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Correlation of PSA Level and ISUP Grade Group with Scintigraphic Bone Metastases Detection in 36 Prostate Cancer Patients

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Abstract

Background: We need population-specific clinical features that can predict bone metastases as an affordable therapeutic decision-making tool in newly diagnosed prostate cancer patients as scintigraphy or positron emission tomography are not available and as no such study had ever been performed in our country. **Objective:** To determine biologic and pathologic criteria that can predict the scintigraphic detection of bone metastases in our prostate cancer patients. **Patients and Method:** We analyzed with student's t test and logistic regression the PSA level, the ISUP grade and the scintigraphic data retrospectively collected in newly diagnosed prostate cancer patients. **Results:** In ten years, 36 prostate cancer patients were sent to the Korle Bu Teaching Hospital in Accra (Ghana) for bone scintigraphy (mean age = 63.9 years; 55.6%, 19.4% and 25.0% ISUP grade ≤ 2, 3 or ≥4). Among 28 patients who had performed the bone scintigraphy, 6 (21.4%) presented bone metastases, 22 (78.6%) had no bone metastasis. The mean PSA level was 36.7ng/mL in the non-metastatic patients and 97.7 ng/mL in the metastatic patients. The difference in PSA level between the 2 groups was significative ($p = 0.041$). 63.6% of the non-metastatic cancers versus 16.7% of the metastatic cancers were ISUP grade 2 or less. Inversely, 36.4% of the non-metastatic cancers versus 83.3% of the metastatic cancers were ISUP grade 3 or more. The difference was significative in the ISUP grade 2 or less ($p = 0.035$), was significative in the ISUP grade group 3 or more ($p = 0.035$). Metastasis was more likely in prostate cancer patients with PSA equal 30 ng/mL or more and ISUP grade 3 or more (83.3%) than in prostate cancer patients with PSA less than 30 ng/mL and ISUP grade less than 3 (16.7%) [OR = 13.7; CI 95% (1.59; 31.0); $p = 0.035$]. **Conclusion:** The scintigraphic detection of bone metastases is low in patients

with PSA < 30 ng/mL and ISUP grade < 3. This can be helpful in curative therapy decision making for prostate cancer when nuclear medicine or other metastases detection tools are lacking.

Keywords

Metastasis, Prostate Cancer, Bone Scintigraphy

1. Introduction

Prostate cancer is the second cause of cancer death in males [1]. The practice of prostate biopsy has recently been introduced in Benin [2] [3], triggering the local need for curative therapy against prostate cancer. Nevertheless, the lack of sound imaging tools to evaluate tumor extension may be a therapeutic hindrance in poor clinical settings. Bone scintigraphy or positron emission tomography are not available in Benin. Therefore, we do refer prostate cancer patients to the nuclear medicine unit of Korle Bu Teaching Hospital in Accra, Ghana. But that process consumes time, money, and physical strength. It has been established that prostate-specific antigen (PSA) level and tumor grade are independent predictors of bone metastasis [4] [5]. European Association of Urology and American Urological Association recommend that bone scintigraphy can be omitted in asymptomatic patients with PSA ≤ 20 ng/mL and ISUP grade ≤ 2 [6] [7]. Nevertheless, most of the studies that have generated the risk stratification of prostate cancer in those guidelines have been conducted outside black Africa. Thus, evidence from our setting may provide us with a population-specific clinical parameters to identify localized prostate cancer without imaging and possibly contribute to knowledge on the matter.

2. Objective

This study aimed to determine the clinical or biological criteria that could predict the detection of bone metastases at scintigraphy. Specifically, it looked for any link between the findings at bone scintigraphy and the patients' PSA level at biopsy or the ISUP grade determined at the pathological examination of the patients' prostate biopsy cores.

3. Patients and Method

From medical records, we retrospectively collected age, PSA level, ISUP grade and data of bone scintigraphy in all patients newly diagnosed with prostate cancer and sent to Accra for bone scintigraphy from 2012 to 2022. We considered only the newly diagnosed prostate cancer patients in whom all the needed information was available. We excluded all cases of prostate cancer that were not newly diagnosed, all newly diagnosed prostate cancer who had not accepted to perform bone scintigraphy or who had performed bone scintigraphy but in

whom data were not available. Amoako has described the bone scan procedure in Korle Bu Teaching Hospital [4]. We used the software R version 4.0.2. to analyze the data. We stratified the newly diagnosed prostate cancer patients into classes of PSA level using a cut-off of 10, 20, 30, and 100 ng/mL. As there were no metastatic patient with PSA < 30 ng/mL but one with PSA = 7.73 ng/mL, we only considered the PSA cut-offs of 30 and 100 ng/mL. We expressed qualitative variables as proportions. We calculated the means and standard deviations of quantitative variables as their distributions were normal. The proportions were compared by means of the ki square test, the Fischer's exact test or the corrected test of Yates. The means were compared by using the t test of Student. A univariate logistic regression was used to determine the association between the PSA level and the bone metastases detection at scintigraphy.

4. Results

In ten years, 36 newly diagnosed prostate cancer patients were sent to the Korle Bu Teaching Hospital in Accra (Ghana) for bone scintigraphy. Their clinical and scintigraphic characteristics are summarized on **Table 1**. Their mean age was 63.9 years. Their mean PSA level was 45.02 ng/mL. The ISUP grade was 2 or less in 20 patients (55.6%) and 3 or more in 16 patients (44.4%). Eight patients were lost to follow-up. 28 patients had performed the bone scintigraphy. 6 patients were metastatic. 22 patients had no detected bone metastasis.

The comparison of the metastatic to the non-metastatic patients enabled us to notice several facts (**Table 2** and **Table 3**). The metastases affected varied bones in the 6 metastatic patients: vertebra, sternum, pelvis, scapula, femur, ribs, skull, and clavicle. The metastases were located on the spine in 4 of the 6 metastatic patients. The metastases involved the whole skeleton in 1 patient with PSA = 100 ng/mL and ISUP grade 5. The number of metastatic sites seemed to be more elevated in patients with PSA level above 100 ng/mL ($p = 0.10$). Five or 38.5% in the 13 patients with ISUP grade 3 or more were metastatic. Only one or 6.7% in the 15 patients with ISUP grade below 3 was metastatic. The ISUP grade was 3 or more in 5 or 83.3% of the 6 metastatic patients and in 8 or 36.4% of the 22 non-metastatic patients. The proportion of metastatic patients was significantly higher in patients with ISUP grade ≥ 3 than in patients with ISUP grade < 3 ($p = 0.035$). The mean PSA level was 97.7 ng/mL in the metastatic patients and 36.7 ng/mL in the non-metastatic patients. Among the 12 patients with PSA level 30 ng/mL or more, 5 (41.7%) and 7 (58.3%) were respectively metastatic and non-metastatic. Only one (6.3%) in 16 patients with PSA level below 30 ng/mL was metastatic. Five (83.3%) of the 6 metastatic patients had a PSA level of 30 ng/mL or more. Two (33.3%) in 6 patients with PSA level below 100 ng/mL versus 4 (18.2%) in 22 patients with PSA level above 100 ng/mL were metastatic. The mean PSA level was significantly more elevated in the metastatic patients than in the non-metastatic patients ($p = 0.041$). The proportion of metastatic patients was significantly higher in patients with PSA ≥ 30 ng/mL than in the patients with

Table 1. Disease's characteristics in the patients.

Patients sent to Accra for Bone Scintigraphy (N = 36)	
mean age (age range)	63.9 (42 - 77)
mean PSA (PSA range)	45.02 (5.2 - 287.4)
ISUP grade group	*n* (%) of patients
1	11 (30.6)
2	9 (25.0)
3	7 (19.4)
4	5 (13.9)
5	4 (11.1)
Patients who performed the Bone Scintigraphy (n = 28)	
mean age (age range)	63.04 (48 - 77)
mean PSA (PSA range)	50.22 (5.2 - 287.4)
n (%) with PSA < 30	16 (57.1)
n (%) with PSA ≥ 30	12 (42.9)
n (%) with PSA < 100	23 (82.1)
n (%) with PSA ≥ 100	5 (17.9)
ISUP grade group	*n* (%) of patients
1	11 (39.3)
2	4 (14.3)
3	6 (21.4)
4	3 (10.7)
5	4 (14.3)
n (%) of bone metastatic patients	6 (21.4)
n (%) of bone metastasis-free patients	22 (78.6)
number of bone metastatic sites	*n* (%) patients
<3	3 (10.71)
≥3	3 (10.71)

Table 2. Comparison of metastatic and non-metastatic patients.

	Metastatic	**Non-metastatic**	***p* value**
Patients *n* (%)	6 (21.4)	22 (78.6)	
***n* (%) *of* patients by affected bones**			
Spine	4 (66.7)	0 (0.0)	
other bones	2 (33.3)	0 (0.0)	
Number of metastatic sites			
PSA < 100 ng/ml	≤2		0.10

Continued

PSA ≥ 100 ng/ml	>2		
***n* (%) Patients with ISUP grade group**			
<3	1 (16.7)	14 (63.6)	0.035
≥3	5 (83.3)	8 (36.4)	
PSA level (*ng/ml*)			
mean (range)	97.7 (7.73 - 287.4)	36.7 (5.2 - 270.6)	0.041
n (%) of patients with PSA level			
<30	1 (6.3)	15 (93.8)	0.035
≥30	5 (41.7)	7 (58.3)	
<100	2 (33.3)	4 (66.7)	0.10
≥100	4 (18.2)	18 (81.8)	

Table 3. Correlation between PSA level, ISUP grade group and metastases detection.

	n* (%) MP	***n* (%) MP < 3 sites**	***n* (%) MP ≥ 3 sites**	***p* value**
PSA level (*ng/ml*)				
<30	1 (6.25)	1 (6.25)	0 (0.00)	0.035
≥30	5 (41.67)	2 (16.67)	3 (25.00)	
<100	3 (13.04)	3 (13.04)	0 (0.00)	0.10
≥100	3 (60.00)	0 (0.00)	3 (60.00)	
ISUP grade group				
<3	1 (6.67)	1 (6.67)	0 (0.00)	0.035
≥3	5 (38.46)	2 (15.38)	3 (23.08)	
≤3	3 (14.29)	2 (9.52)	1 (4.76)	0.10
>3	3 (42.86)	1 (14.29)	2 (28.57)	

*MP = metastatic patient.

PSA < 30 ng/mL (p = 0.035). 63.6% of the non-metastatic cancers versus 16.7% of the metastatic cancers were ISUP grade 2 or less. Inversely, 36.4% of the non-metastatic cancers versus 83.3% of the metastatic cancers were ISUP grade 3 or more. The difference was significative in the ISUP grade 2 or less ($p = 0.035$), was significative in the ISUP grade 3 or more ($p = 0.035$). Metastases were more likely in prostate cancer patients with PSA ≥ 30 ng/mL and ISUP grade ≥ 3 than in prostate cancer patients with PSA < 30 ng/mL and ISUP grade < 3 [OR = 13.7; CI 95% (1.59; 31.0); $p = 0.035$].

5. Discussion

Prostate cancer is more and more diagnosed in Benin since the introduction of TRUS-guided prostate biopsy in 2013 [2] [3]. But sound tumor extension evalu-

ation tools such as nuclear medicine or positron emission tomography are not yet available. That situation is a big hindrance to curative decision-making for prostate cancer. This study has demonstrated that we can omit bone scintigraphy in some selected newly diagnosed prostate cancer patients and safely decide a curative therapy. In fact, metastases were unlikely in patients with PSA < 30 ng/mL and ISUP grade group < 3. A recent study found that the chance of getting positive bone scan for skeletal metastasis is less in prostate cancer patients with PSA < 29.16 ng/mL [8]. Most studies support that bone scintigraphy value is limited in patients with PSA < 20 ng/mL and Gleason score < 8 (*i.e.*, ISUP grade group < 4) [9] [10]. Khalid has noticed that the prevalence of bone metastases is negligible in Sudanese patients with PSA ≤ 10 ng/mL who also tend to have low grade tumor [5]. According to Qureshi, 22.2% of native African patients with PSA < 20 ng/mL have bone metastases which indicates that bone scan should not be omitted because of PSA < 20 ng/mL [11]. Clearly, the literature reveals that PSA level with variable cut-offs below 30 ng/mL and ISUP grade ≤ 3 are predictive of less scintigraphic detection of bone metastases.

The advent of choline and PSMA positron emission tomography has revealed that the whole-body scintigraphy can miss up to 24% bone metastatic prostate cancer patients [12]. The computed tomography is available in our country, but it does not perform better than bone scintigraphy [13]. The whole-body magnetic resonance imaging if it is available, may be helpful in non-claustrophobic patients [14] [15]. Beyond being a therapeutic decision-making tool, the presence of bone metastases at scintigraphy is predictive of a shorter survival [16], axial metastases carrying a better prognosis than appendicular metastases [17]. Still, in clinical settings which lack both scintigraphy and positron emission tomography, patients can be selected based on low PSA level and low ISUP grade for curative therapy.

6. Conclusion

The scintigraphic detection of bone metastases is low in patients with PSA < 30 ng/mL and ISUP grade < 3. This can be helpful in curative therapy decision making for prostate cancer when nuclear medicine or other metastases detection tools are lacking.

Limitations of This Study

The greatest limitation of this study is the small size of the population of newly diagnosed prostate cancer patients that have performed the bone scintigraphy.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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