFS

	Mean				p-value
	Estimate	Std. Error	95% CI		
Age					
<60	2.333	.400	1.550	3.117	0.025
60-80	2.603	.145	2.318	2.888	
80+	2.220	.212	1.806	2.635	
Overall	2.469	.116	2.241	2.696	
Stage					
I	2.136	.180	1.784	2.489	0.124
II	2.643	.199	2.254	3.033	
III	2.220	.231	1.767	2.673	
IV	2.814	.276	2.273	3.355	
Overall	2.469	.116	2.241	2.696	
Histopathology					
Adenocarcinoma	2.540	.122	2.301	2.778	0.006
Sarcoma	1.536	.317	.915	2.157	
Overall	2.469	.116	2.241	2.696	

Discussion

Based on the finding of this study due to the specific conditions in this region as a result of environmental and epidemiological changes, changes in lifestyle, and the effect of chemical hazards because of wars, there has been an increase in the incidence rate of prostate cancer over the past decades [12].

The results of the present study revealed that most of the patients (60% of the cases and 58.7% of the controls) were 65-80 years old. This finding is in good agreement with the report by Williams and Powell (2009) who referred to old age as the most significant risk factor for prostate cancer. Although research has regarded family history as a well-established risk factor for prostate cancer [13], the results showed that most of the patients (88% of the cases and 85.3% of the controls) did not have a positive family history of prostate cancer.

As revealed by the results of the present study, all of the patients in the case group (100%) and most of those in the control group (94%) had adenocarcinoma, while sarcoma was diagnosed in none of the cases and in a very few control (5.3%). This finding is in line with the results of the studies carried out in Iran [14]. Moreover, most of the patients in the current study were diagnosed to be at stages I and II. Research has indicated that there is a significant direct correlation between stage of disease and PC survival rate, such that patients who are at stages I and II have a higher survival rate[15].

In the present study, it was seen that the mean overall survival (OS) time for the patients was 4.46 years, with the longest OS (4.47 years) belonging to the age group 60-80 years. This finding is partly in agreement with previous studies which reported that survival maximizes in men who are 60-69 years old at the time of diagnosis[16,17].

The results of the present study showed no significant relationship between the patients' age and their survival rate ($p>0.05$). However, it was observed that older patients with prostate cancer had higher survival durations. This finding is supported by the results of the study carried out by Yang et al. (2013) who reported that older patients with single-bone metastasis had a higher survival rate [18]. It was also seen that there was a significant difference between prostate cancer patients with tumors of different stages in terms of their overall survival time ($p>0.001$), such that patients with tumors stages I had the longest survival duration, followed by those with stages II and II. This finding is well supported by previously conducted studies [16, 17].

In this study, there was a significant difference between different age groups in terms of their PFS at a p-value of 0.025, such that the longest PFS belonged to the age group 60-80 years, followed by <60 years, and over 80 years. Similar results were reported in a study conducted in the US to analyze survival in 275,280 histologically confirmed adult cases of PC [19].

In the present study, no significant relationship was observed between the stage of tumor and PFS. Also, low probability of progression-free survival was seen in patients with stage I of tumor, which can be related to the late diagnosis of prostate cancer. PFS can be influenced by several factors such as screening program which is absent in Kurdistan, lack of specialized units for detection of PC, and lack of an efficient reporting system. The lowest PFS was observed in the patients are stage IV, which is in line with the results of the study carried out in the USA [19].

Results revealed a significant relationship between the patients' histopathology results and their PFS, such that patients with adenocarcinoma had remarkably higher progression-free survival of 2.54 compared to those with sarcoma who had a PFS time of 1.536 years (p=0.006). This finding can be due to the small number of patients with sarcoma, which is in line with Alizadeh's study[14].

Conclusion

Prostate cancer is more likely to develop in males aged 65 to 80 year. Patients' overall survival is not correlated with their age, while there is a correlation between the stage of their tumors and their overall survival. The patients' their progression-free survival was found to be significantly affected by their age and histopathology, while the stage of their tumors was not in a significant correlation with their progression-free survival.

Conflict of Interest: Not

Ethical Clearance: The study was approved by the ethical committee of the High Institute of Public Health (HIPH) - Alexandria University, Egypt and Ministry of Health, the Kurdistan Region of Iraq .

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