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Predictive Factors of Castration Resistance in Prostate Cancer in Guinean Men : A Retrospective Study of 90 Cases

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Abstract

Introduction :

Prostate cancer (CaP) is common in sub-Saharan Africa, often diagnosed at an advanced stage. The objective of this study was to identify clinical and paraclinical factors predictive of the development of castration resistance in Guinean patients.

Material and methods

This was a retrospective analytical study conducted in Conakry, Guinea, between January 1, 2019, and December 31, 2023. All patients followed for locally advanced or metastatic hormone-naïve prostate cancer were included. Castration resistance was defined according to the Prostate Cancer Clinical Trials Working Group 3 (PCWG3) criteria. Data were analyzed using univariate and multivariate logistic regression (significance threshold $p < 0.05$).

Results

Ninety patients were included. The mean age was 70.48 ± 9.15 years. The median baseline PSA was 221 ng/mL. After a median follow-up of 41.4 months, 46 patients (51.11%) developed castration resistance. In univariate analysis, younger age ($p = 0.007$), high baseline PSA ($p < 0.001$), ISUP score ≥ 3 ($p < 0.001$), number of metastases > 6 ($p < 0.001$), and time to PSA nadir > 6 months ($p < 0.001$) were associated with resistance. In multivariate analysis, only an ISUP score ≥ 3 remained an independent predictive factor (ORa = 5.47; 95% CI : 1.84–16.24 ; $p = 0.002$).

Conclusion

A high ISUP score is a strong predictor of castration resistance in Guinean men. These results highlight the importance of early histological diagnosis and prognostic stratification.

Introduction

Prostate cancer (CaP) is the second most common cancer worldwide and the fifth leading cause of cancer death [1]. CaP is primarily a public health issue, as its incidence has increased significantly in recent decades, particularly since the introduction of prostate-specific antigen (PSA) testing as a screening tool [2].

In low- and middle-income countries, especially in sub-Saharian Africa, diagnosis is often delayed, with a high proportion of locally advanced or metastatic forms at the time of treatment. The incidence of hormone-naïve metastatic prostate cancer is estimated at approximately 10% in Europe, compared to much higher rates in Africa, reaching 68.23% in Côte d'Ivoire and 45.9% in Senegal [3, 4, 5].

Prostate cancer is a heterogeneous disease whose progression can lead to a phase of castration resistance, defined by biological, clinical, or radiological progression despite a castration testosterone

level (< 50 ng/dL). Despite therapeutic advances (taxane chemotherapy, next-generation hormone therapies, targeted therapies), the prognosis for metastatic castration-resistant prostate cancer (mCRPC) remains poor, with a median survival of less than three years [6].

In Guinea, data on predictive factors for this progression are limited.

Identifying these factors is essential to optimize patient management and improve prognosis. The objective of this study was to identify the clinical and paraclinical factors associated with the development of castration resistance in Guinean patients with prostate cancer.

Material and methods

study framework – Study Type and Period : This was a retrospective analytical study conducted in the urology department of the Ignace Deen University Hospital and at the Perchin Specialties Clinic in Conakry, Guinea, over a five-years period from January 1, 2019, to December 31, 2023.

Inclusion and Exclusion Criteria : All patients admitted for locally advanced (stage T3–T4, N0–N1, M0) or metastatic (M1) hormone-naïve prostate cancer during the study period were included. The diagnosis was confirmed by histology (prostate biopsy). An exhaustive sampling was performed (inclusion of all records meeting the criteria).

Incomplete records (lacking essential data such as baseline PSA, testosterone levels, or a minimum 6-month follow-up) were excluded.

Data collection : Data were collected from medical records, radiological, surgical, and pathology reports.

Variables studied : The variables analyzed included :

- Sociodemographic : age at diagnosis, socioeconomic status (low, middle, stable according to local criteria)
- Clinical : reasons for consultation, disease progression, TNM stage (8th edition UICC), ECOG score, neurological deficit (Frankel classification)
- Paraclinical : initial PSA (ng/mL), minimum testosterone level (< 50 ng/dL defining castration), Gleason score, ISUP grade, staging imaging (bone X-ray, CT scan of the chest, abdomen, and pelvis, MRI, scintigraphy), number and location of metastases.
- Therapeutic : hormone therapy (pulpectomy + bicalutamide or LH-RH agonists + bicalutamide), chemotherapy (docetaxel), zoledronic acid, radiotherapy.
- Follow-up : time to reach PSA nadir (PSA > 2 ng/ml), time to onset of castration resistance, 5-year status (improvement, death, worsening, stable).
- Definition of castration resistance : we used
- The Prostate Cancer Clinical Trials Working Group 3 (PCWG3) criteria

- Maintained serum testosterone < 50 ng/dl
- Biological progression : PSA increase ≥ 25% and ≥ 2 ng/ml from the nadir, confirmed by a second measurement at least 3 weeks later, or radiological progression : appearance of at least two new bone lesions on scintigraphy, or progression of visceral lesions according to RECIST
- or clinical progression : worsening of pain, or deterioration of general condition attributable to cancer.

Statistical analysis : Data were analyzed using KoboCollect v2022.1.2, Microsoft Excel 2016, and Epi Info version 7.2.2.2.

- Descriptive analysis : means (± standard deviation), medians (interquartile range or extremes), proportions
- Univariate analysis : Chi-square test or Fisher's exact test for categorical variables, Student's t-test or Mann-Whitney U test for continuous variables
- Multivariate analysis : binary backward logistic regression (enter method) including variables with p < 0.20 in univariate analysis. Results are expressed as adjusted odds ratios (ORa) with a 95% confidence interval.
- Significance threshold: p < 0.05 (two-tailed).

Ethical considerations : Information was collected anonymously, and strict confidentiality was maintained. Due to the retrospective nature of the study, individual informed consent was waived. But, the absence of objection was verified.

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The study was approved by the Research Ethics Committee for Health Research of the Urology Department (CERHUD), under reference number CER/Chaire-Uro/009/2026.

Limitations and Challenges :

- Selection bias related to the retrospective nature of the study and incomplete records
- Small sample size (90 patients) limiting the power of the multivariate analysis (risk of overadjustment)
- Lack of standardization of staging assessments (not all patients underwent scintigraphy or CT scans)
- Unavailability of certain therapies (radiotherapy, next-generation hormone therapy) which may have influenced resistance-free survival.

Results

We recorded 90 patient records of individuals admitted for locally advanced or metastatic prostate cancer. The mean age of the patients was 70.48 ± 9.15 years [50 to 87 years]. The majority of patients,

61.11% (n = 55), had a low socioeconomic status, a minority, 11.11% (n = 10), had a stable socioeconomic status, while 27.77% (n = 25) had a medium socioeconomic status.

All patients presented with lower urinary tract symptoms (LUTS), 100% of whom presented with symptoms predominantly complete or incomplete urinary retention (73.33%). Bone pain was reported in 78.88% (n = 71) and hemospermia in 8.88% (n = 8). The mean time to consultation was 16.75 ± 7.64 months [6–26 months]. Half of the patients (50.00%) had consulted a general practitioner as their first point of contact.

At admission, the ECOG scores were: ECOG 0 (22.22%), ECOG 1 (31.11%), ECOG 2 (35.56%), and ECOG 3 (11.11%). The initial median PSA level was 221 ng/mL [range: 43.32–1072.5 ng/mL]. Histopathological examination of prostate biopsies revealed adenocarcinoma in all patients (100%). The distribution according to ISUP grade was: group 1 (43.33%), followed by group 4 (22.22%) and group 3 (15.55%), while groups 2 and 5 were less represented, at 7.77% and 11.11%, respectively.

The staging procedures were as follows: radiography of the pelvis, cervicothoracolumbar spine, and lungs in 22.22% (n = 20) of patients; CT scan of the chest, abdomen, and pelvis in 66.66% (n = 60); MRI in 12.22% (n = 11) of patients; and scintigraphy in 8.88% (n = 8) of patients. Metastases were present in 94.44% (n = 85) of patients (bone only in 69.41%, bone and visceral involvement in 30.58%). The number of metastases was 2 to 5 in 63.52% (n = 54), a single metastasis in 25.89% (n = 22), and 6 or more in 10.58% (n = 9). The distribution according to the TNM classification is presented in Table 1.

Table 1
Distribution according to the TNM classification

Stage TNM	Frequency (n)	Percentage (%)
T4N1M1c	23	25.55
T4N1M1b	18	20.00
T3N0M1b	18	20.00
T4N0M1b	12	13.33
T3N1M1b	8	8.88
T4N0M0	*5*	5.56
T3N1M1c	3	3.33
T2cN0M1b	3	3.33
Total	90	100

All patients received hormonal therapy: pulpectomy combined with bicalutamide (33.33%) or LH-RH agonists + bicalutamide (66.66%). Chemotherapy (docetaxel) was used in 13.3% of patients, always in combination with hormonal therapy and zoledronic acid.

After a median follow-up of 41.4 months (range 3–60 months): 47.78% of patients had improved clinical status; 33.33% had died; 13.3% had worsened (bone pain in all, motor deficit in 8, pathological fracture in 4); 5.56% had stable clinical status. The median PSA at 12 months was 0.82 ± 151.66 ng/ml. The median time to PSA nadir was 6.96 ± 4.32 months (range 3–18 months); 6.66% of patients never reached nadir. The median time without biochemical progression was 34.02 ± 14.87 months (range 3–60 months). The median time to castration-resistant survival was 41.43 ± 19.83 months. Of 90 patients, 46 (51.1%) developed castration resistance according to PCWG3 criteria.

Univariate analysis (Table 2) showed a significant association between castration resistance and: younger age (68.2 vs 73.6 years; p = 0.007); higher initial PSA (median 500 vs 167 ng/ml; p < 0.001); ISUP score ≥ 3 (OR = 8.06; p < 0.001); time to PSA nadir > 6 months (OR = 2.01; p < 0.001); number of metastases > 6 (p < 0.001); however, time to consultation was not associated with castration resistance (p = 0.64). In multivariate analysis (Table 3), after adjusting for age, baseline PSA, time to nadir, and number of metastases, only an ISUP score ≥ 3 remained an independent predictor of castration resistance (ORa = 5.47; 95% CI: 1.84–16.24; p = 0.002).

Table 2
Univariate analysis of predictors of castration resistance

Variable	**OR**	**IC95%**	**P**
Age (years)	0,93	0,88–0,98	0,007
Initial PSA (ng/mL)	1,005	1,002–1,007	< 0,001
ISUP score	8,06	3,72–17,44	< 0,001
Time to reach PSA nadir	2,01	1,48–2,73	< 0,001
Time to consultation (months)	1,02	0,95–1,08	0,64
Number of metastases	significant association	—	< 0,001

Table 3
Multivariate analysis of predictive factors for castration resistance

Variable	**OR ajusté**	**IC95%**	**P**
Age (years)	1,05	0,89–1,24	0,546
Initial PSA (ng/mL)	0,77	—	0,665
ISUP score	**5,47**	**1,84–16,24**	**0,002**
Time to reach PSA nadir	1,74	0,90–3,39	0,101
Time to consultation (months)	1,00	0,85–1,17	0,987
Number of metastases	4,62	0,49–43,8	0,182

Discussion

Our study shows that, in a Guinean population of patients followed for advanced prostate cancer, more than half (51.1%) develop castration resistance within five years, and that the ISUP grade (score ≥ 3) is the only independent predictive factor.

The mean age of our patients (70.48 ± 9.15 years) is comparable to recent African data : 73 years in Guinea by Cissé D et al. [7], 71.15 years in Mali [8].

The clinical presentation was dominated by urinary symptoms and bone pain (78.88%), reflecting late diagnosis, linked to low socioeconomic status, recourse to traditional medicine, and a lack of awareness of early signs. Mbamba OFM et al. [8] and Cissé [7] reported 54% and 83.3% of cases, respectively, of bone pain as the reason for consultation. The initial median PSA (221 ng/mL) was very high compared to European standards [9], but lower than that reported in Cameroon (305.5 ng/mL) [10]. All cancers were adenocarcinomas, consistent with the literature [11]. The high proportion of high ISUP grades (groups 4 and 5: 33.33%) reflects the tumor aggressiveness in our setting. In contrast, Konan PG [12] et al. and Mbamba OFM et al. [9] found ISUP group 3 to be 48.58% and 51.5%, respectively.

Bone metastases (94.4%) predominated, as expected in prostate cancer [13].

The number of metastases (> 6) was a major prognostic factor in univariate analysis but lost its significance in multivariate analysis, probably due to a lack of statistical power.

In our series, the castration resistance rate (51.1% at 5 years) was high. Sun et al. [14] reported a 3-year overall survival rate of 46% in patients undergoing chemical castration, but our mean time to resistance (41.4 months) was longer, perhaps due to differences in management or definition. The association between younger age and castration resistance (68.2 vs. 73.6 years; p = 0.007) was described by Sanjoy KS et al. [15] in India but remains debated. Conversely, some authors find a more unfavorable prognosis in older subjects [16]. This could be explained by genetic factors or a more aggressive tumor biology in young African patients.

A high baseline PSA level is a classic predictor of progression [15], but it is no longer independent after adjustment in our series, probably because PSA is correlated with ISUP grade.

The main finding of our study is that an ISUP score ≥ 3 increases the risk of castration resistance by a factor of 5.47 (p = 0.002). The literature is divided on the prognostic value of histological grade in metastatic forms : some find no influence [17, 18], others do [19]. Our results, in an African context of late diagnosis, support the major prognostic impact of ISUP grade.

Conclusion

An ISUP score ≥ 3 is an independent predictor of castration resistance in Guinean patients with advanced prostate cancer. These results underscore the crucial importance of high-quality prostate biopsy and

standardized histopathological reading, even in resource-limited settings.

Early identification of high-risk patients (ISUP ≥ 3) could allow for more intensive surveillance and faster consideration of next-generation therapies when they become available.

Declarations

Funding :

This research received no specific grants from public, commercial, or not-for-profit organizations.

• Ethical considerations : Information was collected anonymously, and strict confidentiality was maintained. Due to the retrospective nature of the study, individual informed consent was waived. But the absence of objection was verified.

Author Contribution

BANGOURA MF1,2, CISSE D1,2, BARRY AO1,2, KEITA Y1,2, BALDE M1, BAH MD1, DIALLO TMO1, BAH MB1, BAH I1, DIALLO AB1, BAH OR1,2.All authors contributed to data collection, analysis, and writing. The final version was approved by all authors.

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