Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

Bone Scintigraphy and Initial Stagging of Prostate Cancer in Burkina Faso: Preliminary Study of 71 Cases

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DOI: 10.36347/sjams.2023.v11i12.019 | **Received:** 06.11.2023 | **Accepted:** 11.12.2023 | **Published:** 30.12.2023

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Abstract **Original Research Article**

Introduction: Prostate cancer (PCa) is the second most common cancer in men, behind lung cancer. Bone scintigraphy (BS) is available, accessible and easy to perform, making it the test of choice for the detection of bone metastases for all cancers. We proposed to clarify the contribution of SO in the initial expansion report of the PCa in Burkina Faso. ***Materials and Method:*** We carried out a retrospective single-center descriptive cross-sectional study over the period from January 1, 2018 to January 1, 2021. It included the files of patients with CaP confirmed on histology and scored according to the Gleason score in whom an OS was performed. Demographic and histological variables were entered on the scintigraphic examination request forms. The descriptive study consisted of calculating frequencies for qualitative variables and means for quantitative variables. The comparison of variables was made using the Chi-Square contingency or Fisher tests depending on their conditions of applicability. The test was significant if $p \leq 0.05$. ***Results:*** We collected 71 patient files, all with histologically confirmed prostate adenocarcinoma and initial BS. Their average age is 68.81 ± 8.70 years. The extreme ages were 50 and 88 years. Patients aged 60 to 70 were the most represented (38%). The PSA level ranged from 4.8 to 1030 with a mean PSA level of 304.94 ± 332.70 ng/ml. 34 patients had a Gleason score ≤ 6 (47.88%): Group A; 35 patients had a Gleason score between 6 and 8 (49.29%): Group B; 02 patients had a Gleason score greater than 8 (2.81%): Group C. BS+ were 46 (64.78%) patients compared to 25 BS- (35.21%). All patients with a Gleason score 6 are classified BS-. Among the 35 patients with a Gleason score = 6, 48.57% had BS+ and 51.42% had BS–. Among the 35 patients with a Gleason score between 7 and 8; 80% had an BS+ and 20% an BS-. The only patient with a Gleason score between 9 and 10 had BS+. ***Conclusion:*** Our study shows that OS+ is associated with an age greater than 70 years and a Gleason score greater than or equal to 7. It specifies that for patients with a Gleason score less than or equal to 6, OS is only justified 'in the event of painful bone symptoms. Local studies should be considered to evaluate the contribution of SO in the monitoring of PCa bone metastases.

Keywords: Prostate cancer (PCa), Bone scintigraphy, Chi-Square contingency, prostate adenocarcinoma.

INTRODUCTION

Worldwide, prostate cancer (PCa) is the second most common cancer in men, behind lung cancer. PCa is more common in developed countries, but rates are increasing in developing countries as well. Due to the large number of PCa cases detected by screening, it is estimated that in just over ten years, PCa will overtake lung cancer and become the most common cancer in men worldwide [1]. Ethnic origin is a recognized risk factor for PCa: sub-Saharan Africa and the Antilles have incidences higher than the world average [2]. In the United States, African-American men are 1.6 times more likely to develop PCa than white men. These tumors are usually discovered at a more advanced stage and at a higher grade. Imaging of PCa metastases plays an important role in the implementation of the therapeutic strategy. Thus the detection of metastases has a prognostic value and helps guide treatment [3]. Also, the Gleason score is a major prognostic factor for PCa. Described by Donald Gleason in 1966, it was modified in 2005 by the ISUP (International Society of Uro-Pathology) and has three grades, from 3 to 5 [4]. The tumor aggressiveness demonstrated by the Gleason score is often associated with metastases and overall with a poor cancer prognosis. The high sensitivity of BS and the

simplicity of its performance make it the examination of choice in the detection of bone metastases for all cancers. BS has been available in Burkina Faso since 2012. We proposed to specify the contribution of BS in the initial expansion report of the PCa.

PATIENTS AND METHODS

We carried out a retrospective single-center descriptive cross-sectional study over the period from January 1, 2018 to January 1, 2021. It included the files of patients with PCa confirmed on histology and scored according to the Gleason score in whom an BS was performed. Demographic and histological variables were entered on the scintigraphic examination request forms.

The BS was carried out in the nuclear medicine department of Yalgado Ouédraogo University Hospital. For exploration, a diphosphonate derivative (hydroxy methylene diphosphonate: HMDP) labeled with technetium 99m (99mTc) was injected intra venous vein at the bend of the elbow at a dose of 300 µCi/Kg or 740 MBq for an adult weighing 70 Kg. The acquisition was carried out on patients in supine position, three hours after injection of the radiotracer using a scan of the whole body (anterior and posterior faces) by a SpectMédiso double-head Gamma Camera with a Low Energy High Resolution (LEHR) Collimator at a speed of 15 cm per minute. Additional images were taken for better definition of the area of interest, the site of the bone lesions. The interpretation of BS images is done by 01 junior nuclear doctor and confirmed by a nuclear doctor with 12 years of practical experience in nuclear medicine.

The descriptive study consisted of calculating frequencies for qualitative variables and means for quantitative variables. The comparison of variables was made using the Chi-Square contingency or Fisher tests depending on their conditions of applicability. The test was significant if $p \leq 0.05$.

RESULTS

Main Features

We collected 71 patient files, all with histologically confirmed prostate adenocarcinoma and initial BS. The average age of the patients was 68.81 ± 8.70 years. The extreme ages were 50 and 88 years. Patients aged 60 to 70 were the most represented (38%).

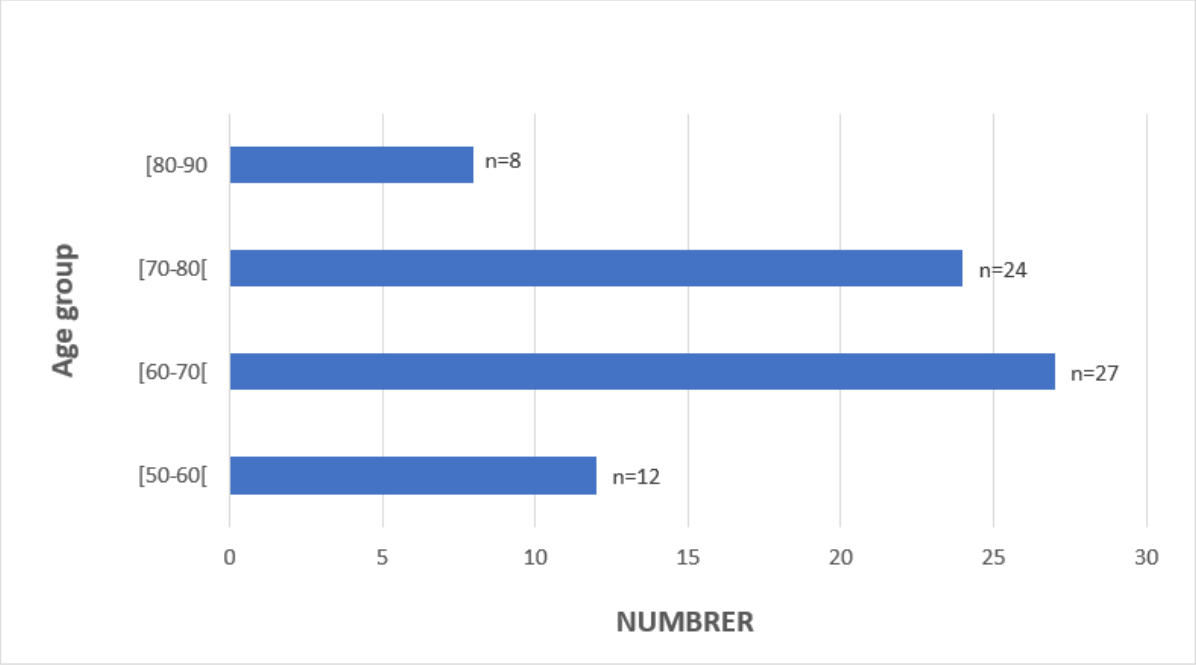

Figure 1: Distribution of patients by age

PSA rate

The PSA level ranged from 4.8 to 1030 with a mean PSA level of 304.94 ± 332.70 ng/ml. Figure 2 shows the distribution of patients according to PSA level.

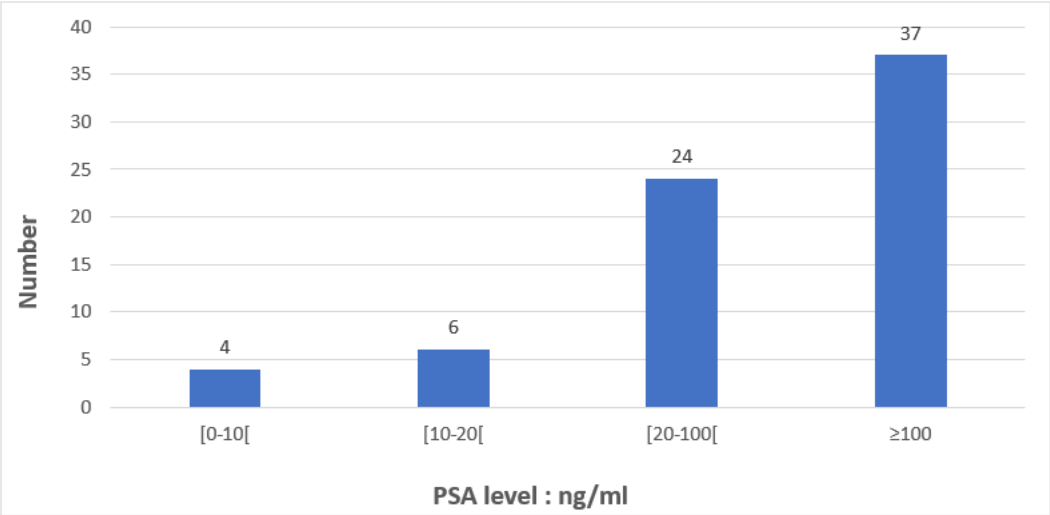

Figure 2: Distribution of patients according to PSA level

Based on the PSA level we classified our patients into 3 groups.

Group I represented by patients with PSA levels between 0 and 10 ng/ml (n= 4). Group II represented by patients with a PSA level between 10 and 20 ng/ml (n=6). Group III represented by PSA levels greater than 20 (n = 61).

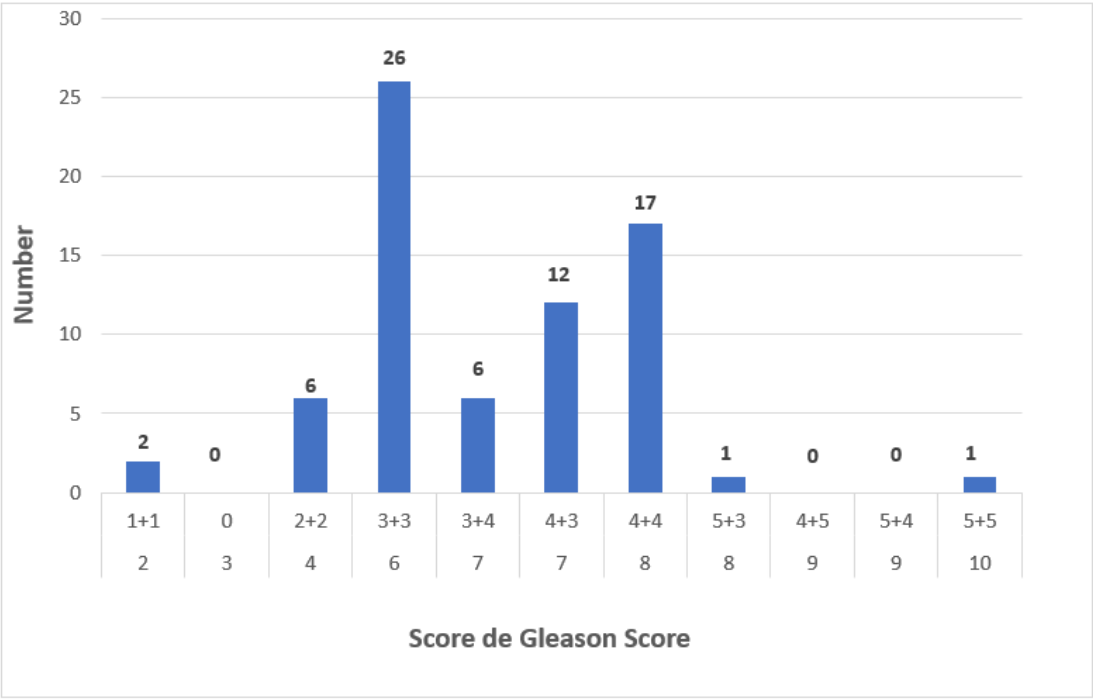

Figure 3: Distribution of patients according to Gleason score

34 patients had a Gleason score ≤ 6 (47.88%): Group A
35 patients had a Gleason score between 6 and 8 (49.29%): Group B
02 patients had a Gleason score greater than 8 (2.81%): Group C

BS results

The BS+ numbered 46 (64.78%) patients compared to 25 BS- (35.21%).

Location of secondary lesions

Of 46 BS+, 17.39% (n=8) had single lesions including 3 costal and 5 vertebral, all requiring additional images (static and/or tomography). The appendicular skeleton was free from any single lesions.

Multiple lesions (n= 32) were the most represented (69.56%). The three sites most affected by multiple lesions are the spine (19%), the rib cage (17.4%)

and the pelvis (12.62%). Furthermore, appendicular damage represented 11.4%.

Finally, 6 patients had diffuse secondary lesions throughout the skeleton (13%).

Correlation between Gleason score and BS

Table I shows the correlation between Gleason score and BS results.

Table I: Gleason score and BS correlation

Gleason Score	BS+		BS-	
	Number	Percentage	Number	Percentage
6	17	48,57 %	18	51,42 %
7	13	37,14 %	4	11,42 %
8	15	42,85 %	3	8,57 %
9	0	0 %	0	0 %
10	1	100 %	0	0 %

All patients with a Gleason score 6 are classified BS-. Among the 35 patients with a Gleason score = 6, 48.57% had BS+ and 51.42% had BS–. Among the 35 patients with a Gleason score between 7 and 8; 80% had an BS+ and 20% an BS-. The only patient with a Gleason score between 9 and 10 had BS+.

Correlation of PSA and BS levels

Table II shows the correlation between PSA level and BS.

Table II: Correlation of PSA and BS levels

PSA	BS+		BS-	
	Number	Percentage	Number	Percentage
0-10	2	22,22 %	7	77,77%
10-20	2	22,22 %	7	77,77%
20-50	6	54,54 %	5	45,45%
50-100	4	36,36%	2	63,63%
+ de 100	32	88,88 %	4	11,11%

Correlation of age and BS

Table III compares BS+ and BS- in the different age groups.

Table III: BS correlation and patient age

Age group	BS+		BS-	
	Number	**Percentage**	**Number**	**Percentage**
50-60	5	41,66 %	7	58,33 %
60-70	18	66,66 %	9	33,33%
70-80	21	72,41 %	8	27,58%
80-90	2	66,66 %	1	33,33 %

DISCUSSION

Our study follows that of Tapsoba *et al.*, in 2013 on the contribution of BS to the spread of cancers in Burkina Faso [5]. It is the first in Burkina Faso to specifically correlate BS results and the Gleason score. As the clinical stages were insufficiently documented, our study did not take into account the D'AMICO prognosis stage in the correlation calculations. Another limitation of our study is the non-integration of prognostic parameters (Crawford and Soloways classifications) for BS+. In addition, patients who did not benefit from an assessment before treatment were not included, which significantly reduced the number of files.

General Characteristics

The average age of our patients was 68.81 ± 8.70 years. The most represented age group was that of]60-70 years old].

Our results are superimposable to those found in general in sub-Saharan Africa, marked by the strong representation of the 60-70 year old age group.

Thus, in Senegal, Jallow M *et al.*, [6] reported in 2018 an average age of 65.61 years (n=67) compared to 66.71 years for Ndong *et al.*, in 2012 (n=45) [7].

In Cameroon [8], Dong found an average age of 67 years (n=360) with extremes of 50 and 85 years. In Ghana, the average age was 70 years in the 669 cases in the series by Yeboah *et al.*, [9]. In Nigeria the average

age found is 60.8 years in a series of 4172 men [10]. South Africa had the highest average age of 72 years [11]. In other parts of the world the results are no different [12]. It is therefore generally accepted that black subjects present forms at a younger age than white subjects [2].

PSA values

In our study, the mean PSA level was 304.94 ± 332.70 ng/ml. 85.91% of patients had a PSA level ≥20ng/ml.

Most West African studies confirm the high PSA trend in their series [9-11]. Note that Niang *et al.*, in Senegal [14] reported a particularly high average PSA level of 1447.57ng/mL in Senegal.

Prostate specific antigen (PSA) or human kallikrein 3 (hK3), is a serine protease secreted by prostate epithelial cells in immature form (pro-PSA) and transformed into mature forms only capable of binding to anti proteases (mainly alpha-1-antichymotrypsin [ACT]) to form complexed PSA. Serum total PSA (PSAT) includes inactive free forms (ALPS) and complexed forms (PSAC). PSA production by healthy tissue is around 0.3 µg/L/g and approximately ten times higher in prostate cancer. Early detection of prostate cancer is based on a PSAT assay combined with a rectal exam. The accepted decision threshold for prescribing a biopsy is now 2 to 3 µg/L at 45 years of age for assay methods using the international standard. To interpret the results, the age, volume and cell density of the prostate must be taken into account [13].

PSA is specific to the prostate and not to cancer [14]. There are no normal PSA values since it is a tissue marker. Values may vary depending on the test used. The most common standard is a level below 4 ng/ml.

PSA screening at a threshold of 4 ng/mL has maximum sensitivity and specificity in men under 70 years of age. It is currently proposed to lower it to 3 ng/mL, particularly for men under 70 years of age, since more than 20% of diagnosed cases present at diagnosis with a PSA lower than 4 ng/mL. A PSA cutoff value of 3ng/mL would improve the predictive value of PSA.

Gleason score

All patients had prostate adenocarcinoma. Furthermore, 52.12% of patients had a Gleason score greater than or equal to 6. Jallow M *et al.*, found in Senegal a Gleason score greater than or equal to 6 in 42% of patients.

The Gleason score is the most used histoprognostic criterion in prostate cancer because it assesses the aggressiveness and evolution of this cancer.

Prostate biopsies are indicated in men whose life expectancy is estimated to be greater than or equal to 10 years and who have a clinical or biological suspicion of prostate cancer: suspicious abnormality on digital rectal examination or elevated serum PSA. In men with reduced life expectancy, the benefit of performing prostate biopsies must be discussed on a case-by-case basis, depending on the situation, the clinical stage, the PSA value and the need for initiation. of treatment [4].

The Gleason score was performed in 100% of cases on biopsy specimens. No Gleason score was made after prostatectomy.

Peko *et al.*, compared biopsy Gleason scores with gGeason scores on surgical specimens in 2011 in Brazaville and concluded that the Gleason score on biopsies showed some limitations in the application.

The Gleason score was performed in 100% of cases on biopsy specimens. No Gleason score was made after prostatectomy.

In 2011 in Brazaville, Peko *et al.*, compared biopsy Gleason scores with gGeason scores on surgical specimens and concluded that the Gleason score on biopsies showed some limits in the assessment of the prediction, especially since prostate cancer is a heterogeneous cancer. Classifying patients according to the three distinct groups of degree of differentiation would increase the correlation between the biopsy Gleason score and that of the surgical specimen [15].

Scintigraphy Result

The BS+ numbered 46 (64.78%) patients compared to 25 BS- (35.21%).

This high rate of BS+ is explained by a delay in diagnosis and an advanced stage of the disease at the time of diagnosis. This trend specific to sub-Saharan Africa is confirmed by Dong *et al.*, in Cameroon with 61% BS+ (n=360). Similar studies in SENEGAL notably by Jallow *et al.*, and by Ndong *et al.*, found lower BS+ rates of 36% and 33%. However, the sizes of these two series were smaller than ours.

Prostate cancer is an osteophilic cancer for which BS plays a leading role. According to B. Erra *et al.*, BS is indicated in prostate cancer [16].

- in the initial extension assessment at the localized cancer stage;
- in the event of biochemical recurrence after total prostatectomy if the patient presents painful bone symptoms;
- for the evaluation of the response to systemic treatments (hormonotherapy, chemotherapy) of bone metastases from prostate cancer.

However, he specifies that BS is not indicated in the monitoring of patients during treatment in the absence of symptoms or biochemical recurrence.

Multiple secondary bony locations were the most represented (69.56%) and were located preferentially in the spine (19%), in the rib cage (17.4%), in the pelvis (12.62%).

All sub-Saharan series consulted confirm the predominant involvement of the axial skeleton in secondary bony locations of PCa. This is how Jallow *et al.,* calculate 62.5% axial localization.

This confirms international data on the site of secondary bone lesions in PCa.

Age and BS$^+$

In our study, age over 70 years is associated with an increased risk of BS+. For patients whose age was between 65 and 81 years, the bone scan was positive in 48.65% of cases, compared to the result of patients aged less than 65 years, with a proportion of 20% ($p< 0.05$).

Multiple secondary locations on the skeleton are associated with a form of prostate cancer with a poor prognosis. In our study, 9 out of 24 patients (37.5%) had multiple locations. In the age group [70-81 years], multiple localization (axial, appendicular, skull) was predominant with 63.64% of cases compared to 15.38% of cases in the age group [50-70 years].

PSA and BS$^+$ rates

Our study shows a risk of BS+ which increases as the PSA increases. From 20ng/ml the risk of BS+ is 1.21 times higher. This risk is multiplied by 2 from a PSA greater than 50 ng/ml and by 8 when the PSA is greater than 100 ng/ml. These findings are corroborated by the literature, only the degree of correlation varies depending on the studies.

According to the recommendations of the European Association of Urology (EAU), a PSA level between 3.1ng/ml and 4ng/ml is associated with a risk of PCa of 26.9%.

The PSA level increases with age but also with the spread of the disease, which explains these high values in our regions where prostate cancer is diagnosed at an advanced, sometimes metastatic, stage [17].

Gleason and BS$^+$ Correlation

All patients classified Gleason less than or equal to 6 were BS-.

84.21% of patients with a Gleason score greater than 8 are BS+.

These observations confirm the fact that a score less than or equal to 6 is associated with a low risk of BS+ while scores above 8 are associated with a high risk of BS+.

These observations, consistent with those of the international literature on the subject, are corroborated by other sub-Saharan studies. Thus Ndong *et al.,* [5] in 2011 found 80% BS+ with a Gleason score ≥7. Dong *et al.,* found a lower rate, i.e. 59.09% of BS+ with a Gleason score ≥7.

According to our study, patients with a Gleason score > 6 had a 4.53 times greater risk of developing bone metastases visible on scintigraphy than those with a Gleason score = 6. This difference was statistically significant ($p<0.005$; CI= [1.53-13.35]).

These results show a possible correlation between the Gleason score and the positivity of the bone scan.

CONCLUSION

Nuclear medicine plays an important role in the evaluation and management of prostate cancer. Its recent development, particularly through metabolic imaging and isotope therapy, makes it a major player in the management of metastatic prostate cancer. In Burkina Faso only the BS is available to support the urologist in taking PCa. Our study shows that BS+ is associated with an age greater than 70 years and a Gleason score greater than or equal to 7. It specifies that for patients with a Gleason score less than or equal to 6, BS is only justified 'in the event of painful bone symptoms. Local studies should be considered to evaluate the contribution of BS in the monitoring of PCa bone metastases.

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