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Hormone-Naïve Metastatic Prostate Cancer: A Presentation of 110 Cases in a Urology Center in the City of Douala, Cameroon

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Abstract

Aim: According to World Health Organization, prostate cancer is one of the increasing malignancies in men worldwide. This paper aims to describe the epidemiological, clinical, diagnostic, therapeutic, and evolutionary aspects of patients with early metastatic prostate cancer in a urology center in the city of Douala in Cameroon. **Materials and Methods:** It is a retrospective and descriptive study of 110 patients with prostate cancer that was immediately metastatic at diagnosis over a period of six years (from January 2014 to December 2020). **Results:** The average age of patients at diagnosis was 67.5 years (range: 45 years to 88 years) and 53.63% of patients had body mass indexes greater than 25. Disorders of the lower urinary tract were the main presenting complaint in 55.45% of cases, followed by bone and joint pain in 46.36% of cases. Digital rectal examination was suggestive of prostate cancer in 96.36% of cases with an average total prostatic specific antigen (PSAT) level of 676.9 ng/ml (range: 21.8 to 8832 ng/ml). The diagnosis was made through prostate biopsy in 57 (51.81%) patients or after palliative endoscopic resection of the prostate indicated for lower urinary tract symptoms or even acute urinary retention in 53 (48.18%) patients. Adenocarcinoma of the prostate was the main histologic type, and in 47.27% of cases, the tumor was poorly differentiated with a Gleason's score of greater than 7. The sites of metastasis were mainly the lymph node (87.27%), bone (56.36%), and both (44.54%). The treatment was palliative and dominated by bilateral pulpectomy in 60% of cases and luteinizing hormone-releasing hormone agonists (Triptorelin 11.25

mg every 3 months) in 44 (40%) of cases. **Conclusion:** Prostate cancer is a real public health problem in developed countries but also in Africa, especially in Cameroon. It is aggressive cancer that is often diagnosed when metastasis has already occurred. Its management is essentially palliative.

Keywords

Prostate Cancer, Metastasis, Hormone Therapy, Palliative Treatment

1. Introduction

Prostate cancer is one of the malignant conditions whose prevalence is on the rise in men worldwide [1]. There is a distinct geographical variation in the incidence of prostate cancer. It is the most frequently diagnosed cancer among men in over half (105 of 185 of the countries of the world, especially in the Americas, Northern and Western Europe, Australia/New Zealand, and much of Sub-Saharan Africa. GLOBOCAN estimates of the incidence and associated mortality worldwide for 36 different types of cancer in 185 countries [2]. It is the leading cause of cancer-related death among men in 46 countries, especially in Sub-Saharan Africa and the Caribbean. The prevalence rates are highest among men of African descent in the United States and the Caribbean, reflecting an ethnic and genetic predisposition [3]. The diagnosis of prostate cancer has improved over the years. A suspicious digital rectal examination is an indication for prostate biopsies regardless of the serum PSA level. Magnetic resonance imaging (MRI) can increase the rate of identification of clinically detectable prostate cancer and guide prostate biopsies of these lesions [4]. The metastatic disease burden of the population is high in prostate cancer patients because of its long natural history and the quality of life decrements associated with its treatment [5]. Hormone-naïve prostate cancer is generally subdivided into two categories, which are biochemical recurrence and metastatic prostate cancer, and are characterized by no prior hormonal therapy or Androgen deprivation therapy [6]. The basis for the treatment of metastatic prostate cancer at diagnosis is the knowledge of the natural history of the disease, the biology of the primary tumor, and its metastases. This is to improve the survival of patients with advanced disease [7]. Laville *et al.* demonstrated that the management of early metastatic prostate cancer was based on a systemic treatment via Androgen deprivation therapy with or without chemotherapy or new-generation anti-androgen therapies [8]. This study aimed to describe the clinical characteristics and outline the treatment delivered to patients with metastatic hormone-naïve prostate cancer (mHNPC) and evaluate factors that may predict the survival of patients followed up in a specialized urology institution in the city of Douala, Cameroon.

2. Patients and Methods

This was a retrospective, population-based study of all patients diagnosed with

prostate cancer at the *Centre medico-chirugicale d'urologie* in Douala, Cameroon, between January 2014 and December 2020. We included 110 patients who underwent transrectal ultrasound-guided biopsy (TRUS-guided), patients who were determined to have prostate cancer by Gleason's score criteria, and patients known to have distant metastases at diagnosis. Patients with any previous Androgen deprivation therapy, radiotherapy, or radical prostatectomy were excluded. Pre-tested questionnaires were used to collect data from our study participants. The data collected included age, family history of prostate cancer, lower urinary tract symptoms, body mass index (BMI), digital rectal examination (DRE) findings, PSA, hemoglobin level, Gleason score, serum creatinine, prostate volume, and urinary tract dilatation. An extension workup was performed to look for metastases. It included the abdominal, pelvic, and thoracic computed tomography, bone scan, and MRI. The minimum follow-up period was four months. All treatments delivered were recorded: pulpectomy, LHRH agonists, Abiraterone, Enzalutamide, Docetaxel, and Bisphosponates. Survival was considered as the time-lapse between the date of diagnosis of metastases and the date of demise due to disease or any other cause, or the date of last known follow-up. For overall survival (OS), hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using the univariate Cox proportional hazards models. Median survival times were estimated using the Kaplan-Meier method. Continuous variables were presented using the mean standard deviation for normally distributed variables and the median and interquartile range for variables with skewed distributions. Categorical variables were presented as frequencies and percentages. The data collected using pre-tested questionnaires were entered into Microsoft excel 2016 and exported to SPSS version 23.0 for statistical analysis. Values of $P \leq 0.05$ were considered statistically significant.

3. Results

3.1. Patient Characteristics

In total, 110 patients with metastatic prostate cancer were diagnosed in the *Centre d'Urologie* in Douala, Cameroon, between January 1, 2014, and December 31, 2020 (**Figure 1**). The median age of patients was 69 years [61 - 73].

At diagnosis, 61 (55.45%) patients complained of lower urinary tract symptoms, 39 (35.45%) patients presented with acute urinary retention, 51 (46.36%) patients presented with bone and joint pain, two patients presented with paralysis of the lower limbs, one patient thigh pain, one other patient with pathological hip fracture, and six (5.45%) patients were asymptomatic, as can be seen in **Figure 2**.

The median body mass index (BMI) of all the patients was 25.25 [23.1 - 27.4].

Among the 110 patients, 10 (9%) patients had a family history of prostate cancer. The findings of the digital rectal examination were indicative of prostate cancer in 106 (96.3%) patients. The median PSAT was 226.95 [115 - 528] ng/ml. The distribution of the study participants according to PSAT levels is presented

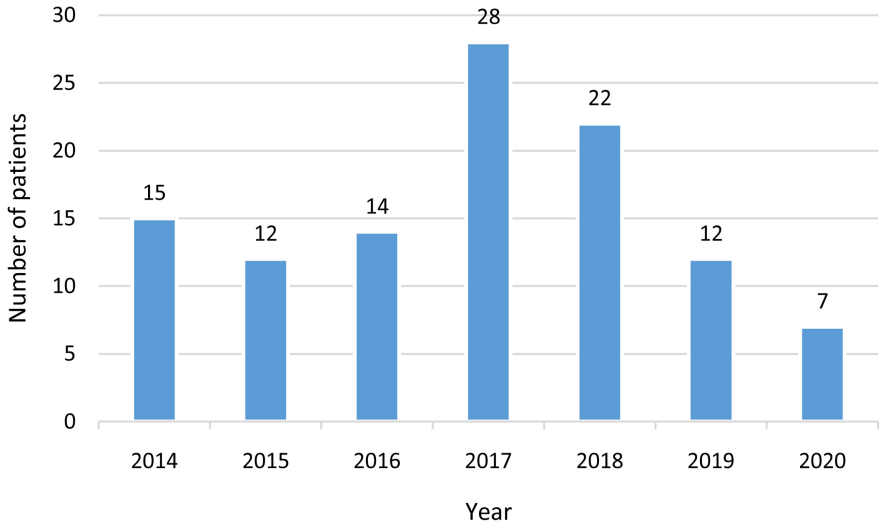


Figure 1. Distribution of the study participants by year.

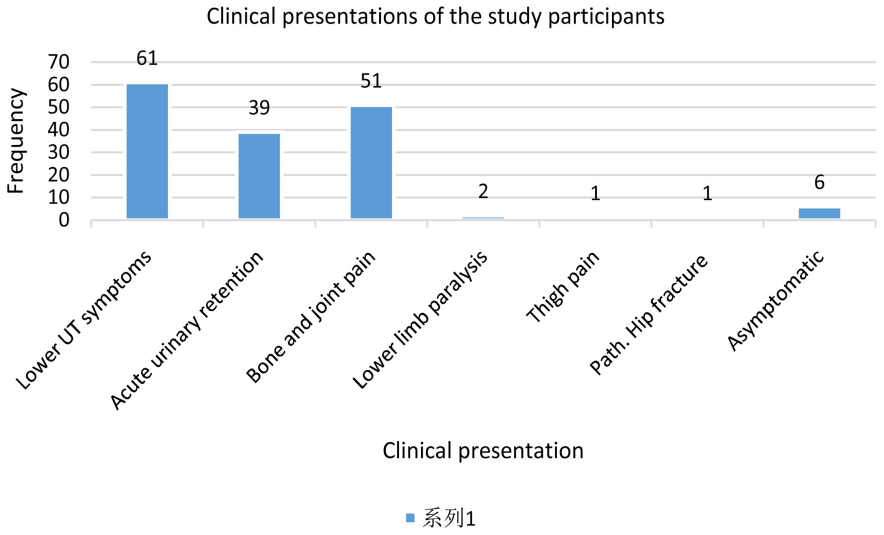


Figure 2. Clinical presentations of the study participants.

in **Figure 3**.

The median hemoglobin level was 10.55 [8.9 - 12.2] g/dl. The median prostate volume was 70 [50 - 98] ml. The measurement of kidney function by assaying serum creatinine showed a median value of 13 [11.6; 21] mg/L. Then, prostate biopsies were performed on 57 (51.9%) patients. There were 53 (48.1%) patients diagnosed following endoscopic palliative resection of the prostate. The distribution of Gleason's score features of prostate biopsies is presented in **Table 1**.

Thoraco-abdomino-pelvic CT scans were performed in 40 (36.36%) patients, abdominopelvic CT scans were done in 70 (63.63%) patients, and bone scans were done in 11 (9.09%) patients. The magnetic resonance imaging of the prostate was performed in 8 (7.27%) patients (**Table 2**).

Concerning urinary tract examination, we found unilateral hydronephrosis in 21 (19.09%) patients and bilateral hydronephrosis in 11 (10%) patients. **Figure 4**

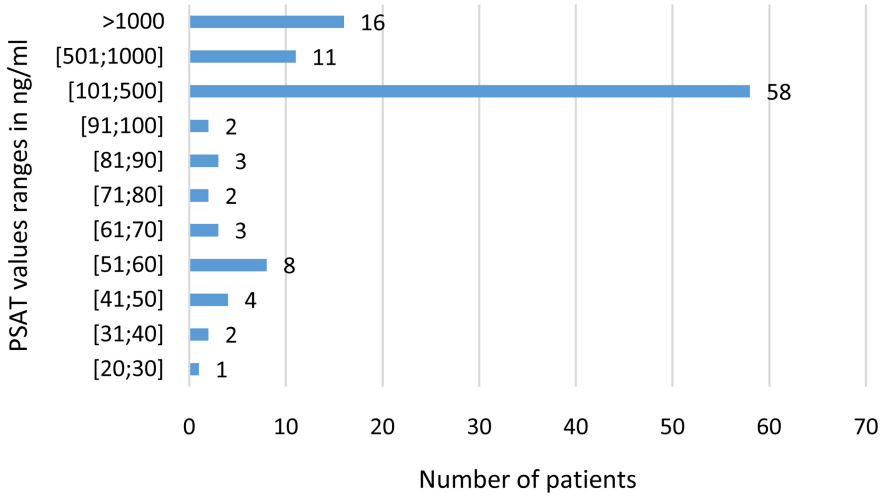


Figure 3. Ranges of PSAT values in the patients.

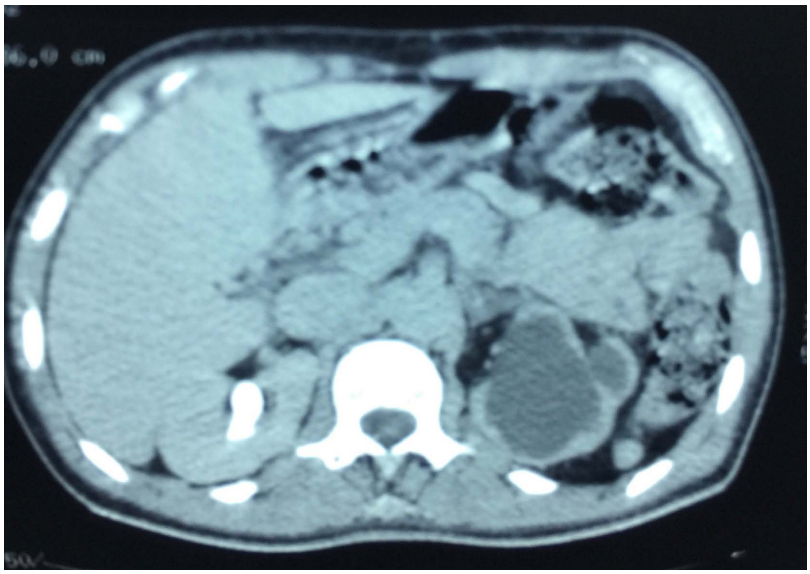


Figure 4. Left ureterohydronephrosis.

Table 1. Gleason score and ISUP grade 2016.

Gleason score	Frequency (N = 110)	Percentage (%)
6 (3 + 3) (ISUP 1)	20	18.18
7 (3 + 4) (ISUP 2)	28	25.45
7 (4 + 3) (ISUP 3)	10	9.09
8 (4 + 4) (ISUP 4)	13	11.81
8 (3 + 5) (ISUP 4)	10	9.09
8 (5 + 3) (ISUP 4)	6	5.45
9 (4 + 5) (ISUP 5)	12	10.9
9 (5 + 4) (ISUP5)	09	8.18
10 (5 + 5) (ISUP 5)	02	1.81

Table 2. Characteristics patients that underwent magnetic resonance imaging of the prostate.

Age	DRE	PSAT (ng/ml)	Prostate volume (ml)	Gleason score
61	Positive	55.50	65	9 (5 + 4)
68	Positive	54.77	100	7 (3 + 4)
75	Positive	43.40	80	9 (4 + 5)
67	Negative	88.00	53	6 (3 + 3)
75	Positive	59.00	94	6 (3 + 3)
56	Positive	21.80	60	8 (4 + 4)
62	Positive	70.00	54	7 (4 + 3)
60	Negative	50.00	64	7 (4 + 3)

shows the MRI of a patient with ureterohydronephrosis who was managed at the *Centre d' Urologie*.

In our series, various types of metastases were found in patients (Table 3).

Some distant metastases are illustrated in Figure 5.

3.2. Treatment Modalities

Treatment modalities included bilateral pulpectomy in 66 (60%) patients, luteinizing hormone-releasing hormone agonists (Triptorelin 11.25 mg every 3 months) in 44 (40%) patients, Abiraterone 1000 mg with Prednisone 10 mg and Enzalutamide 160mg were prescribed in 13 (11.81%) and 04 (3.63%) patients, respectively, Docetaxel (DOC) 75 mg/m^2 intravenously every 3 weeks with oral prednisone at a daily dose of 5 mg was delivered in 14 (12.72%) patients, Bisphosphonate (Zoledronic acid 4 mg intravenous) was given in 58 (52.72%) patients (Table 4).

3.3. Survival

The median survival time was 95 weeks and the five-year overall survival was approximately 96% (Figure 6(a) and Figure 6(b)). The mortality rate after a median follow-up of 26.25 months was 40% (N = 44). Descriptive characteristics of death patients are listed in Table 5.

Some factors were associated with the survival of the patients in our study. These factors include age > 70 years, chemotherapy, orchidectomy, treatment with LHRH analogs. The presence of hydronephrosis tended to be associated with patients' survival, although the association was not quite statistically significant. The factors associated with patients' outcomes are presented in Table 6.

4. Discussion

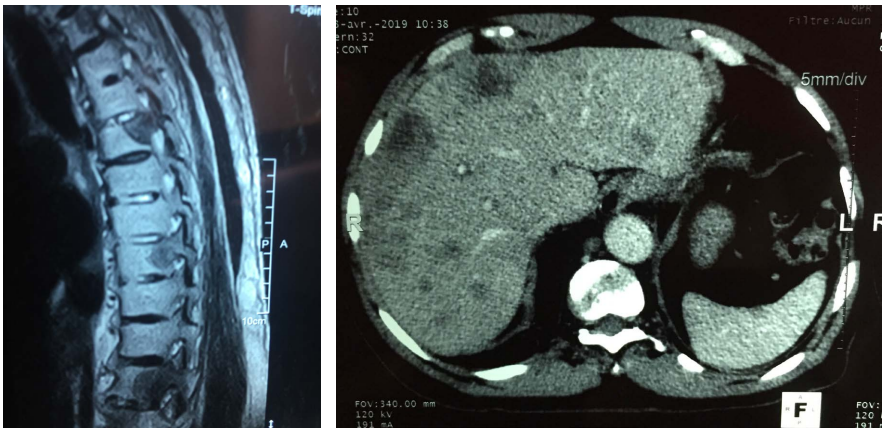
In this study, we aimed to describe the epidemiological, clinical, diagnostic, therapeutic, and evolutionary aspects of patients with early metastatic prostate cancer in a urology center in the city of Douala in Cameroon. Hence, we recruited

Table 3. Locations of metastases in the series.

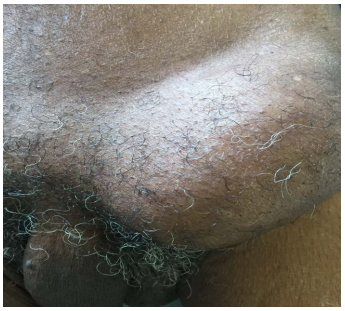
Metastases	Effective (N = 110)	Percentage (%)
Lymph nodes	96	87.27
Bone	62	56.36
Lymph nodes and bone	49	44.54
Liver	04	3.63
Rectum	01	0.9
Seminal vesicles	01	0.9
Lungs	03	0.27
Lung and liver	02	0.18

Table 4. Treatment modalities.

Treatment	Effective (N = 110)	Percentage (%)
bilateral pulpectomy	66	60
LHRH agonists	44	40
Abiraterone	13	11.81
Enzalutamide	04	3.63
Docetaxel	14	12.72
Bisphosphonates	58	52.72

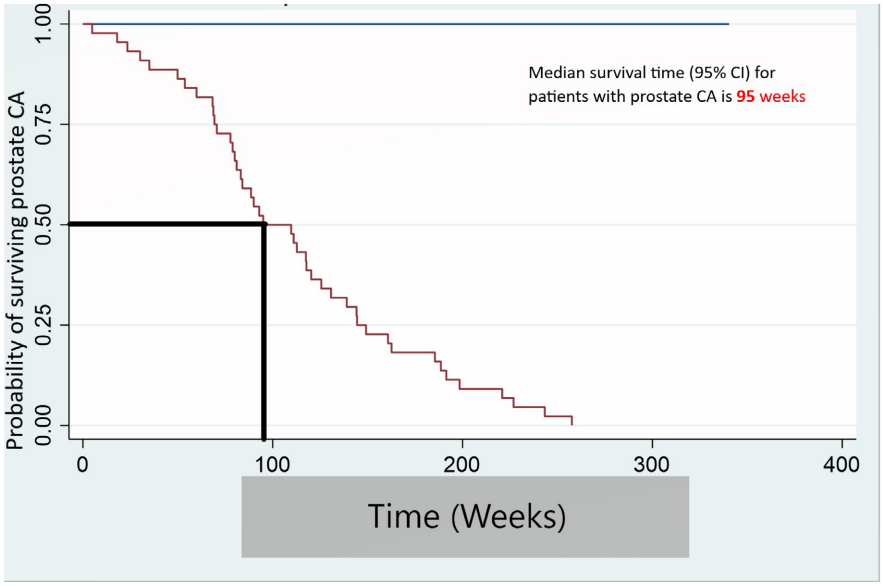


(a) (b)

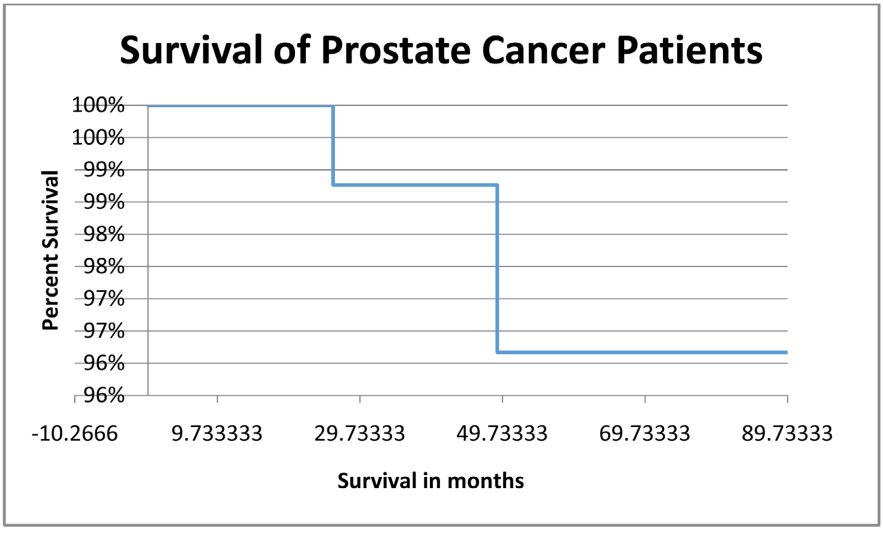


(c)

Figure 5. Metastases at different sites: bone metastasis (a); liver metastasis (b); lymph node metastasis (c).



(a)



(b)

Figure 6. Kaplan-Meier survival estimates ((a): Median survival duration; (b): Overall survival).

110 patients with prostate cancer that was immediately metastatic at diagnosis from January 2014 to December 2020. The median age of the patients was 69 years, which is similar to the values reported by Niang in Senegal and Fofana in Cote d'Ivoire (65 and 68 years, respectively) [9] [10].

A continuously increasing number of new cases of prostate cancer has been reported in some countries in Africa (Cameroon, Gambia, and South Africa) [11]. There is also an association between prostate cancer and family history [12] [13] [14]. In our study, 10 (10%) patients had had a family history of prostate cancer. Although previous studies have identified a contributive family as a risk factor for prostate cancer [15], it was not significantly associated with patients' survival in our study. Lower urinary tract symptoms were the most common

Table 5. Characteristics of patients who died.

Patients		Number (N = 44)	Percentage (%)	Follow-up Duration (weeks)
Age (years)	<55	1	2.27%	112.714286
	55 - 59	9	20.45%	1000.28571
	60 - 64	5	11.36%	759.857143
	65 - 69	5	11.36%	519.285714
	70 - 74	9	20.45%	1222
	75 - 79	8	18.18%	803.428571
	80 - 84	3	6.82%	240.142857
	>85	4	9.09%	302.714286
PSA (ng/ml)	<4	0	0.00%	0
	4 - 19.9	0	0.00%	0
	20 - 99.9	5	11.36%	651.142857
	100 - 199.9	7	15.91%	947.571429
	200 - 499.9	19	43.18%	2245
	500 - 999.9	6	13.64%	602.714286
	>1000	7	15.91%	514
Gleason Score	6	7	15.91%	845.6
	7 (3 + 4)	12	27.27%	1186.9
	7 (4 + 3)	4	9.09%	383.7
	8	9	20.45%	1095.6
	9	10	22.73%	1121.1
	10	2	4.55%	327.6
Metastasis	Lymph nodes	40	90.91%	
	Bone	26	59.09%	
	Lymph node and bone	22	50.00%	
	seminal vesicles	1	2.27%	
	Liver	3	6.82%	
	Lungs	2	4.55%	
	liver and lungs	2	4.55%	
Creatinine (mg/l)	≤13	22	50.00%	2572
	>13	22	50.00%	2388.42857
Hemoglobin (g/dl)	<5	0	0.00%	0
	5 - 10	26	59.09%	2954.57143
	>10	18	40.91%	2005.85714

Continued

Primary Treatment	Pulpectomy	31	70.45%	3168.0
	LHRH Analogues	13	29.55%	1792.4
	Bisphosphonates	25	56.82%	2822.6
	Abiraterone	3	6.82%	470.1
	Enzalutamide	2	4.55%	101.1
	Docetaxel	12	27.27%	1663.7

Table 6. Factors associated with outcome.

EXPOSURE VARIABLE	SURVIVED (%)	DIED (%)	OR [95% CI]	P-value
Orchidectomy	35 (50.03)	31 (46.97)	2.11 [0.94 - 4.74]	**0.05**
Hydronephrosis	16 (48.48)	17 (51.12)	1.97 [0.86 - 4.50]	0.08
Chemotherapy	2 (15.38)	11 (84.62)	0.47 [0.21 - 1.06]	**<0.001**
Obesity	7 (63.64)	4 (36.36)	0.84 [0.23 - 3.06]	0.53
Hb level < 10	23 (52.27)	21 (47.73)	1.71 [0.78 - 3.72]	0.12
Age > 70 years	18 (45)	22 (55)	6.67 [1.20 - 5.94]	**0.013**
Gleason ≥ 8	31 (59.62)	21 (40.38)	1.03 [0.48 - 2.21]	0.55
LHRH Analogs	31 (70.45)	13 (29.55)	1.03 [0.48 - 2.21]	**0.05**
Bisphosphonates	33 (56.90)	25 (43.10)	1.32 [0.61 - 2.8]	0.3
Positive rectal exam	62 (58.49)	44 (41.51)	Undefined	0.12
Bone Scintigraphy	3 (27.27)	8 (72.73)	4.67 [1.16 - 18.7]	0.02
Family history	6 (60)	4 (40)	1 [0.26 - 3.77]	0.62

presentation of patients with prostate cancer. This was in line with the findings of Merriel *et al.* in 2018 [16]. Niang *et al.* [9] also reported that patients having metastatic prostate cancer in Senegal complained of similar symptoms. Other clinical presentations included acute urinary retention and bone and joint pain.

The median BMI in our study was 25.25 kg/m^2. The findings of previous studies on the association between BMI and prostate cancer risk have been conflicting. While some studies reported that aBMI is associated with an increased risk of prostate cancer [17] [18] [19], Giovannucci *et al.* [20] reported that the risk of prostate cancer in men with a higher BMI (≥30 kg/m^2) was lower than that in men with a lower BMI (23 - 24.9 kg/m^2). We found no significant association between the BMI and the outcome of prostate cancer patients.

DRE findings are subjective and have a poor performance in detecting prostate cancer, especially when PSA levels are low [21]. A total of 96.36% of the patients that underwent DRE in this study were suspected to have prostate cancer, probably because most of the participants of this study were recruited at an advanced stage of the disease. However, this method has been associated with low

sensitivity for prostate cancer diagnosis, as Leslie *et al.* reported that abnormal findings on DRE were present only in 20% of patients with prostate cancer [22]. The serum PSA level was higher than 100 ng/ml in all patients; this result underlines the fact that Africans are more likely to have high serum levels of PSA when diagnosed with prostate cancer as reported by previous studies [3] [9].

The median prostate weight was 70 g. Freedland and al. evaluated the association between prostate weight with pathologic tumor grade found that men with smaller prostates had a higher prevalence of high-grade cancer and more advanced disease [23]. The aggressiveness of prostate cancer also depends on the Gleason score; in this series, 58 (52.72%) and 52 (47.27%) patients were diagnosed with Gleason scores of ≤7 and ≥8, respectively. Similar results were reported by Rebbeck *et al.* in 2013 [3]. It has also been reported that patients with metastatic prostate cancer tend to be anemic [24], probably due to the invasion of the bone marrow by the tumor. However, in our study, we found a median hemoglobin level of 10.55 g/dl and no significant association between anemia and the outcome of prostate cancer patients.

The extension workup included ultrasound, CT-Scan, bone scintigraphy, and MRI. The latter was more associated with the younger of the 110 patients to assess the possibility of curative surgery. MRI can assess the local and locoregional spread of newly diagnosed prostate cancer by detecting extracapsular extension, seminal vesicle invasion, and lymph node invasion MRI [25] [26]. Out of 110 patients, 96 and 62 had lymph node and bone metastases, respectively. These two were the most common sites of metastases. Bone metastases are common in advanced prostate cancer [27]. Konan *et al.* also found different metastases during their examinations (bone (61%), lung (13%), bladder (8%), lymph node (7%), and liver (5%) [28].

Androgen deprivation therapy (ADT) has been the gold standard in the treatment of metastatic hormone-naïve prostate cancer for the past years. Therefore, the initial management of metastatic prostate cancer is based on androgen deprivation to achieve castrate levels (<50 ng/dl) of circulating testosterone, thereby depriving the cells of their primary fuel for growth [29]. All the patients in this study received ADT either medically or surgically. We found that treatment with LHRH agonists was significantly associated with patients' outcomes. Chemotherapy was also significantly associated with the outcome of patients in our study. Sixty percent of our study participants underwent surgical Androgen deprivation therapy in the form of orchidectomy, which was also significantly associated with patients' outcomes. ADT in monotherapy was the standard treatment for these patients until a combination therapy with New-Generation Hormonal Therapy (NGHT) or chemotherapy came into use and now appears to be indicated in most cases [4]. It consisted of Abiraterone, Enzalutamide, and Docetaxel chemotherapy. Less than 30% of our patients benefited from this regimen. The higher cost and unavailability of NGHT is a limit to their prescription in our milieu. A recent study carried out in the US demonstrated that Docetaxel

was substantially more cost-effective than Abiraterone in the treatment of metastatic hormone-naïve prostate cancer [30].

Overall, 44 (54.5%) of the patients that died were aged between 70 and 79 years. This age range is near the median age (69) at the beginning of the study. Thirty-two (72.7%) of these 44 patients had PSA levels of ≥200 ng/ml and 21 (47.72%) others had Gleason scores of ≥8. However, we found no significant association between Gleason scores of ≥8 and patients' outcomes. Our median survival duration was small; it was 21.848 months. Although DOC is strongly recommended for patients with a high burden of disease and is a treatment limited in time, abiraterone seems to be an option for a broader population, has better tolerability, and improves patient-reported outcomes [31]. The five-year overall survival in our study was approximately 96%, which differs from the 100% five-year survival rate reported by Leslie *et al.* [22] This difference could be due to the fact that Leslie *et al.* studied patients who were at an early stage of the disease and were in the western world, unlike our study that had African participants who were mostly at an advanced stage of the disease.

However, this study had certain limitations. First, due to the retrospective nature of the study, cause-to-effect relationships between the associated factors and patient survival could not be established. Second, the study was carried out at a single center, which means the study sample is not quite representative of the entire Cameroonian population. Thus, we recommend that similar cross-sectional and prospective studies should be carried out to further investigate our findings.

5. Conclusion

Metastatic hormone-naïve prostate cancer, due to its prevalence and significant risk of mortality, has become a real public health problem not only in developed countries but also in Africa, especially in Cameroon. It is an aggressive type of cancer with synchronous metastases to different sites, including the lymph nodes, bones, and viscera. Its management is essentially palliative. Androgen deprivation therapy (which is associated with accessible new-generation hormonal therapy) and chemotherapy are major ways of increasing patients' overall survival. Early detection is associated with a reduced number of advanced or metastatic cases, which reduces the morbidity and mortality associated with prostate cancer.

Acknowledgements

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Availability of Data and Materials

The data analyzed in this study are available from the corresponding author upon reasonable request.

Ethics Statement

Ethical approval was obtained from the institutional review board of the Faculty of Medicine and Pharmaceutical Sciences and the ethics committee of the *Centre medico-chirugicale d'urologie* in Douala, Cameroon. The requirement for informed consent was waived due to the retrospective nature of the study.

Conflict of Interest Statement

The authors have no conflicting interests to declare.

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