Original Article

Determinants of Mortality among Patients Managed for Prostate Cancer: Experience from Korle Bu Teaching Hospital in Ghana

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Abstract

Background: Over the past two decades, diagnosis and treatment approaches for men with prostate cancer have changed dramatically, with improvements in established prostate cancer treatments and new treatment strategies. However, In sub-Saharan African countries, there is a paucity of data on the characteristics and treatment of men who eventually die from Prostate Cancer (PCa). We used the clinical records of patients who died from PCa to describe the natural history and treatment PCa patients in Ghana. **Methods:** From 2013 to 2022, the medical records of 234 men who died of PCa at a tertiary hospital in Ghana were prospectively collected and retrospectively analysed. **Results:** The mean age at death was 71.6 years, and the median was 72.5 years. 51.3% died within 24 months of diagnosis, 23.0% between 2 and 5 years after diagnosis, and a quarter survived for more than 5 years. Over 80% presented with advanced disease, characterised by high prostate-specific antigen (PSA) levels, a high T stage on DRE, and evidence of metastasis. 43.6% presented with haemoglobin levels below 10ng/dl at diagnosis. These patients had the worst outcome, with 73% dying less than 2 years after diagnosis. The 5-yr survival rate of patients who presented with metastatic disease was 21.2 %. Over 80% were treated with bilateral total orchidectomy, with less than 10% receiving treatment intensification with the newer generation antiandrogens or chemotherapy. **Conclusion:** Our analysis shows that patients who die from PCa have aggressive disease, are diagnosed at an advanced stage, and are relatively younger than in Western countries. There is also a slow uptake of newer treatment strategies for metastatic prostate cancer. These results confirm literature suggesting that blacks have poorer outcomes due to the disease's aggressive nature. Further research is needed to understand the mechanisms and also define appropriate management for metastatic PCa in sub-Saharan Africa.

Keywords: *Africa, mortality, prognosis, prostate cancer, treatment*

Introduction

Prostate cancer (PCa) is the second most frequently diagnosed cancer worldwide and the fifth leading cause of cancer death among men in 2020.[1] In Ghana, it is the second leading cause of male cancer death[2] and the leading male cancer seen at Korle Bu Teaching Hospital.[3] In western countries, routine prostate-specific antigen (PSA) testing has contributed to an increase in the prevalence of PCa and a change in the stage at which it is typically diagnosed, with the incidence of detectable metastases at diagnosis decreasing from more than 50% of the cases in the 1970s to less than 10% currently.[1] Additionally, the recent introduction of treatment intensification for metastatic disease with new-generation antiandrogens and chemotherapy has significantly changed the PCa landscape in western countries.[4] It is, therefore, essential to study the situation in developing countries to understand the current state of PCa and identify areas for improvement.

PCa is a disease with a long natural history, and many patients diagnosed with it may not ultimately die from it.[5,6] In the United States, the lifetime risk of being diagnosed with PCa is approximately 11%, and the lifetime risk of dying of PCa is 2.5%.[7] Therefore, it is important to identify the characteristics of lethal PCa and accurately differentiate them from most patients with the indolent, slow-growing disease, who will likely die with, rather than of, the disease. Because the natural history of PCa can span from a few years to decades,[5] following up can be challenging in countries without a sophisticated cancer registry. One way to overcome this challenge is through the retrospective analysis of the records of patients who have died from PCa.

How to cite this article: Mensah JE, Amoah Y, Ofori E, Albezel M, Vanderpuye V. Determinants of mortality among patients managed for prostate cancer: Experience from Korle Bu Teaching Hospital in Ghana. J West Afr Coll Surg 2023;13:65-70.

Received: 29-Jan-2023
Accepted: 01-Mar-2023
Published: 27-Jun-2023

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Access this article online

Website: www.jwacs-jcoac.com

DOI: 10.4103/jwas.jwas_26_23

Quick Response Code:

This study aimed to describe the characteristics and natural history and treatment received by patients dying of PCa in Ghana

Patients and Methods

Study population

The study was conducted at the Korle-Bu Teaching Hospital (KBTH) in Accra. The hospital is presently the leading national referral healthcare facility in Ghana, with a bed capacity of 2000. The study population included all patients diagnosed with PCa at the hospital during the study period who died of the disease. Patients were excluded if they did not have complete medical records or had been diagnosed with PCa but did not die of PCa.

Data collection

Medical records were obtained from the patient's folder, death certificates, and the hospital's electronic medical record system. Data were extracted using a standardised data collection form that included Demographic information, initial PSA levels, haemoglobin level, Gleason scores, staging data, and primary treatment modality. Data were collected by urology registrars who reviewed the medical records and extracted relevant information from the data collection form. The date of diagnosis was the date of histopathological confirmation for PCa. For those without histopathological confirmation, the diagnosis date was determined based on PSA, digital rectal examination (DRE), and imaging results. After the history, physical examination, and imaging tests, the stage at diagnosis was classified as local, locally advanced/lymph node-positive, or metastatic disease. The interval from diagnosis to death was used to calculate the length of survival

Data analysis:

Descriptive statistics were used to summarise the demographic and clinical characteristics of the study population. Chi-square tests of independence were used to estimate P values by comparing the association between the various parameters and survival duration. Statistical analyses were performed using STATA software (version 14).

Ethics:

The study was approved by the institutional review board at the hospital, and all patient data were deidentified to protect patient privacy. Informed consent was not required for the use of medical records in this study.

Results

Study cohorts

A total of 234 medical records were obtained over 10 years between 2013 and 2022. The number of records examined each year ranged from 20 to 28.

Age at death

Most patients who died from PCa were aged 60 to 79. The mean age at death was 71.6 years, and the median was 72.5 years. The percentage distribution of deaths according to specified age groups is shown in Tables 1 and 2. The highest frequency of patients was in the age range 70–79, with 100 patients, followed by the age range 60–69, with 74 patients. The lowest frequency of patients was in the age range 45–49, with 2 patients, and in the age range 90 and above, with 2 patients [Table 1].

Survival time

Most patients (51.3%) died within 24 months of diagnosis. A significant percentage of patients, 23.0%, died between 2 and 5 years after diagnosis, while a quarter of the cohort survived for more than 5 years after diagnosis [Table 2].

Prostate-specific antigen

The highest proportion of patients (60.7%) had PSA values of 100 or above at the time of diagnosis and had the shortest survival period, with 56% living less than two years following diagnosis. Patients with PSA values of less than 10 at diagnosis had the best survival, with 50% living more than six years [Table 2].

Gleason score

In a significant proportion of the patients (38%) in this study, a Gleason score could not be assigned because a biopsy was not performed. These patients presented with PSA over 100, T3 or T4 disease on digital rectal examination, evidence of osteoblastic deposits on X-ray and were deemed too frail for biopsy due to the high risk of complications. Not surprisingly, these patients had a poor outcome similar to those with Gleason scores of 8–10 on biopsy, with 72% and 50% dying within 2 years of diagnosis, respectively. There is a clear trend of decreasing survival time as the Gleason score increases. Patients with a Gleason score of 6 & below had the most prolonged duration of survival, with almost a quarter surviving for more than 6 years [Table 2].

DRE

Most patients (39.7%) had T2 results on the DRE at diagnosis, followed by T3 (26.9%), T4 (23.0%), and T1 (7.2%). There is a trend of decreasing survival time as

Table 1: Age ranges of the cohort

Age range (years)	Frequency	%
40–49	2	0.85
50–59	24	10.26
60–69	74	31.53
70–79	100	42.68
80–89	32	13.68
90 and above	2	0.85
Total	234	100

Table 2: Clinical parameters and duration of survival

Years of Survival					Percentage	Chi-square
PSA (ng/mL)	**Total**	**Less than 2 years**	**2 to 5 years**	**Over 5 years**		**(*P* Value)**
< 10	12	4 (33.3%)	2 (16.7%)	6 (50.0%)	5.10%	16.07(0.065)
10-50	51	21 (41.2%)	11 (21.6%)	19 (37.3%)	21.80%	
50-100	29	15 (51.7%)	5 (17.2%)	9 (31.0%)	12.40%	
> 100	142	80 (56.3%)	36 (25.4%)	26 (18.3%)	60.70%	
Total	234	120 **(51.3%)**	54 **(23.0%)**	60 **(25.6%)**	100%	
Gleason score						
No Gleason	89	64 (71.9%)	16 (18.0%)	9 (10.1%)	37.90%	15.40(0.017)
6 & Below	17	5 (29.4%)	4 (23.5%)	8 (47.1%)	7.20%	
7	38	10 (26.3%)	5 (13.2%)	23 (60.5%)	16.20%	
8-10	90	45 (50.0%)	29 (32.2%)	16 (17.8%)	38.30%	
Total	234	124 (53.0%)	54 (23.0%)	56 (23.9%)	100.00%	
DRE						
Not available	10				4.30%	
T1	14	4 (28.6%)	2 (14.3%)	8 (57.1%)	6.00%	15.40(0.080)
T2	86	44 (51.2%)	21 (24.4%)	21 (24.4%)	36.60%	
T3	63	36 (57.1%)	14 (22.2%)	13 (20.6%)	26.90%	
T4	61	41 (67.2%)	12 (19.7%)	8 (13.1%)	26.10%	
Total	234	125 (53.4%)	49 (20.9%)	60 (25.6%)	100.00%	
Haemoglobin levels						
Not available	4				1.70%	
< 10	102	74 (72.6%)	16 (15.7%)	12 (11.8%)	43.40%	22.99(0.0010)
10-13	76	38 (50.0%)	19 (25.0%)	19 (25.0%)	32.50%	
> 13	52	7 (13.5%)	18 (34.6%)	27 (51.9%)	22.40%	
Stage						
Localised	19	0 (0.0%)	6 (31.6%)	13 (68.4%)	8.10%	Not done
Locally advanced	22	10 (45.5%)	6 (27.3%)	6 (27.3%)	9.40%	
Metastatic	193	111 (57.5%)	41 (21.2%)	41 (21.2%)	81.70%	
Total	234	121 (51.7%)	53 (22.6%)	60 (25.6%)	100.00%	

the DRE finding becomes more advanced. Patients with DRE T4 had the shortest survival, with 67% dying within two years and only 13% living for more than 5 years after diagnosis. Patients with T1 DRE results had a more indolent course, with 57% surviving more than 5 years [Table 2].

Haemoglobin levels

One hundred two patients (43.6% of the cohort) had haemoglobin levels below 10 at diagnosis. These patients had the worst outcome, with 73% living for less than 2 years after diagnosis. Only 12% survived for more than 5 years. There is a clear trend of increasing survival time as haemoglobin levels at diagnosis increase. Patients with haemoglobin levels above 13 had the best survival duration, with more than half living for more than 5 years after diagnosis [Table 2].

Stage at presentation

Approxomately 81.7% of the patients included in the analysis presented with metastatic stage cancer at diagnosis. Even though most of these patients (57.5%) died within two years, a significant proportion (25%) survived for more than five years after diagnosis. As expected, the survival time decreases as the cancer stage at presentation advances. However, some patients who presented with localised stage cancer and received curative treatment still progressed and died within 5 years, possibly due to advanced disease that was not detected during staging tests

Univariate analysis

PSA at PCa diagnosis, total Gleason score, DRE, T stage, and haemoglobin level were all associated with length of survival. The strength of the association varied, with haemoglobin level having the strongest association and PSA having the weakest association [Table 2].

Treatment received

Androgen deprivation therapy (ADT) was the predominant treatment, with bilateral orchidectomy performed for 83.9% of patients. The second most common treatment was Zodalex/Lupron, given to 36.9% of patients. Oestrogen was the third most common treatment, prescribed to 32% of patients. Local curative treatment in the form of

Table 3: Primary treatment received by the cohort

Treatment	Frequency	%
Bilateral Orchidectomy	204	83.9
Zodalex/Lupron	84	36.9
Oestrogen	75	32.0
RP, EBRT, Brachy	14	9.1
Palliative RT	32	13.0
Abiraterone/Enzalutamide	19	8.0
Chemotherapy	7	3.0

radical prostatectomy, external beam radiotherapy, and brachytherapy was provided to 6.0% of patients, while palliative radiation therapy was administered to 13%. Finally, Abiraterone/Enzalutamide was given to 8.0% of patients, and chemotherapy was prescribed to 3.0% [Table 3].

Discussion

The median age at death in the study was 72 years, which was lower than 79.5 years in the US,[8] but similar to other African countries.[9,10] Approximately 43% of the deaths occurred before 70 years. This finding suggests that PCa may disproportionately affect relatively younger men in this population and may have a more significant impact on their lives and the lives of their families. This could be due to various factors, including poorer access to quality healthcare and screening services and the impact of poverty on overall health and access to treatment. It is also possible that the biological aggressiveness of the disease may be more pronounced in this population, which could contribute to a higher mortality rate. These findings highlight the importance of addressing the factors contributing to the higher prevalence of PCa and poorer outcomes in African populations.

Eleven per cent of patients died before age 60. Since the relative 10-year survival rate for patients with PCa is 100% for localised disease,[8] it implies that at least 11% of patients were affected by the disease in their forties or early fifties. The recommendations by NCCN that black men should commence screening earlier, during an annual physical examination at age 40 and no later than 45,[11] appear very reasonable if the disease is to be detected when a cure is anticipated.

The study found that more than 80% presented with advanced-stage disease at diagnosis, characterised by high levels of PSA and higher T stage and evidence of metastasis, which is consistent with reports from several African[10,12] and Caribbean countries[13] but contrasts with developed countries, where more patients present with early-stage disease.[14]

The 5-year survival rate of 21.2% in our patient who presented with metastatic disease was lower than the 31.6% reported for blacks in the United States.[8] In a large retrospective study of 26,168 patients with metastatic PCa, Elmehrath *et al.*[15] found that most deaths (59%)occurred within 2 years of diagnosis, with black patients having a higher risk of excess death overall compared to white patients. Out of all deaths in their cohort, 77.8% were due to PCa, with 5.5% due to other cancers and 16.7% non-cancer causes. High PSA and T stages have all been associated with increased PCa mortality.[16] The Late presentation could be due to poor access to healthcare, a less educated population, and a lack of screening services.[17] However, the patients could also have advanced diseases because they had biologically aggressive diseases. PCa in Africans tends to be more aggressive and has a higher mortality rate than other populations.[18,19] While some studies suggest that socioeconomic factors may contribute to this trend,[20,21] the biological aggressiveness of the disease appears to play a significant role. Our data supports this, showing that patients with short survival times often had high Gleason score tumours, which are a marker of aggressiveness.[22] These cancers have a limited window of curability and tend to progress rapidly. Ongoing work by several groups to identify genomic markers of aggressiveness of PCa in Africans may be crucial for early detection and improving outcomes.[23,24] The MADCAP team's research,[25] which included patients from this study, may provide valuable insights into specific genomic markers of lethal PCa in Africans.

A finding worth discussing is the small cohort of patients(8.1%) who presented with localised disease and received curative treatment in the form of radical prostatectomy, brachytherapy or external beam radiotherapy but still died of PCa. An explanation for this could be inadequate local treatment or undetected metastatic deposits (Under staging). When a patient with PCa develops metastatic disease within 5 years of treatment for local disease, it can be devastating for the patient and the healthcare team. This is because the patient may have already experienced the costs and complications associated with local treatment. Therefore, patients, especially those with high-risk localised disease, must be made aware of the possibility of undiagnosed metastatic disease so they can make informed decisions about their treatment and manage their expectations about the course of their disease. In addition, healthcare providers should counsel these patients about the potential for cancer to spread without any evidence on traditional staging tests like bone scan, CT scan and MRI,[26] and the importance of regular follow-up after curative treatment. The availability of PSMA (prostate-specific membrane antigen) PET scans in West Africa may help reduce the incidence this problem. These scans are more sensitive than traditional imaging modalities and may be able to detect smaller metastatic deposits that other tests may miss.[27,28]

Our study found that haemoglobin levels were the most significant predictor of survival duration, with 73% of patients with haemoglobin less than 10mg/dl dying within

2 years after diagnosis. Therefore, it is essential to carefully evaluate patients with low haemoglobin levels and consider their overall health and fitness for treatment before initiating therapy with newer medications that may be expensive and may not provide significant survival benefits. This is especially important in a third-world environment where the patient's family may struggle to bear treatment costs. Focusing on supportive care and comfort measures may be more appropriate in some cases than attempting aggressive treatment[29,30]

ADT is a standard metastatic PCa treatment that slows the disease's progression and improves the quality of life. Bilateral Total Orchidectomy (BTO), LHRH agonists, and oestrogens are all equally effective forms of ADT,[31] with BTO often the most affordable option.[32] As a result, it is the most commonly used form of ADT, with about 80% of patients receiving this treatment. Intensification of treatment with second-generation antiandrogens (such as abiraterone or enzalutamide) or chemotherapy is now recommended for metastatic PCa.[11] However, less than 10% of patients received this more aggressive treatment, despite the availability of level 1 evidence from clinical trials and several guideline recommendations from the US and Europe indicating that the addition of these treatments may improve survival outcomes for certain patients with metastatic PCa.[11] There are several potential explanations for this finding. One possibility is that the cost of these treatments is a barrier to their use. It is also possible that some urologists and oncologists may not be aware of the studies demonstrating the potential benefits of these treatments or may not feel confident in their ability to administer them; furthermore, some patients may not be fit for these treatments, for example, patients with low haemoglobin levels. It is important to note that patients recruited into clinical trials evaluating the use of abiraterone and chemotherapy in PCa generally had an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2,[4,33]which may limit the generalizability of these findings to the very sick. The uptake of ADT intensification with abiraterone, enzalutamide, or chemotherapy has been slow, with a reported usage of 11%, even in well-resourced countries.[34] Cost is often cited as the most significant factor contributing to this trend. In developing countries, the cost of these treatments may be a substantial barrier to their use. However, with the recent reduction in the cost of these drugs,[35] more eligible patients in these settings may benefit from improved survival outcomes demonstrated in clinical trials. As ADT intensification becomes more widespread in Africa, it will be necessary to monitor the uptake and impact of these treatments in these settings to understand the factors that influence their utilisation and to identify strategies to improve access.

Limitations

The study may be biased towards patients with shorter survival durations as their medical records are more likely to be complete and up-to-date, increasing the likelihood of their inclusion in the analysis. This should be taken into account when interpreting the results.

Conclusion

In conclusion, this study analysed the characteristics and treatment patterns of patients with PCa who died in Ghana. The analysis results suggest that these patients generally have aggressive disease, are diagnosed at an advanced stage, and have shorter 5-yr survival, with the survival time being highly dependent on haemoglobin levels at diagnosis. Most of these patients received BTO as treatment, with less than 10% receiving ADT intensification with newer-generation antiandrogens or chemotherapy. These findings suggest opportunities for increasing the life expectancy of PCa patients. Further research is needed to understand the reasons for the advanced presentation and the potential impact of the current recommendation of ADT intensification on survival outcomes. Encouraging screening for PCa beginning at age 40 and ending at age 75 may be an important strategy for reducing PCa mortality in Africans.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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