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Prognostic Factors for Prostate Cancer at the Brazzaville University Hospital Center

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Abstract: Second cancer frequently diagnosed in men; prostate cancer is responsible for high mortality. His prognosis has benefited from significant technical improvements. Determining prognostic factors in prostate cancer is an integral part of the therapeutic decision-making process. The aim of this study was to determine the prognostic factors of prostate cancer in the cancer department of University Hospital of Brazzaville in Congo. This was a retrospective descriptive study, which took place from 1 January 2016 to 31 December 2020, in the cancer department of the University Hospital of Brazzaville in Congo. During the study period, 118 files were retained. The survival curves were realized according to the Kaplan-Meier model, and the statistical comparison according to the Log-Rank model. The significance threshold was set at 5%. The results found that mean age was 68 ± 7.74 years. Low urinary tract symptoms accounted for 68.64% of the discovery circumstances. The Initial PSA was greater than 100 ng/ml in 65.25% of patients. Metastases were found in 95.76% of patients. Overall survival at 3 years was 15%. Survival differed significantly by age ($p = 0.0017$); WHO performance status ($p = 0.0000$); clinical stage ($p = 0.0000$) and metastatic site ($p = 0.0022$). Finally, the incidence of prostate cancer is increasing worldwide, hence the interest of defining a screening strategy, allowing to institute management with better results.

Keywords: Prostate Cancer, Prognostic Factors, Brazzaville

1. Introduction

Prostate cancer (Pca) is the second most frequently diagnosed cancer in men, and the fifth leading cause of cancer death in the world [1]. Its incidence is gradually changing, due to the increase in life expectancy, and the improvement of screening techniques [2]. Individual screening by prostate specific antigen (PSA) and digital rectal examination (DRE) have allowed in Western countries to diagnose this disease most often at an early stage where curative treatment is possible and still effective [3]. Late diagnosis is often the rule in developing countries, jeopardizing any possibility of curative treatment. Its management at the metastatic stage remains a clinical challenge in terms of survival and improvement of the quality of life of patients [3]. Responsible for high mortality, the prognosis of this cancer has benefited from significant technical improvements, both for surgery and for medical treatments [4]. The prognostic factor is a characteristic of the cancer or patient, which affects the outcome of the disease [4]. Determining prognostic factors for prostate cancer is an integral part of the treatment decision process. It makes it possible to establish the indication of the treatment, to reduce the side effects of a treatment whose probability of being

useful is sometimes low and to better adapt the therapeutic follow-up [5].

The aim of this study was to determine the prognostic factors of prostate cancer in the cancer department of Brazzaville University Hospital Center (CHUB).

2. Patients and Methods

This was a retrospective descriptive study, conducted over a period of five (5) years, from January 1, 2016 to December 31, 2020 in the cancer service of the CHUB. Were included, all histologically confirmed prostate cancers, with a complete medical record (prostate specific antigen (PSA), TNM classification, imaging, treatments received). Data were collected from medical records. The variables studied were epidemiological, clinical, histological, and therapeutic. For quantitative variables, mean and standard deviations, median with the first (Q1) and third quartile (Q3); for qualitative variables, absolute and relative frequencies were calculated.

The endpoint for defining a prognostic factor was patient survival calculated in months. Since this was a retrospective study and the difficulties in collecting all data, only overall survival was studied. As the study ended in December 2020, patients were considered alive, deceased or lost to sight at that time. A univariate logistic regression was performed to determine factors associated with survival; and a multivariate logistic regression including variables with a p-value of 20% or less in univariate analysis was performed. The significance threshold was set at 5%. The survival curves were carried out according to the Kaplan-Meier model for each criterion analyzed. The statistical comparison between the survival curves was made according to the Log-Rank model.

3. Results

During the study period, 118 files were retained. The average age was 68 ± 7.74 years, with extremes of 48 and 85 years. The 60-69 age group was the most represented, as shown in Figure 1. Symptoms of the lower urinary tract were the most common discovery (77.97%).

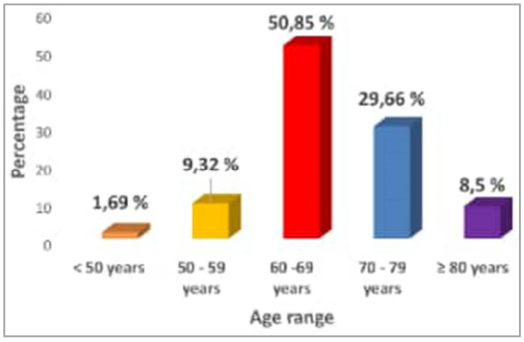

Figure 1. *Age distribution of patients (n = 118).*

The average consultation time was 8.9 ± 7.3 months, with extremes of 0 and 36 months.

The median initial PSA was 122.93 ng/mL, with Q1 at 70.81 ng/mL and Q3 at 317 ng/mL. The initial PSA was greater than 100 ng/mL in 65.25% of patients.

Prostatic ultrasound was performed by 88.98% of patients, thoraco-abdominal CT was performed by 98.31% of patients and pelvic magnetic resonance imaging (MRI) by 53.39%. Bone scan and positron emission tomography, were achieved by 3.39% and 1.69% respectively.

The histological type found was adenocarcinoma. Table 1 shows the distribution of patients according to the circumstances of discovery, ISUP grade and clinical stage. According to D'Amico classification, one patient was classified as high risk and four as intermediate risk.

Table 1. *Distribution of patients by ISUP grade and clinical stage.*

Variables	Effective	Percentage (%)
Circumstances of discovery		
Symptoms of the lower urinary tract	92	77,97
Paraplegia	18	15,25
Chance discovery	5	4,24
Pathological fracture	3	2,54
ISUP grade		
1	13	11,02
2	12	10,17
3	22	18,64
4	27	22,88
5	44	37,29
Stages		
1	2	1,69
2	2	1,69
3	1	0,85
4	113	95,76

Metastases were bone in 53.98% of patients. Other metastatic sites were hepatic (13.27%), pulmonary (23.90%), rectal and vesical (8.85%).

The average Gleason score was 8.02 1.27, with extremes of 6 and 10.

In univariate and multivariate analysis, spine disease, comorbidities, and WHO performance status (WHO PS) were significantly associated with survival, as shown in Tables 2 and 3.

Table 2. *Univariate analysis of significant prognostic factors associated with survival.*

Variables	OR (IC 95 %)	*p*-Value
Rachialgies		
Yes (15)	0,20 (0,04 – 0,96)	0,04
No (103)		
Comorbidities		
Yes (46)	2,34 (1,07 – 5,12)	0,03
No (72)		
WHO Performance Status		
0-1 (57)	0,32 (0,14 – 0,69)	0,003
2-3 (61)		

Table 3. *Multivariate analysis of prognostic factors associated with survival.*

Variables	OR (IC 95%)	*p*-Value
Rachialgies	0,1292 (0,0196 - 0,8515)	0,0334
Comorbidities	5,4678 (1,8130 -16,4900)	0,0026
WHO Performance Status	0,2593 (0,0827 - 0,8137)	0,0207
PSA at 3 months	9,7833 (0,851-112,4635)	0,0672
Alkaline phosphatase	0,4819 (0,1892 - 1,2275)	0,1259
RT	1,3183 (0,3850 - 4,5137)	0,6599

In our study, 111 patients received hormonal therapy. In 3 patients, it was surgical hormonal therapy. The molecules used for hormone therapy were antiandrogens associated with LHRH analogues.

Docetaxel was the chemotherapy molecule used in combination with hormone therapy.

Two patients received second-line hormone therapy with abiraterone acetate.

The mean follow-up time was 12.12 ± 9.21 months, with extremes of 1 and 48 months.

The castration resistance defined by the reappearance of clinical signs and the re-escalation of the total PSA level with testosteronemia at a castration threshold was observed at 12 months in 2 patients. At the end of our study, 61.02% of patients had died.

Median survival (MS) was 22 months. Overall survival (OS) at 3 years was 15%. Survival differed significantly by age, WHO PS, clinical stage, and metastatic site, as shown in Figures 2, 3, 4, 5, and 6.

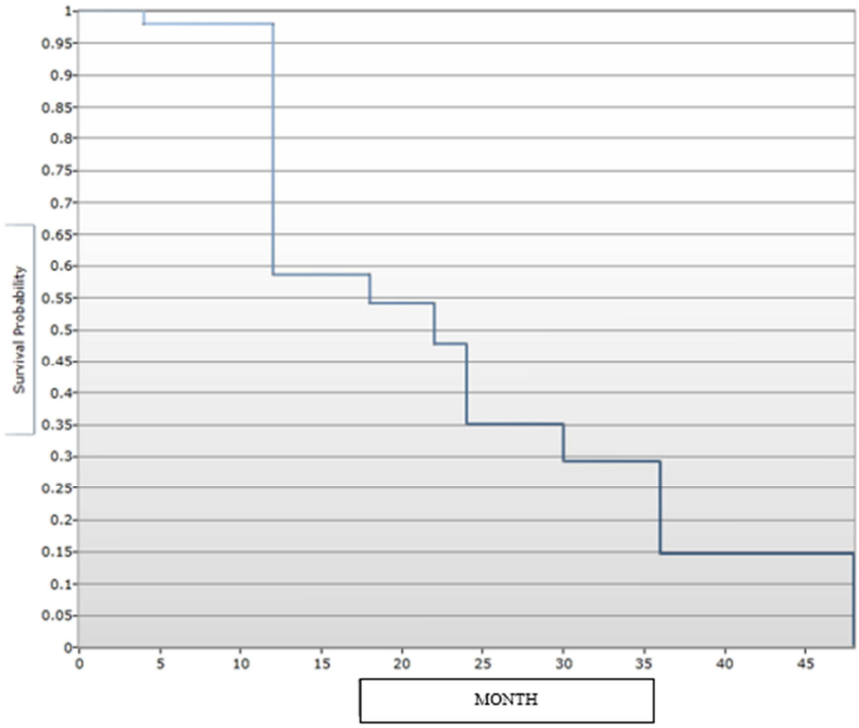

Figure 2. *Overall Survival Curve.*

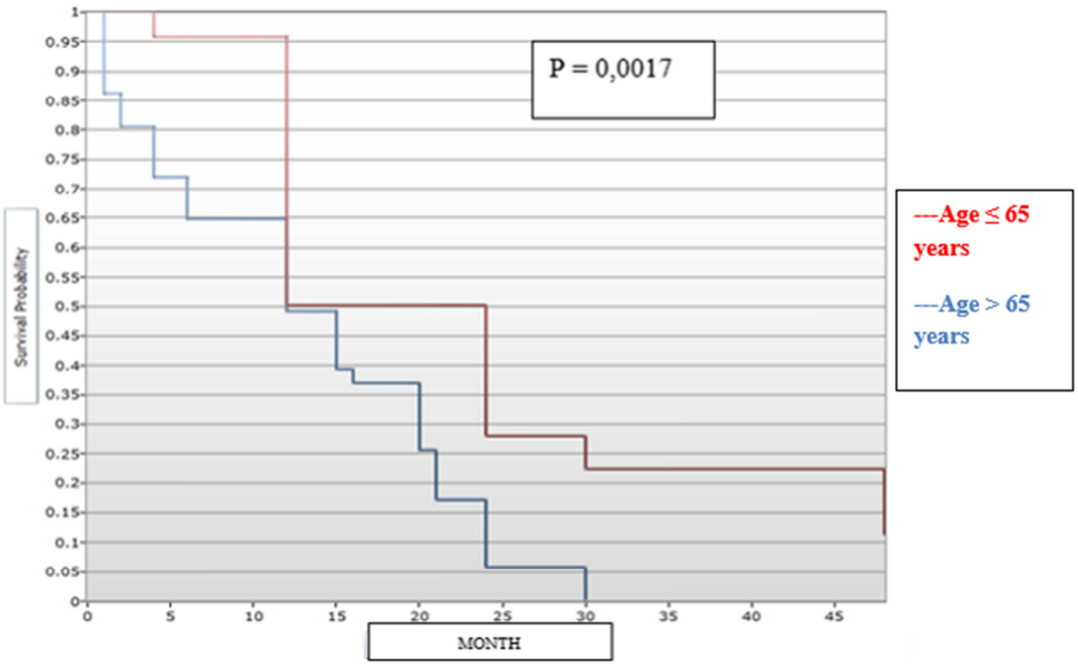

Figure 3. *Survival curve by age.*

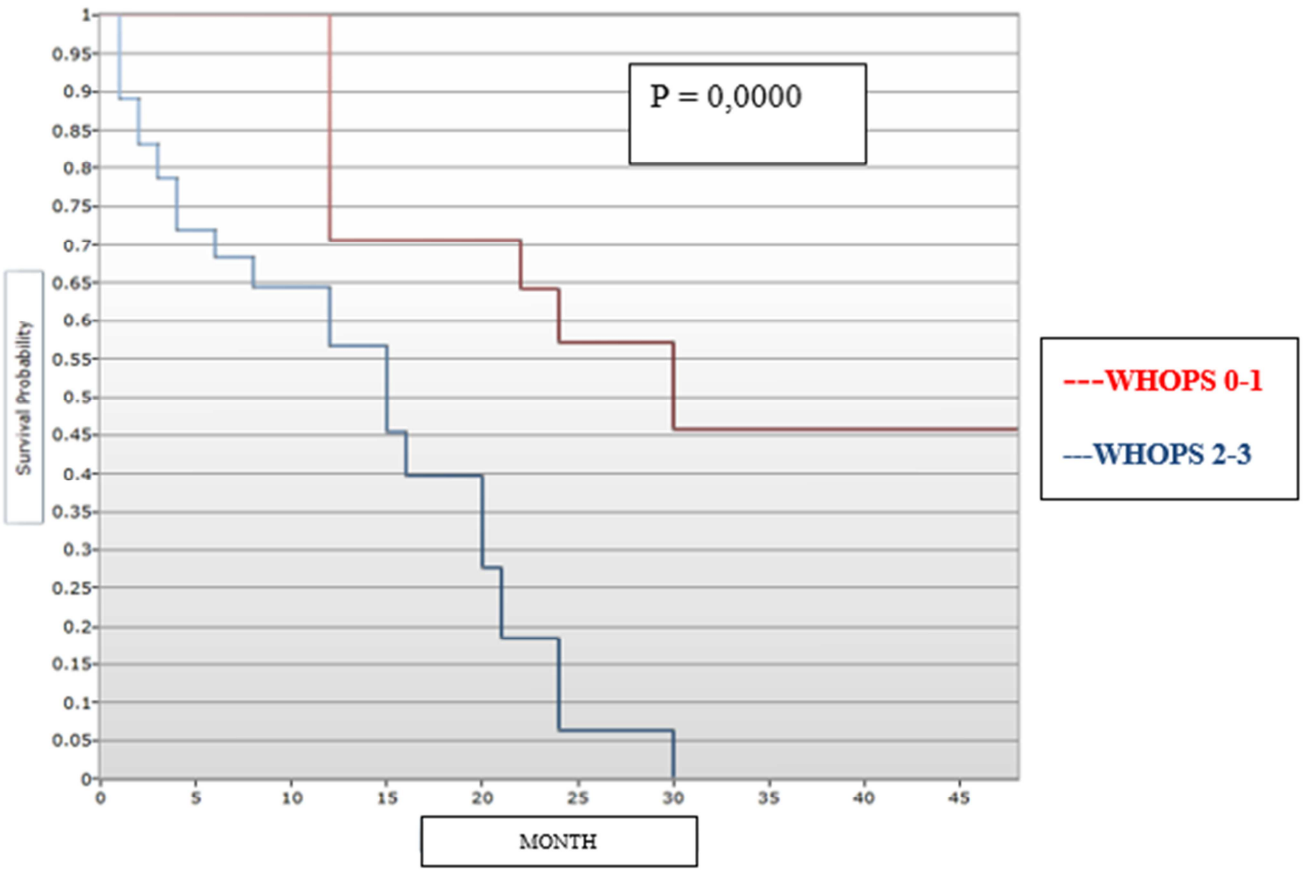

Figure 4. *Survival curve by WHO performance status.*

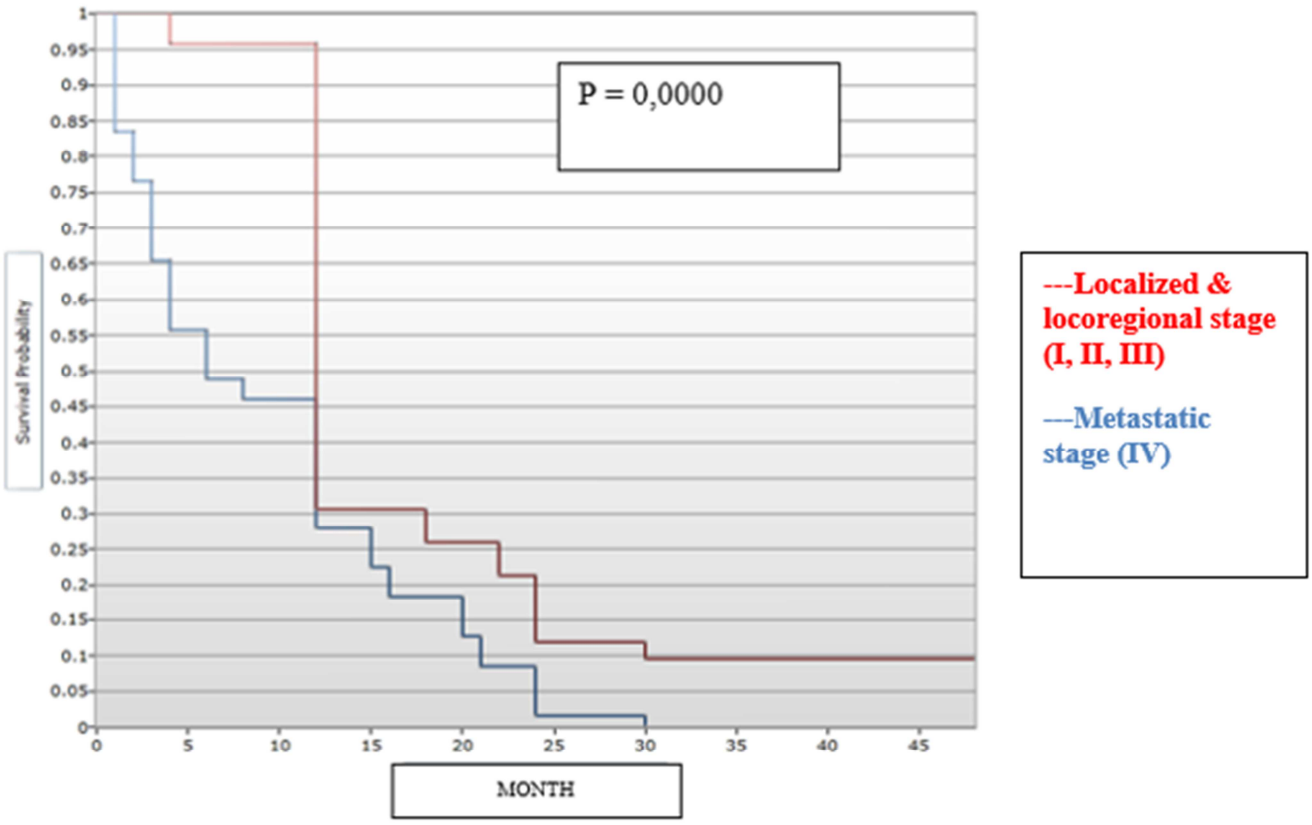

Figure 5. *Survival curve by stage.*

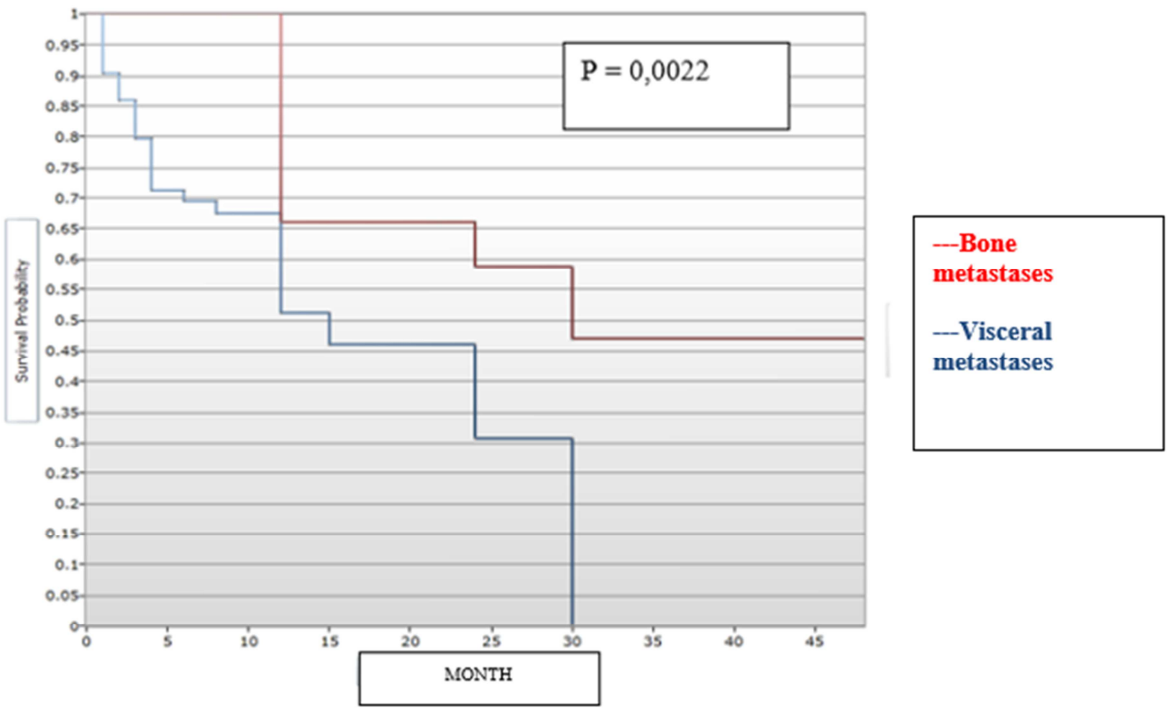

Figure 6. *Survival curve by metastatic site.*

4. Discussion

Our study has experienced limitations due to its retrospective nature. The balance of extension carried out within the limits of our means, did not allow us a satisfactory staging.

The average age of our patients was 68 years. Our data are comparable to those found in the literature [2, 3, 6, 7]. The probability of getting Pca increases with age. Prostate cancer is rare before 50 years old (< 0.1% of cases) but its incidence then increases strongly and more than 75% of new cancer cases are diagnosed after 65 years, with a considerable decrease in incidence after 79 years [8].

The circumstances of discovery were dominated by symptoms of the lower urinary tract. The revealing circumstances of prostate cancer are very variable. Often, patients are seen for symptoms unrelated to the urinary tract. The existence of functional signs reflects a locally advanced or metastatic stage as demonstrated by Cussenot and Teillac in France [9], which showed that a prostatic adenocarcinoma actually localized to the gland is asymptomatic. With the advent of screening, incidental discoveries just on the rise in PSA levels without clinical signs become frequent [10].

The initial PSA level was above 100 ng/mL in 65.62% of our patients. The interest of PSA dosage is threefold (diagnosis, prognosis, monitoring). The RT/PSA association plays an important role in the diagnosis of prostate cancer in our context. There is a correlation between the value of PSA and the extent of prostate cancer; beyond 50 ng/ml, extraprostatic involvement exists in 80% of cases; and beyond 100 ng/ml, metastatic bone involvement is evident [5].

Adenocarcinoma was the only histological form found. These results are similar to those in the literature [2, 7, 12–14]. Prostatic adenocarcinoma is by far the most common pathological form [5]. The diagnosis of Pca was mainly made at stages IV (95,76 %). These results could be explained by the long consultation time in our study. The metastases were bone in 53.98% of our patients. Pca is an osteophilic cancer, in the absence of bone scans and given the high PSA levels in our sample, our results may be underestimated.

In univariate and multivariate analysis, spine (p=0.0334), comorbidities (p=0.0026), and WHO performance status (p=0.0207), were statistically associated with patient outcomes. The rachialgia, are the witness of a bone damage vertebral. Vertebral metastases occurring after the disease are responsible for skeletal complications that can be life-threatening.

Therapeutically, the majority of our patients had received hormone therapy. This is indicative of the advanced stage of the disease. Patients who had locally advanced cancer, had benefited from radiotherapy/ hormone therapy outside the country, due to lack of adequate technical plateau. Androgen suppression (SAd) remains the basic treatment for metastatic prostate cancer. The treatment of patients from metastatic to diagnosis, hormone-sensitive, has evolved considerably in recent years. A therapeutic intensification, by combination of a SAd either with docetaxel in case of high tumor volume, or with hormone therapy of new generation (HTNG) whatever the tumor volume, improves the overall survival [11].

Overall survival at 3 years was 15%. The overall survival of cancer patients, including Pca, is still subject to a number of prognostic factors that influence patient outcomes. Data on the survival of cancer patients in sub-Saharan Africa are very scarce despite high prevalence and mortality in the region [15,

16]. Age was significantly associated with survival in our study (*p=0.0017*). Older age is generally associated with poor prognosis, which further increases mortality. In the case of advanced disease, many parameters related to the general condition, comorbidity factors and the impact of the disease on the body were identified as prognostic factors [8].

Survival differed significantly by clinical stage (*p = 0.0001*). A Tanzanian study reported [17] a significant association (*p = 0.018*) between clinical stage and 5-year Gleason score rate in patients with Pca. Xu et *al*., in China, reported that the 5-year Gleason score rate decreased with increasing clinical stages in Pca patients, and the difference was statistically significant (*p = 0.0002*) [18]. Delay in diagnosis is often the rule in our context, in addition to the lack of public information and awareness policy on this condition. Visceral metastases were associated with a significant decrease in survival (*p = 0.0022*). The presence of metastases is recognized as a factor of very poor prognosis. Metastatic tumors are more aggressive than recurrences after the management of a localized disease [8]. Metastatic prostate cancer has a tropism mainly lymph nodes and bone; visceral damage is rare and late in the history of the disease, or the prerogative of aggressive forms not sensitive to hormonal treatments [11].

5. Conclusion

The incidence of prostate cancer is increasing worldwide. At the end of our study, prostate cancer was discovered as a result of symptoms of the lower urinary tract, at an advanced age, and an initial high level of PSA. The diagnosis was most often made at the metastatic stage, with a Gleason score greater than 7. Adenocarcinoma was the histological type found. Hormone therapy was the most appropriate treatment. Overall survival at 3 years was relatively low. It was statistically associated with age, spinal, comorbidities, general condition, clinical stage, metastatic sites. The lack of screening in our country plays an important role in the clinical presentation of this cancer. Hence the interest of defining a screening strategy aimed at increasing awareness and early detection, thus making it possible to institute management with better results.

Abbreviations

Pca: Prostate Cancer
CHU: University Hospital Centre
HTNG: New Generation Hormone Therapy
MRI: Magnetic Resonance Imaging
ml: Millilitre
ng: Nanogram
PSA: Prostate Specific Antigen
WHO PS: WHO Performance Status
Q1: First Quartile
Q3: Third Quartile
SAd: Androgen Suppression
OS: Overall Survival
MS: Median Survival
RT: Rectal Examination

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Conflicts of Interest

The authors declare no conflicts of interest.

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