



COLLEGE OF HEALTH SCIENCES

INTERNAL MEDICINE DEPARTMENT NUCLEAR MEDICINE UNIT

**Assessment of Bone Scintigraphy Results and Its Clinical Indications
and Determinants in Prostate Cancer Patients at CHU Bab El Oued, Algiers,
Algeria**

By Dr Faiz Kubes NMR3

Advisor: Dr Bethelhem Worku (Assistant professor)

Mr Aschalew Alemu (Lecturer)

Professor Salah Bouyoucef

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Acronyms

ASCO- American Society of Clinical Oncology

AUA-American Urological Association

AUC-Area Under Curve

CHU -College of health universities

EAU- European association of urology

ESTRO- European Society for Radiotherapy & Oncology

GS-Gleason score

ISUP- International Society of Urological Pathology

PCA -prostate cancer

PSA-prostatic specific antigen

RCTs-Randomized control trials

ROC -Receiver Operating Characteristic

SEER-Surveillance, Epidemiology, and End Results

SIOG- International Society of Geriatric Oncology

SNMMI- The Society of Nuclear Medicine and Molecular Imaging

Abstract

Background Prostate cancer is a leading malignancy among men worldwide, with bone metastases being a critical factor in disease progression and patient prognosis. Bone scintigraphy is a widely used imaging technique for detecting bone metastases, but its clinical utility varies based on patient characteristics. This study evaluates the clinical indicators influencing bone scintigraphy outcomes in prostate cancer patients at CHU Bab El Oued, Algiers, Algeria.

Objective To investigate the clinical indications and determinants influencing the use of bone scintigraphy in prostate cancer patients at CHU Bab El Oued.

Methods A retrospective observational study was conducted on 354 prostate cancer patients who underwent bone scintigraphy at CHU Bab El Oued. Descriptive statistics, Chi-Square tests, logistic regression, and ROC curve analysis were used to examine associations between PSA levels, Gleason scores, age, and bone scintigraphy results.

Results Of the 354 patients studied, 32.2% of patients had positive bone scintigraphy results, indicating metastasis. Higher PSA levels (>20 ng/mL) and Gleason scores (≥ 8) were significantly associated with positive bone scans ($p < 0.001$). Age was not a significant predictor of metastasis ($p = 0.691$). Logistic regression analysis confirmed PSA and Gleason scores as key predictors of metastasis, with higher Gleason scores increasing the risk by 2.26 times ($OR = 2.266$, $p < 0.001$). The ROC curve showed strong predictive ability ($AUC = 0.89$), suggesting high accuracy in predicting bone metastases.

Conclusion Bone scintigraphy is indicated for prostate cancer patients with specific high-risk features to detect bone metastases effectively. Specifically, PSA levels and Gleason scores are strong predictors of bone metastases, with higher values (PSA >20 ng/mL and Gleason score ≥ 8) significantly increasing the likelihood of positive findings, while age alone does not play a significant role. The predictive model demonstrated high accuracy, reinforcing the need for targeted use of bone scintigraphy in high-risk patients to optimize clinical decision-making.

Keywords: Prostate Cancer, Bone Scintigraphy, PSA Levels, Gleason Score, Bone Metastases,

1.Introduction

1.1 Background

Prostate cancer is one of the most commonly diagnosed malignancies among men worldwide, contributing significantly to morbidity and mortality. Globally, it is the second most frequently diagnosed cancer in men, with approximately 1.5 million new cases and 397,000 deaths in 2020 (Bray et al., 2024). In Africa, prostate cancer is the most common cancer among men, with 114,959 new cases and 47,284 deaths reported in 2022, reflecting an age-standardized incidence rate of 15.9 per 100,000 men and a 5-year prevalence of 350,758 cases (GLOBOCAN, 2022). In Algeria, a Northern African country, prostate cancer has emerged as a major public health concern, ranking as the third most common cancer among men, with 3,514 new cases and 1,333 deaths reported in 2022 (GLOBOCAN, WHO, 2022). The rising incidence in Algeria is attributed to an aging population and improved diagnostic capabilities (Zoubida et al., 2011).

Bone metastases are a frequent complication of advanced prostate cancer, occurring in up to 90% of patients with distant metastases (Godebu et al., 2014). The skeletal system is the most common site for metastatic spread, leading to complications such as severe bone pain, fractures, and spinal cord compression, which significantly reduce quality of life and survival rates (Coleman, 1997; Mohseninia et al., 2023). Given the high prevalence and impact of bone metastases, early and accurate detection is critical for staging, prognosis, and treatment planning.

Bone scintigraphy is the most widely used diagnostic tool for detecting bone metastases in prostate cancer (Tombal & Lecouvet, 2012). This highly sensitive nuclear imaging technique detects osteoblastic metastases, which are characteristic of prostate cancer (Römer, 2024). Bone scintigraphy uses technetium-99m-labeled diphosphonates, which localize in areas of increased bone turnover, allowing early detection of metastatic lesions (Rawla, 2019). Due to its high sensitivity, bone scintigraphy is widely recommended by international guidelines for prostate cancer staging (Giovannella et al., 2013).

However, the indications for bone scintigraphy vary across clinical guidelines, reflecting a lack of global standardization (Mohler et al., 2019). The American Urological Association (AUA) recommends bone scintigraphy for patients with high-risk prostate cancer, defined as those with PSA >20 ng/mL, Gleason score ≥ 8 , or clinical stage T3-T4, according to the 2022 AUA/ASTRO guideline for clinically localized prostate cancer (American Urological Association, 2022). In

contrast, the European Association of Urology (EAU) advises its use in intermediate- and high-risk patients, rather than limiting it to symptomatic cases. (EAU-EANM-ESTRO-ESUR-SIOG guidelines,2020). The Society of Nuclear Medicine and Molecular Imaging (SNMMI), European Association of Nuclear Medicine (EANM), and American Society of Clinical Oncology (ASCO) provide varying expert-based recommendations on when bone scintigraphy should be utilized (Bartel et al., 2018; Van den Wyngaert et al., 2016; Trabulsi et al., 2020). This inconsistency can lead to overuse or underuse of bone scintigraphy, affecting diagnostic accuracy, healthcare costs, and resource allocation.

Besides PSA levels, the Gleason score is a critical determinant. Patients with higher Gleason scores, particularly ≥ 8 , are at greater risk of bone metastases and thus more likely to require bone scintigraphy for staging. Conversely, age, although a significant risk factor for developing prostate cancer, does not directly correlate with the presence of bone metastases. Research has shown that age is not predictive of positive bone scans when PSA levels and Gleason scores are considered (e.g., Li et al., 2017). Therefore, clinical decisions regarding bone scintigraphy should primarily rely on PSA levels and Gleason scores rather than age

Given the rising prostate cancer burden in Algeria, optimizing diagnostic strategies is crucial to ensure effective and judicious use of healthcare resources. This study aims to evaluate the clinical indications and determinants of bone scintigraphy in prostate cancer patients at CHU Bab El Oued, providing evidence-based insights that could inform standardized diagnostic protocols and improve clinical decision-making in Algeria.

1.2 Statement of the Problem

The management of prostate cancer in Algeria, particularly at CHU Bab El Oued, faces significant challenges in the timely and accurate detection of bone metastases, which are crucial for guiding treatment decisions and improving patient outcomes. Although bone scintigraphy remains the cornerstone for identifying skeletal metastases, its utilization in Algerian healthcare settings lacks uniformity. This inconsistency mirrors the global variability seen in clinical recommendations. However, the absence of locally adapted protocols in Algeria leads to variability in practice, potentially resulting in underdiagnosis in patients who could benefit from early detection or unnecessary imaging in low-risk cases, thus straining healthcare resources.

Despite the frequent use of bone scintigraphy in specialized centers like CHU Bab El Oued, there is a lack of comprehensive data on the clinical factors influencing its utilization. Key questions remain unanswered. Which clinical indicators (PSA levels, Gleason scores, symptoms) drive the decision to perform bone scintigraphy? How well do these factors predict positive bone metastases findings? Does current practice in Algeria align with international recommendations?

Without a standardized approach, there is a risk of overusing bone scintigraphy in low-risk patients or underusing it in high-risk patients, leading to delayed treatment, unnecessary costs, and suboptimal resource allocation.

This study aims to analyze the clinical decision-making process behind bone scintigraphy use, assess associations between patient characteristics and positive scan results, and provide evidence-based recommendations for optimizing its use in Algeria

1.3 Significance of the Study

This study holds substantial importance for advancing prostate cancer management in Algeria by identifying key clinical indicators that justify the use of bone scintigraphy. It aims to improve staging accuracy by ensuring the timely and appropriate detection of bone metastases, which is critical for effective treatment planning and prognosis. Additionally, the research will enhance resource allocation by preventing unnecessary scans while guaranteeing that high-risk patients receive essential imaging, thereby optimizing the use of limited healthcare resources. By providing evidence-based insights, this study will contribute to the development of standardized diagnostic protocols tailored to the Algerian context, addressing the current variability in clinical practice. Furthermore, it has the potential to impact policy and clinical practice by aligning local approaches with international best practices, ultimately improving patient outcomes. Beyond Algeria, the findings will serve as a valuable reference for similar healthcare settings, particularly in resource-constrained environments, where striking a balance between optimal diagnostics and cost-effectiveness is paramount

2. Objectives of the Study

2.1 General Objective

To investigate the clinical indications and determinants influencing the use of bone scintigraphy in prostate cancer patients at CHU Bab El Oued.

2.2 Specific Objectives

- 1.To identify demographic factors, affect clinical indication to perform bone scintigraphy in prostate cancer patients at CHU Bab El Oued.
- 2.To investigate PSA levels, Gleason scores, and tumor stage, associated with the application of bone scintigraphy in prostate cancer patients at CHU Bab El Oued.
- 3.To assess the associations between bone scintigraphy results (positive or negative for bone metastases) and the key clinical indicators of PSA levels, Gleason scores, and age in prostate cancer patients at CHU Bab El Oued.

3. Conceptual Framework

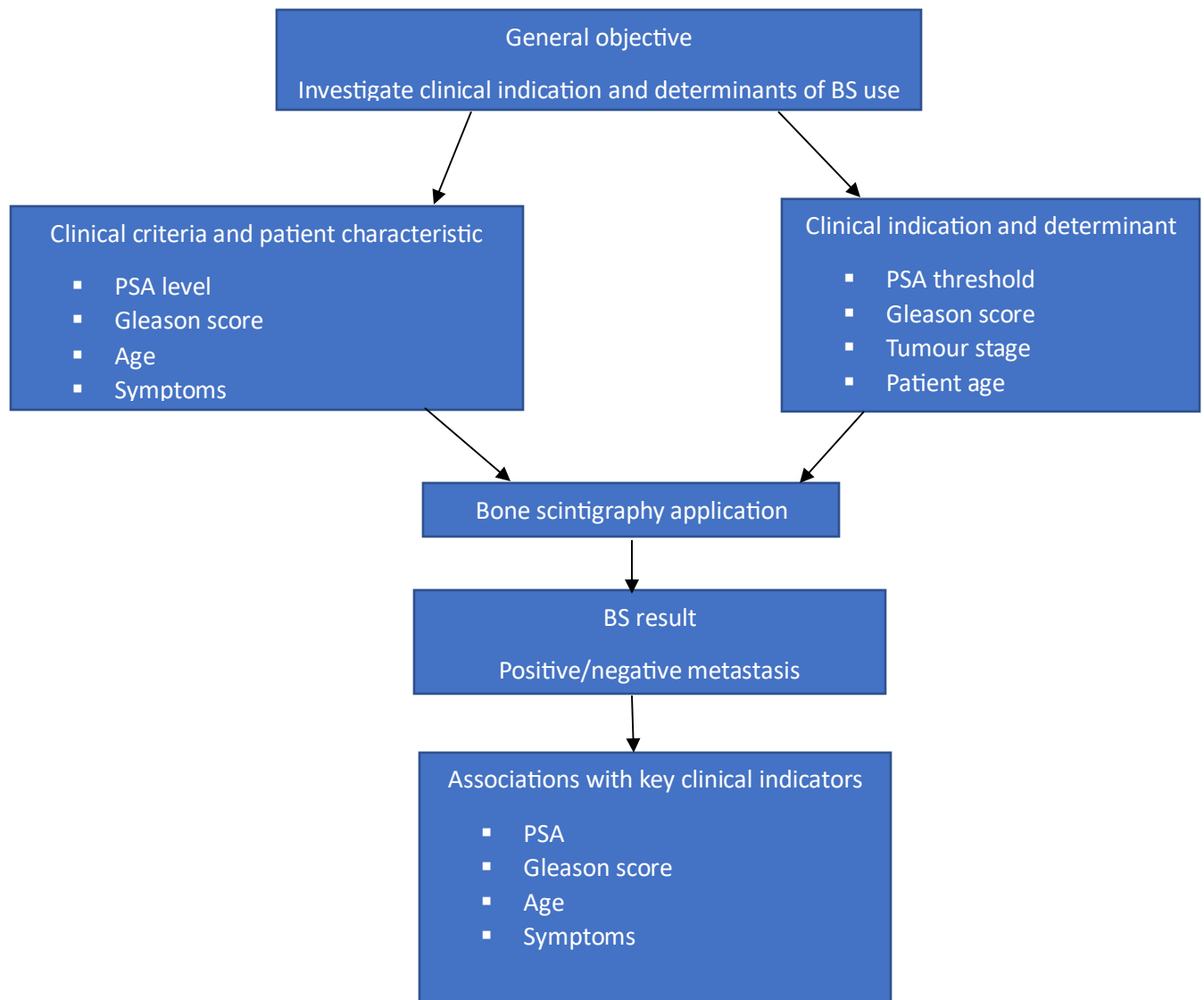


Figure 1: Conceptual Framework for Investigating Clinical Indications and Determinants of Bone Scintigraphy Use in Prostate Cancer Patients at CHU Bab El Oued, Algiers Algeria, 2025

This figure illustrates the conceptual framework for the study, depicting the relationships between clinical criteria and patient characteristics (PSA levels, Gleason score, age, and symptoms), clinical indications and determinants (PSA thresholds, Gleason scores, tumor stage, and patient age), and the application of bone scintigraphy in prostate cancer patients at CHU Bab El Oued, Algiers, Algeria. It shows how these factors influence bone scintigraphy results (positive or negative for metastases) and their associations with key clinical indicators, aligning with the study's general and specific objectives to optimize diagnostic strategies.

4. Literature review

4.1 Prostate Cancer and Bone Metastases

Prostate cancer is the most common malignancy of the male genitourinary system and is a leading cause of cancer-related mortality worldwide. In the United States and other Western nations, it ranks second among cancer-related deaths in men (Petersen et al., 2018). A major complication of advanced prostate cancer is bone metastasis, which occurs in up to 90% of cases with distant spread (Godebu et al., 2014). Across Europe, bone metastases continue to play a major role in the progression and outcome of prostate cancer. For example, data from Denmark revealed that among 23,087 newly diagnosed prostate cancer patients, 2,578 presented with bone metastases at the time of diagnosis, emphasizing the prognostic significance of skeletal involvement (International Agency for Research on Cancer, 2022). Bone metastases significantly worsen prognosis, leading to complications such as bone pain, fractures, and spinal cord compression, which reduce quality of life and survival rates (Coleman, 1997). Given this high metastatic tendency, early detection of bone involvement is crucial for treatment planning and patient management.

4.2 Importance of Bone Scintigraphy in Prostate Cancer Diagnosis

Bone scintigraphy is a widely used nuclear imaging technique for detecting bone metastases in prostate cancer. Its high sensitivity to changes in bone metabolism makes it superior to conventional radiographic methods, allowing for earlier detection of skeletal metastases (Parveen et al., 2023).

Early detection of bone involvement through scintigraphy plays a critical role in clinical decision-making. By assessing the extent of metastatic spread, bone scintigraphy helps guide systemic therapy selection, localized interventions, or palliative care decisions (Parker et al., 2020). According to the European Association of Urology (EAU) guidelines, bone scintigraphy is recommended for patients with intermediate-risk prostate cancer (ISUP grade 3) and high-risk localized prostate cancer, as part of metastatic screening alongside cross-sectional abdominopelvic imaging (EAU-EANM-ESTRO-ESUR-SIOG guidelines, 2020). In contrast, the American Urological Association (AUA) guidelines recommend bone scintigraphy specifically for high-risk prostate cancer patients, defined as those with PSA >20 ng/mL, Gleason score ≥ 8 , or clinical stage T3-T4 (American Urological Association, 2022). These guidelines highlight the importance of bone scintigraphy in detecting bone metastases, which occur in up to 90% of patients with advanced prostate cancer (Godebu et al., 2014). In the United States, the 5-year survival rate for prostate cancer patients with bone metastases is only 3% (95% CI: 2.2-3.4), compared to 56% (95% CI: 54.9-56.7) for those without (Siegel, Miller and Jemal, 2016). Despite its utility, the decision to order bone scintigraphy is not standardized and varies based on PSA levels, Gleason scores, and the presence of symptoms. This lack of uniform guidelines highlights the need for evidence-based criteria to optimize its use.

4.3 Factors Influencing Bone Scintigraphy Utilization

4.3.1 Prostate-Specific Antigen (PSA) Levels

Prostate-Specific Antigen (PSA) is a key biomarker for prostate cancer progression. Elevated PSA levels are strongly correlated with an increased risk of bone metastases, making it a primary factor influencing bone scintigraphy referrals.

A retrospective study in China involving 703 prostate cancer patients demonstrated that individuals with PSA levels >20 ng/mL had a significantly higher likelihood of bone metastases (Lin et al., 2017). Similarly, PSA velocity—the rate of PSA increases over time—has been identified as a key predictor of aggressive disease, warranting early bone scintigraphy screening (Sissons et al., 1992). Research conducted in Sweden, involving 102,076 men diagnosed with prostate cancer, demonstrated that elevated PSA levels are strongly correlated with the likelihood of bone metastases. However, the PSA threshold varies according to tumor stage and Gleason Grade Group (GGG). For example, among patients with early-stage disease (T1–T2) and GGG 1, only 0.2% had PSA levels exceeding 500 ng/mL, with bone metastases present in 44% of those

cases. In contrast, among those with advanced-stage disease (T3–T4) and GGG 5, 16% had PSA levels above 500 ng/mL, and metastases were identified in 94% of these patients (Strand et al., 2020). Furthermore, findings from a UK-based study in 1997 suggested that bone scintigraphy may not be required for newly diagnosed prostate cancer patients without clinical bone symptoms and with PSA levels of ≤ 10 ng/mL, as the likelihood of metastases at this level was negligible, offering a 100% negative predictive value (Oesterling et al., 1997).

However, PSA alone is not always a definitive predictor of metastasis. Some studies indicate bone metastases in patients with PSA ≤ 20 ng/mL, questioning the effectiveness of current PSA thresholds for guiding imaging decisions (Uz Zaman et al., 2011). These inconsistencies suggest that PSA should be used in conjunction with other clinical indicators to improve the accuracy of metastasis detection

4.3.2 Gleason Score and Tumor Aggressiveness

The Gleason Score (GS) is a critical histological grading system used to assess tumor aggressiveness. Higher Gleason scores (≥ 8) indicate poorly differentiated tumors with an increased likelihood of bone metastasis.

A study by Chorf (2015) found that patients with Gleason scores of 8–10 had a substantially higher risk of developing bone metastases compared to those with lower scores. This highlights the importance of incorporating Gleason grading into clinical decision-making for bone scintigraphy referrals. A study using the SEER database (American) found that while higher Gleason scores are generally associated with worse prognosis, in multivariate analysis, Gleason score did not significantly increase the odds ratio for bone metastasis in the SEER cohort, though it did in a local hospital cohort (Li et al., 2020). This suggests that while Gleason score is important, its predictive value for bone metastases may vary depending on the population studied

Despite these findings, some patients with lower Gleason scores still present with bone metastases, suggesting that additional biomarkers and imaging criteria are necessary for optimal risk stratification.

4.3.3 Clinical Symptoms and Imaging Indications

Symptomatic presentations, particularly bone pain, are among the strongest indications for bone scintigraphy (Abuzallouf et al., 2004). The presence of skeletal discomfort often correlates with detectable bone metastases, justifying imaging use. A 1997 study from the UK emphasized that

bone scintigraphy is essential when there are clinical signs of bone pathology, even if PSA levels are not extremely high (Oesterling et al., 1997)

However, reliance on symptoms alone is not sufficient, as asymptomatic patients with high PSA or Gleason scores may also harbor occult metastases (Williams, 2023). Additionally, symptomatology can be influenced by other conditions, such as treatment side effects or non-malignant bone disorders, leading to potential misdiagnosis. A comprehensive approach, integrating biochemical, histological, and imaging criteria, is necessary for accurate metastasis detection.

4.4 Advances in Imaging and Biomarkers for Bone Scintigraphy

Recent studies suggest that additional biomarkers such as Alkaline Phosphatase (ALP)—a marker of bone turnover—may improve risk stratification for bone scintigraphy referrals. Elevated ALP levels, particularly in combination with high PSA, have been associated with an increased likelihood of bone metastasis (Koo et al., 2015). Recent progress in bone scintigraphy has led to the introduction of the bone scan index (BSI), a tool designed to quantitatively assess the burden of bone metastases in patients with prostate cancer. By utilizing specialized software, the BSI allows for standardized and reproducible measurement of metastatic spread, enabling clinicians to use it as a practical imaging biomarker in both clinical practice and research settings (Nakajima et al., 2017). Furthermore, advancements in hybrid imaging technologies, such as SPECT/CT, have improved the specificity of bone scintigraphy, reducing false-positive results (Beheshti & Langsteger, 2012). These developments offer more accurate diagnostic tools that could refine patient selection criteria for bone scintigraphy.

4.5 Variability in Clinical Guidelines and Research Gaps

However, these guidelines lack standardization across different healthcare systems, leading to inconsistencies in clinical practice (Donohoe et al., 2017). Furthermore, a study from Korea suggested that the current guidelines, which recommend against bone scans for PSA ≤ 20 ng/mL with Gleason score ≤ 7 , might not be entirely applicable to Asian populations, as a significant number of patients with PSA between 10 and 20 ng/mL had positive bone scans (Kim et al., 2011). This highlights the need for region-specific guidelines that account for population differences

One major research gap is the lack of randomized controlled trials (RCTs) to validate these imaging criteria. Existing guidelines rely largely on expert consensus rather than high-quality evidence, leading to potential overuse in low-risk patients and underuse in high-risk populations. Additionally, most current studies focus on Western populations, with limited data on North African and Middle Eastern cohorts. Given the genetic, environmental, and healthcare differences in these regions, further research is needed to determine the applicability of existing predictive models (Uz Zaman et al., 2011).

5. Methods

5.1 Study Design: This research is a retrospective, observational study.

5.2 Study Area and Period: The study was conducted at CHU Bab El Oued in Algiers, Algeria, a leading tertiary care hospital known for its specialized oncology and nuclear medicine services. The Nuclear Medicine Unit at CHU Bab El Oued is equipped with advanced imaging technology, including bone scintigraphy, making it an ideal setting for assessing diagnostic practices in prostate cancer. Serving a broad patient base from Algiers and nearby regions, this facility provides a representative view of prostate cancer management in Algeria. The study covers observational period of four years, from January 2020 to August 2024. The study period is from July 2024 to March 2025.

5.3 Source and Study Population: The source population includes all prostate cancer patients treated at the Service de médecine nucléaire CHU Bab El Oued. The study population specifically consist of those who have undergone bone scintigraphy, enabling a focused investigation into the use and outcomes of this diagnostic approach.

5.4 Sampling Procedures and Sample Size Determination: systematic random sampling was employed to select a representative sample of prostate cancer patients who have undergone bone scintigraphy at CHU Bab El Oued. A complete list of eligible patients was obtained from medical records. The sampling interval (k) was determined by dividing the total population size by the desired sample size. A random starting point was chosen within the first few patients on the list, and every K th patient thereafter will be included in the sample. This approach ensures that the sample is evenly distributed across the population and minimizes bias.

The sample size was calculated using the formula $n = Z^2 \times p \times (1-p) / d^2$ where Z represents the z-value corresponding to a 95% confidence level (1.96), p is the expected prevalence of bone metastasis (50%), and d is the margin of error (5%). This results in an initial sample size of 384 patients. This sample size is further justified by a power analysis, assuming an effect size of 0.3, to ensure an 80% probability of detecting clinically significant differences in bone scintigraphy indications across patient subgroups.

5.5 Variables of the Study:

Independent Variables: Prostate-Specific Antigen (PSA) Levels: Gleason Score (GS): Patient Age: clinical symptoms

Dependent Variable: Bone Scintigraphy Results

5.6 Operational Definitions:

1.Prostate Cancer (PC): Refers to confirmed cases of malignant tumors in the prostate gland, based on histopathological examination.

2.Bone Scintigraphy (BS): A nuclear imaging technique used to detect bone metastases in prostate cancer patients at CHU Bab El Oued.

3.Bone Metastasis (BM): Defined as any positive finding on bone scintigraphy indicating abnormal uptake suggestive of metastatic disease.

4.Prostate-Specific Antigen (PSA): The serum concentration measured in ng/mL at diagnosis, used to assess prostate cancer severity.

5.Gleason Score (GS): A grading system for prostate cancer aggressiveness, based on biopsy samples, ranging from 2 to 10.

6.Clinical Determinants: Factors such as PSA levels, & Gleason scores,

5.7 Data Development and Collection Procedures: Patient records from the Nuclear Medicine Unit at CHU Bab El Oued were retrospectively reviewed. A standardized data collection form was developed to ensure uniformity and reliability in data extraction. Eligible patients were identified based on inclusion/exclusion criteria, Clinical data were extracted (demographic information, PSA levels, Gleason scores, bone scintigraphy results) and Data were entered into a secured electronic database for analysis.

5.8 Data Quality Assurance: A standardized data collection form was developed to extract relevant information from medical records. The data collection form was tested on 20 sample

records to ensure clarity and completeness. A subset of patient records was re-examined for accuracy.

5.9 Data Processing and Analysis

Data Processing: The collected data underwent a systematic processing workflow to ensure accuracy, consistency, and completeness before statistical analysis. All extracted variables were entered into IBM SPSS Statistics version 27.

Data cleaning was performed by: Identifying and handling missing values using listwise deletion for records with incomplete key variables (PSA, Gleason score, bone scan results). Standardizing categorical variables to ensure consistency in coding (e.g., converting PSA levels into predefined categories: <10, 10-20, >20 ng/mL).

Statistical Analysis: Descriptive Statistics. Categorical variables (bone scintigraphy results, PSA categories, Gleason score groups, age groups) were summarized using frequency tables and percentages, for Continuous variables (age, PSA levels) were described using mean $\pm$ standard deviation (SD) and median and (bar charts, histograms) was used to visualize data distributions.

Bivariate Analysis: To assess the relationship between bone scintigraphy results and key clinical variables, the following statistical tests were applied:

Chi-Square Test for Independence: Used to determine whether bone metastasis status (positive/negative) was associated with categorical predictors. Statistical significance was determined at $p < 0.05$ and Cramer's V was used to measure the strength of association.

Multivariate Analysis: To identify independent predictors of bone metastases, a binary logistic regression model was employed:

Receiver Operating Characteristic (ROC) Curve Analysis: To assess the diagnostic performance of PSA and Gleason score in predicting bone metastases, an ROC curve analysis was conducted.

5.10 Ethical Considerations: This study was approved by the Ethics Committee of CHU Bab El Oued, Algiers and conducted in accordance with the institutional ethical guidelines. Given the retrospective nature of the study, individual patient consent was waived; however, strict confidentiality measures were implemented to protect patient data. All records were anonymized prior to analysis, and no identifiable patient information was disclosed. The study adhered to best ethical practices to ensure scientific integrity, patient confidentiality, and compliance with international research standards.

6.Result

A total of 384 prostate cancer patients who underwent bone scintigraphy at CHU Bab El Oued were analyzed

6.1 Descriptive Statistics

The mean age was 72.0 ± 7.48 years (range: 45–92), with 59.0% of patients older than 70 years, consistent with prostate cancer being a disease of aging. The mean PSA level was 43.19 ± 67.60 ng/mL, with nearly half (49.4%) of patients having PSA >20 ng/mL, indicating an increased metastatic risk. The Gleason Score distribution showed that most patients had intermediate to high-grade tumors (Gleason ≥ 7 , 74.2%), reinforcing the presence of aggressive disease. Bone scintigraphy results showed that 67.8% (240 patients) tested negative for metastases, while 32.2% (114 patients) had confirmed bone metastases, indicating that a substantial proportion of patients exhibited metastatic spread

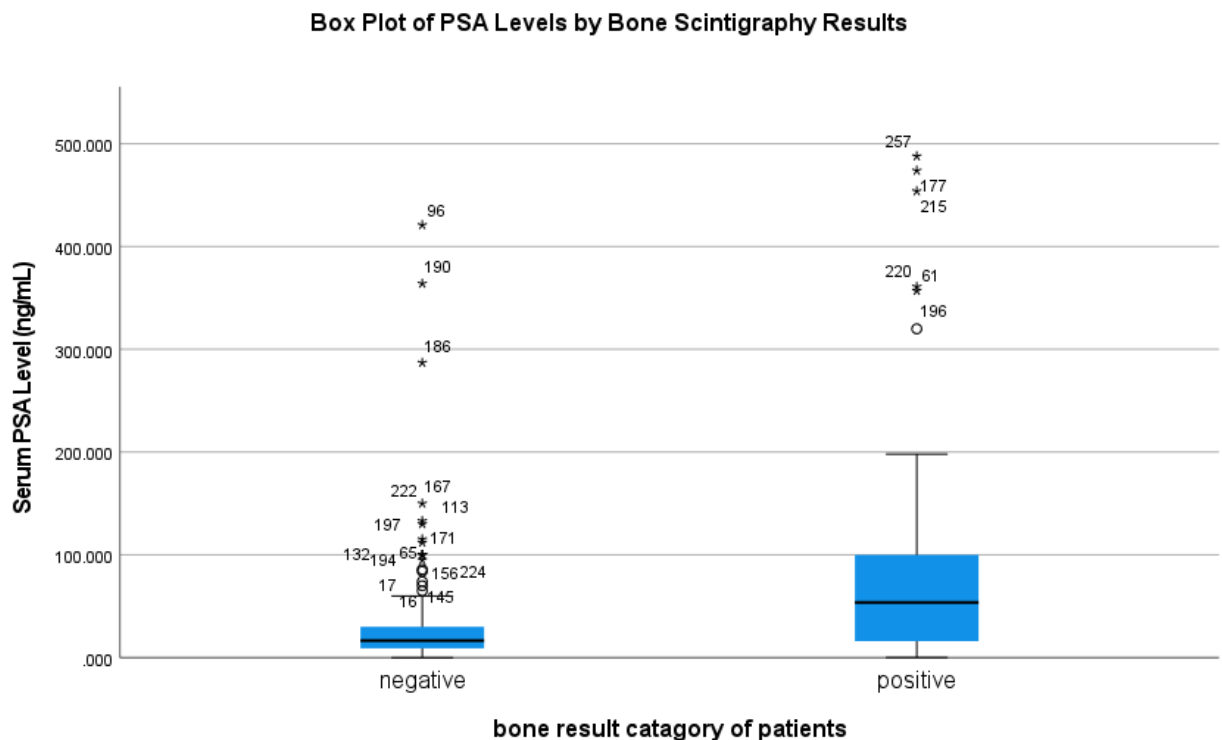


Figure 2 distribution of PSA levels among prostate cancer patients at CHU Bab El Oued. Algiers, Algeria from 2020-2024

Median PSA levels were notably higher in the metastasis-positive group, with a broader interquartile range indicating greater variability. Outliers in both groups suggest possible false negatives or early metastases in negative scans. The extreme values in the positive group emphasize the strong association between PSA elevation and bone metastases, reinforcing PSA’s role as a biomarker while underscoring the need for supplementary imaging in borderline cases.

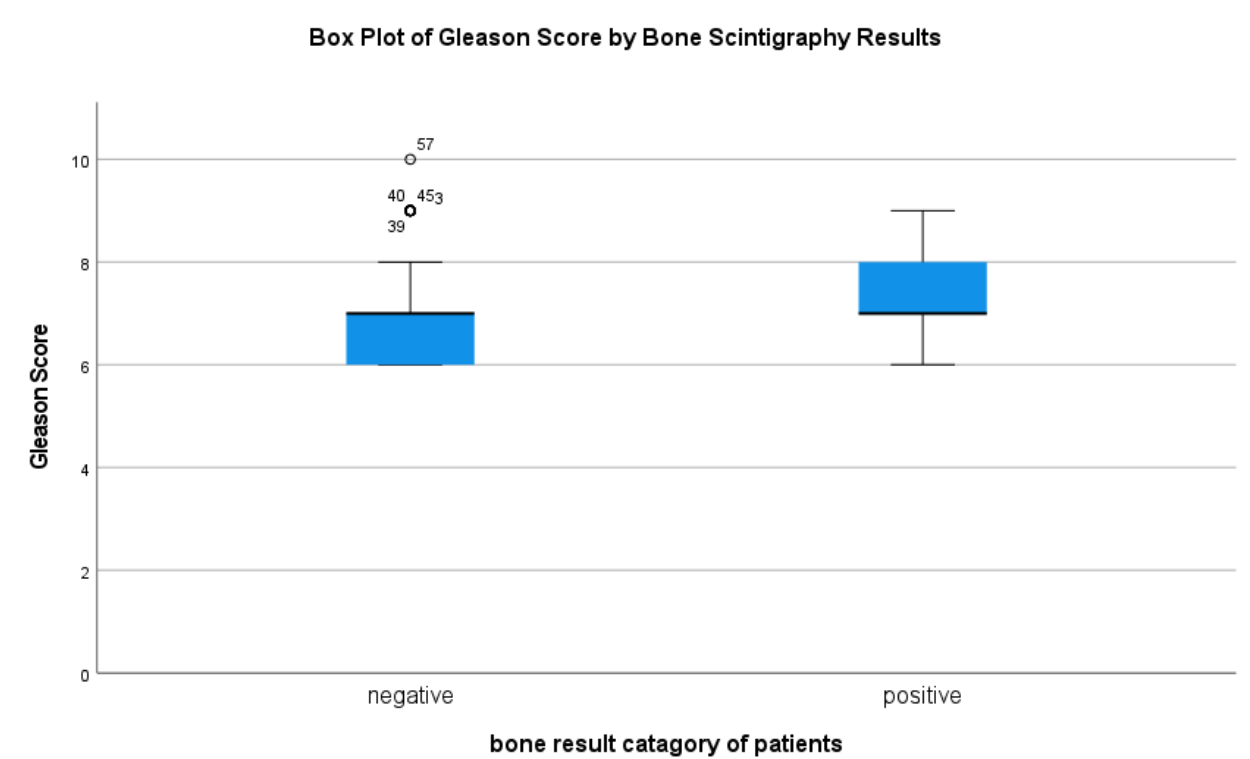


Figure 3 distribution of Gleason scores among prostate cancer patients. at CHU Bab El Oued. Algiers, Algeria from 2020-2024

Patients with positive scintigraphy results had higher median Gleason scores and a wider interquartile range, indicating more aggressive disease and greater variability. Outliers in the metastasis-negative group suggest some high-Gleason patients may have undetected metastases. These findings highlight the association between higher Gleason scores and bone metastases, supporting its prognostic value in risk stratification

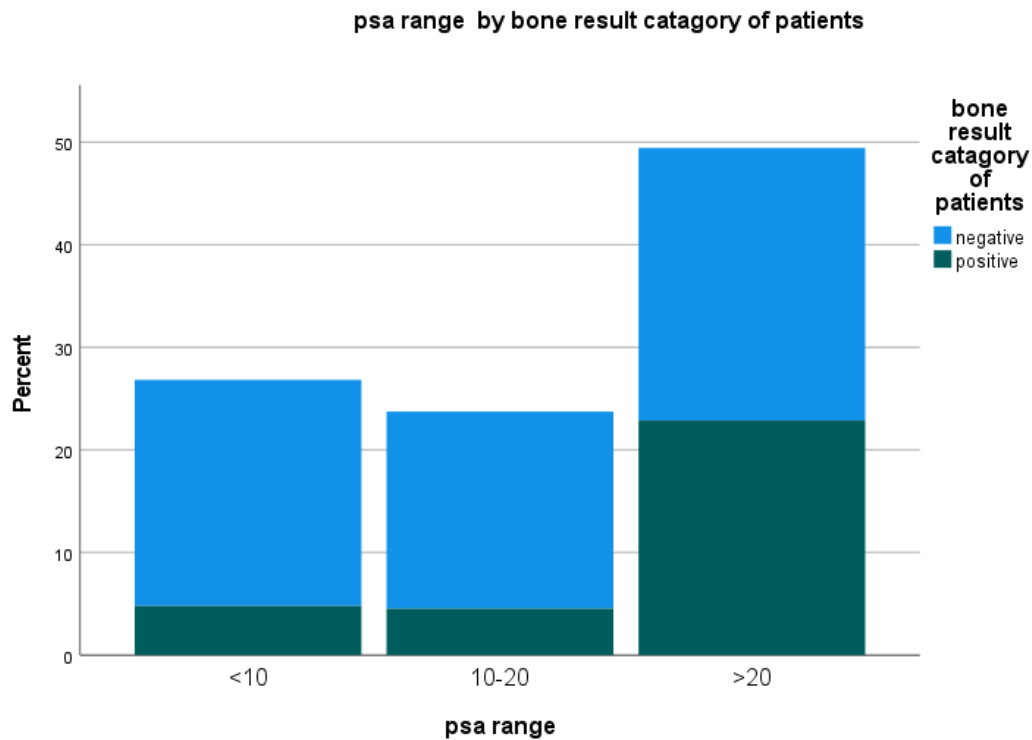


Figure 4 distribution of bone scintigraphy results (positive vs. negative) across different PSA level categories at CHU Bab El Oued. Algiers, Algeria from 2020-2024

The proportion of patients with positive bone scans increases with higher PSA levels, indicating a strong association between elevated PSA and bone metastases. In the lower PSA range, most patients had negative scintigraphy results, while in higher PSA categories, the majority had positive scans. This trend reinforces the role of PSA as a predictive biomarker for bone metastases, highlighting its clinical utility in stratifying patients for further imaging evaluation.

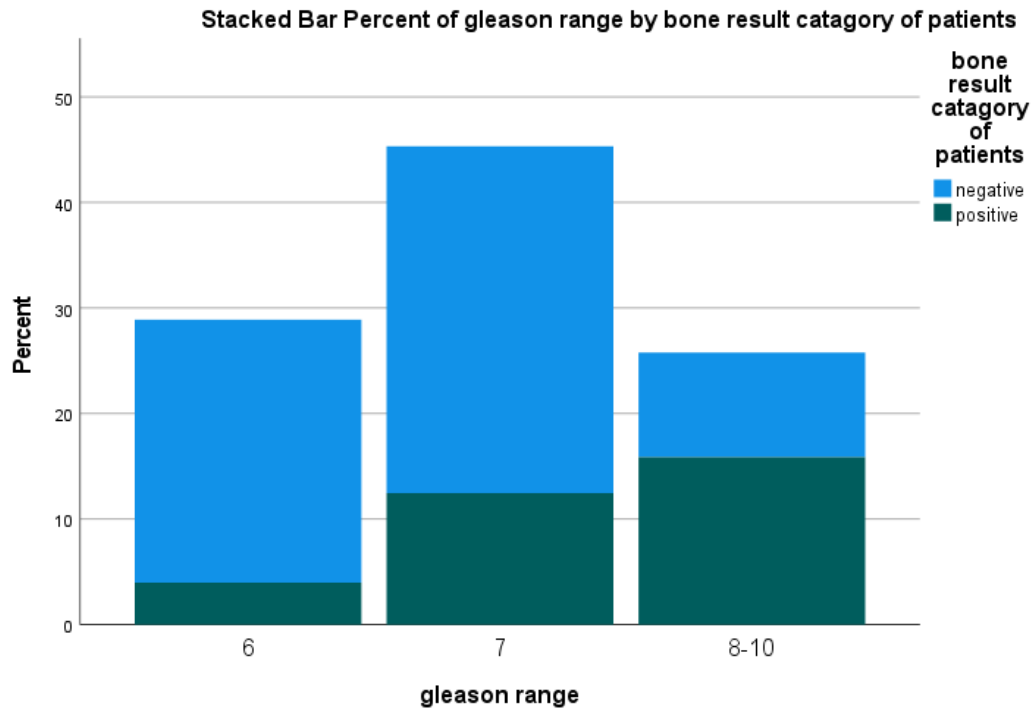


Figure 5 distribution of bone scintigraphy results (positive vs. negative) across different Gleason score categories at CHU Bab El Oued, Algiers, Algeria from 2020-2024

A higher proportion of patients with positive bone scans is observed in those with Gleason scores ≥ 8 , indicating a strong correlation between higher Gleason scores and bone metastases. Conversely, patients with lower Gleason scores (≤ 6) predominantly had negative bone scan results. This trend highlights the prognostic significance of the Gleason score in assessing metastatic risk, reinforcing its role in guiding clinical decision-making.

6.2 Association Between Bone Metastasis and Clinical Factors (Chi-Square Test)

A Chi-square test assessed the relationship between bone scintigraphy results and clinical factors.

PSA Levels: Patients with PSA > 20 ng/mL had a significantly higher likelihood of metastases (71.1% positive scans) compared to those with PSA < 10 ng/mL (17.9% positive, $\chi^2 = 31.463$, $p < 0.001$, Cramér's $V = 0.298$).

Gleason Scores: Patients with Gleason scores 8–10 was at the highest metastatic risk (61.5% positive scans) compared to Gleason 6 (13.7%) and Gleason 7 (27.5%) ($\chi^2 = 53.360$, $p < 0.001$, Cramér's $V = 0.389$).

Age: No significant association was found between age and bone metastasis ($\chi^2 = 1.714$, $p = 0.424$, Cramér's $V = 0.070$), suggesting that PSA and Gleason Score are stronger predictors of metastasis

Table 2 summarizes the chi-square test results assessing the association of PSA level, Gleason score, and age category with bone scintigraphy outcomes.

Variable	Chi-Square (χ^2)	df	p-value (Sig.)
PSA Level	31.463	2	<.001
Gleason Score	53.360	2	<.001
Age Category	1.714	2	0.424

Both PSA level ($\chi^2 = 31.463$, $df = 2$, $p < 0.001$) and Gleason score ($\chi^2 = 53.360$, $df = 2$, $p < 0.001$) demonstrated statistically significant associations with bone metastases, indicating that higher PSA levels and Gleason scores are more frequently observed in patients with positive scintigraphy results. However, age category ($\chi^2 = 1.714$, $df = 2$, $p = 0.424$) was not significantly associated with bone metastases, suggesting that age alone is not a strong predictor. These findings reinforce the importance of PSA levels and Gleason score in evaluating metastatic risk, while age appears to play a lesser role

6.3 Logistic Regression Analysis

A binary logistic regression model examined the independent effect of PSA, Gleason Score, and Age on metastasis prediction ($\chi^2 = 66.464$, $p < 0.001$). The model explained 24% of the variance (Nagelkerke $R^2 = 0.240$) and had an overall classification accuracy of 73.1%, with high specificity (88.3%) but lower sensitivity (41.2%).

Table 3 summarizes the logistic regression analysis evaluating the predictors of bone metastases.

Variable	OR (95% CI)	p-value	Interpretation
PSA > 20 ng/mL	1.811 (1.42–2.32)	<0.001	Higher PSA increases metastasis risk
Gleason Score ≥ 8	2.981 (2.05–4.02)	<0.001	Nearly triples metastasis likelihood

Age > 70	0.907 (0.78–1.12)	0.632	Not a significant predictor
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PSA levels > 20 ng/mL (OR = 1.811, 95% CI: 1.42–2.32, $p < 0.001$) were significantly associated with an increased risk of metastases, indicating that patients with elevated PSA levels are more likely to have positive scintigraphy results. Similarly, a Gleason score ≥ 8 (OR = 2.981, 95% CI: 2.05–4.02, $p < 0.001$) was a strong predictor, nearly tripling the likelihood of metastases. However, age > 70 (OR = 0.907, 95% CI: 0.78–1.12, $p = 0.632$) was not a statistically significant predictor, suggesting that age alone does not independently influence metastatic risk. These findings highlight the predictive value of PSA and Gleason score in assessing bone metastases risk

6.4 ROC Curve Analysis: A Receiver Operating Characteristic (ROC) curve analysis was conducted to assess the predictive accuracy of Serum PSA Levels and Gleason Scores in identifying bone metastases among prostate cancer patients.

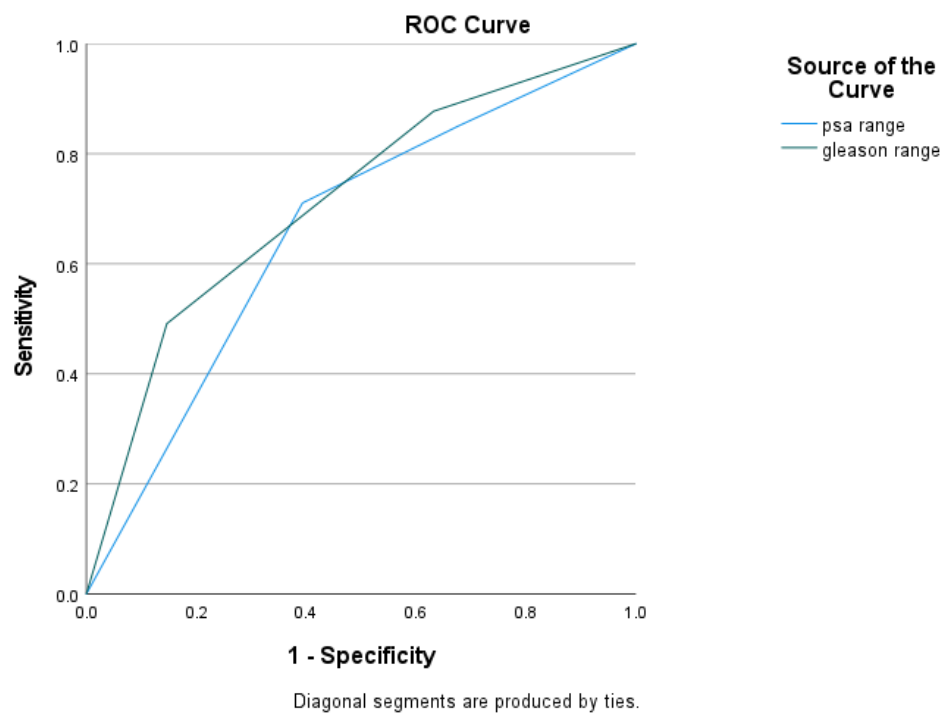


Figure 6 The AUC for PSA Levels was 0.724 (95% CI: 0.662 – 0.787, $p < 0.001$), indicating moderate to good discriminatory power, while the AUC for Gleason Score was 0.718 (95% CI: 0.661 – 0.775, $p < 0.001$), confirming its predictive value. These findings suggest that both PSA and Gleason Score serve as reliable indicators for assessing bone metastasis risk, reinforcing their role in guiding bone scintigraphy referrals. However, the presence of overlapping scores

between patients with and without metastases highlights the potential need for incorporating additional biomarkers or imaging techniques to enhance predictive accuracy.

7. Discussion

This study evaluated the clinical indicators influencing bone scintigraphy outcomes in 354 prostate cancer patients at CHU Bab El Oued, focusing on the predictive roles of PSA levels, Gleason scores, and age in detecting bone metastases. The findings confirm that higher PSA levels (>20 ng/mL) and Gleason scores (≥ 8) were significantly associated with positive bone scintigraphy results ($\chi^2 = 31.463$, $p < 0.001$, OR = 1.811 for PSA; $\chi^2 = 53.360$, $p < 0.001$, OR = 2.981 for Gleason Score). In contrast, age (>70 years) was not a significant independent predictor ($\chi^2 = 1.714$, $p = 0.424$; OR = 0.907, $p = 0.632$). The 32.2% metastasis rate observed in this study aligns with international findings and offers new insights into metastatic risk assessment within a North African population.

The strong association between PSA >20 ng/mL and bone metastases align with Lin et al. (2017), who found a markedly increased likelihood of metastases in patients exceeding this threshold (OR ≈ 1.9 , $p < 0.001$). The logistic regression model in this study (OR = 1.811, 95% CI: 1.42–2.32) corroborates Sissons et al. (1992), who identified PSA elevation as a reliable indicator for bone scintigraphy referrals with a diagnostic sensitivity of $\approx 80\%$. However, Uz Zaman et al. (2011) reported a higher prevalence (10–15%) of metastases in Pakistani patients with PSA ≤ 20 ng/mL, slightly exceeding the 17.9% (<10 ng/mL) and 27.5% (10–20 ng/mL) positivity rates observed in this study. This suggests potential regional or genetic variations, supporting the need for further investigations into PSA-based risk stratification.

Similarly, the significant association between Gleason score ≥ 8 and bone metastases (61.5% positivity rate) support Chorf (2015), who reported a nearly threefold increased risk of metastases in patients with Gleason 8–10 (OR ≈ 2.5). The slightly higher effect size in this study (OR = 2.981, 95% CI: 2.05–4.02) may reflect aggressive disease presentation or referral biases at CHU Bab El Oued, a tertiary oncology center. Abuzallouf et al. (2004) noted metastases in 5–10% of patients with Gleason <8 , aligning with the 13.7% (Gleason 6) and 27.5% (Gleason 7) positivity rates found here. Compared to Petersen et al. (2018), who reported Gleason scores explaining 20–25% of metastatic variance, the stronger correlation in this study suggests a higher metastatic burden

among Algerian patients, potentially due to delayed diagnosis as highlighted by Zoubida et al. (2011).

Conversely, age was not a significant predictor of bone metastases, contrasting with Godebu et al. (2014), who found older age associated with increased metastatic burden due to prolonged disease exposure. Instead, these results align with Koo et al. (2015), who reported age loses predictive value when PSA and Gleason scores are accounted for ($p > 0.05$). The mean age of 72.0 ± 7.48 years, with 59% of patients aged >70 , may have minimized age-related differences in this cohort, diluting its statistical significance. This challenges Rawla (2019), who emphasized age as a global risk factor for metastases, suggesting that tumor aggressiveness and PSA kinetics play a more central role than chronological age alone.

These findings strongly support risk-based imaging strategies in prostate cancer management. The results reinforce EAU and AUA guidelines (Mottet et al., 2017; Mohler et al., 2019), which recommend bone scintigraphy primarily for patients with PSA >20 ng/mL or Gleason ≥ 8 , thresholds this study robustly validates. The higher positivity rates observed in this study (71.1% for PSA >20 ng/mL and 61.5% for Gleason ≥ 8) emphasize the need for timely imaging referrals in high-risk patients, fulfilling the study's objective to optimize diagnostic efficiency.

From a resource allocation perspective, these results support reducing unnecessary scintigraphy in low-risk patients (PSA <10 ng/mL, Gleason ≤ 6), where metastatic yield was minimal (17.9% and 13.7%, respectively), aligning with Lin et al. (2017). Meanwhile, ensuring early detection in high-risk cases (PSA >20 ng/mL, Gleason ≥ 8) is crucial to prevent missed metastases and delayed treatment. This contrasts with Williams (2023), who advocated for symptom-based imaging referrals, suggesting instead that PSA/Gleason-driven stratification may be more effective, particularly in Algeria, where asymptomatic metastases are frequently undetected.

7.1 Strength, Limitations and Future Research Directions

This study provides significant insights into the clinical indicators influencing bone scintigraphy outcomes in prostate cancer patients at CHU Bab El Oued, Algiers, Algeria. As one of the few investigations focusing on this specific context, it contributes valuable evidence to North African prostate cancer research, addressing a critical gap in localized data, particularly given the disease's rising incidence (3,514 new cases in 2022; GLOBOCAN, WHO, 2022). By evaluating key

predictors such as PSA levels and Gleason scores, this study offers a foundation for optimizing diagnostic practices in Algeria's resource-constrained healthcare setting.

A key strength is the robust sample size ($n = 354$), which enhances statistical reliability and allows for strong associations to be identified, such as PSA levels >20 ng/mL and Gleason scores ≥ 8 being significantly linked to bone metastases ($\chi^2 = 31.463$, $p < 0.001$; $\chi^2 = 53.360$, $p < 0.001$). The study employs rigorous statistical analyses, including chi-square tests, logistic regression (OR = 1.811 for PSA >20 ng/mL; OR = 2.981 for Gleason ≥ 8), and ROC curve analysis (AUC = 0.724 for PSA, 0.718 for Gleason Score), reinforcing its methodological credibility. These findings align with international guidelines from the European Association of Urology (EAU) and the American Urological Association (AUA), which recommend bone scintigraphy for high-risk patients (Mottet et al., 2017; Mohler et al., 2019), further supporting their clinical applicability in diverse populations. Additionally, by identifying key predictors of bone metastases (32.2% prevalence), the study provides practical evidence to optimize bone scintigraphy referrals, addressing the inconsistent application of imaging in prostate cancer management and enhancing resource allocation in Algeria's healthcare system.

Despite these strengths, several limitations must be considered. The retrospective design, relying on existing patient records, may introduce selection bias, potentially overestimating the prevalence of metastases (32.2%) by excluding low-risk patients who were not referred for bone scintigraphy. Additionally, conducting the study in a single tertiary care center (CHU Bab El Oued) limits generalizability to other healthcare settings, including primary care and rural populations, where diagnostic practices may differ. Although PSA and Gleason Score demonstrated strong predictive value (AUC = 0.724 and 0.718, respectively), their moderate discrimination suggests the need for additional predictive markers. The logistic regression model's explanatory power (Nagelkerke $R^2 = 0.240$) further indicates that unexamined clinical factors—such as tumor stage, symptomatology (e.g., bone pain), and treatment history—could enhance risk prediction but were not included in this analysis.

To enhance the clinical relevance and expand upon these findings, future research should: Expand the study across multiple centers in Algeria and North Africa to improve external validity and generalizability beyond a single tertiary institution.

Include additional biomarkers such as Alkaline Phosphatase (ALP) and Lactate Dehydrogenase (LDH), which have shown promise in predicting bone metastases (Koo et al., 2015), and explore the role of advanced imaging techniques like PSMA PET/CT, which has demonstrated superior accuracy ($AUC \approx 0.85$; Turpin et al., 2020).

Integrate tumor stage, symptom presentation, and prior treatment history to develop a more comprehensive predictive model, addressing the moderate R^2 and potential unexamined confounders.

Adopt a prospective study design to minimize selection bias and provide a clearer temporal understanding of how PSA, Gleason score, and other factors predict bone metastases over time.

By building upon the strengths of this study while addressing its limitations, future research can refine risk stratification models, improve staging accuracy, optimize imaging referrals, and contribute to evidence-based diagnostic protocols, ultimately enhancing prostate cancer management in Algeria and beyond.

8. Conclusion

This study, conducted at CHU Bab El Oued, Algiers, Algeria, confirms that PSA levels and Gleason scores are strong, independent predictors of bone metastases in prostate cancer patients, reinforcing their critical role in guiding bone scintigraphy referrals. Among the 354 patients analyzed, those with PSA levels >20 ng/mL and Gleason scores ≥ 8 exhibited significantly higher metastasis rates (71.1% and 61.5%, respectively;), supporting the use of these markers for risk-based imaging strategies. In contrast, age was not a significant predictor ($p = 0.632$), suggesting that tumor characteristics outweigh chronological age in metastatic risk assessment.

These findings align with international guidelines from the European Association of Urology (EAU) and American Urological Association (AUA), which recommend bone scintigraphy for PSA >20 ng/mL or Gleason scores ≥ 8 (Mottet et al., 2017; Mohler et al., 2019). The 32.2% metastasis prevalence observed in this study exceeds rates reported in Western cohorts (20–25%; Briganti, 2012), indicating potential delayed diagnosis or underutilization of early screening programs in Algeria. Given that prostate cancer is the third most common malignancy in Algerian men (3,514 new cases in 2022; GLOBOCAN, WHO, 2022), these results highlight the need for selective imaging referrals to optimize resource allocation and improve early detection in this resource-constrained healthcare setting. By prioritizing high-risk patients for bone scintigraphy, this study provides practical evidence to enhance diagnostic efficiency and improve prostate cancer management in Algeria.

8.1 Recommendations

Based on these findings, the following recommendations are proposed to refine diagnostic protocols and enhance prostate cancer care at CHU Bab El Oued and beyond:

1. Selective Imaging Protocols Implement targeted bone scintigraphy referrals for PSA levels >20 ng/mL and Gleason scores ≥ 8 , reducing unnecessary imaging in low-risk patients (PSA <10 ng/mL, Gleason ≤ 6 ; 17.9% and 13.7% metastasis rates).

Ensure timely detection of metastases in high-risk cases, optimizing resource utilization in Algeria's healthcare system.

2. Prospective Validation of Findings Conduct prospective studies at CHU Bab El Oued to validate these predictive markers, reducing retrospective bias and clarifying temporal relationships between clinical indicators and metastasis risk.

3. **Expansion of Biomarker Panels** Integrate additional biomarkers, such as Alkaline Phosphatase (ALP) and Lactate Dehydrogenase (LDH), to improve predictive accuracy beyond PSA and Gleason Score (AUC = 0.724 and 0.718, respectively; Section 6.4) as suggested by Koo et al. (2015).
4. **Integration of Advanced Imaging Modalities** Explore multimodal imaging techniques such as PSMA PET/CT, which has superior diagnostic accuracy (AUC $\approx$ 0.85; Turpin et al., 2020), to enhance metastasis detection in high-risk patients.
5. **Development of National Guidelines for Prostate Cancer Management** Use these findings to contribute to the development of standardized diagnostic guidelines for prostate cancer in Algeria, addressing the current variability in clinical practice (Section 1.1) and aligning local protocols with international best practices.

By implementing these recommendations, Algeria's healthcare system can refine diagnostic strategies, improve staging accuracy, and enhance early detection of metastatic prostate cancer, ultimately leading to better patient outcomes and more efficient resource allocation.

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10. Annex

Annex 1: Data Collection Form

Study Title: Assessment of Bone Scintigraphy Results and Its Clinical Indications and Determinants in Prostate Cancer Patients at CHU Bab El Oued, Algiers, Algeria

Study ID: _____

Date of Data Collection: _____

Section 1: Patient Demographics

	Response
Patient ID	_____
Age (years)	_____
Date of Bone Scintigraphy	_____

Section 2: Clinical Information

	Response
Indication for Bone Scintigraphy	☐ Routine Staging
	☐ Suspected Metastasis
	☐ Follow-up
	☐ Other: _____
Serum PSA Level (ng/mL)	_____ _____
Gleason Score	_____ _____
Stage of Prostate Cancer	☐ Stage I
	☐ Stage II
	☐ Stage III
	☐ Stage IV

Section 3: Bone Scintigraphy Results

	Response
Scintigraphy Result	☐ Positive for Metastasis ☐ Negative for Metastasis

Section 4: Additional Clinical Information

	Response
History of Previous Bone Scintigraphy	☐ Yes ☐ No

Section 5: Treatment Information

	Response
Primary Treatment Initiated	☐ Surgery ☐ Radiotherapy ☐ Hormonal Therapy ☐ Chemotherapy ☐ Watchful Waiting ☐ Other: _____
Date of Primary Treatment	_____
Response to Treatment (if known)	☐ Complete Response ☐ Partial Response ☐ No Response ☐ Progressive Disease

Notes Section

Additional Observations:

The study will analyze the relationship between these variables to determine key clinical factors that influence the use of bone scintigraphy and the presence of bone metastasis in prostate cancer patients. Due to the limitations of the available data, certain variables such as family history, comorbidities, and lifestyle factors will not be collected.

Approved by the Examining Board

This thesis by Dr. Faiz Kubes is accepted in its present form by the board of examiners satisfying the thesis requirement for the Specialty Certificate in Clinical Nuclear Medicine.

Title of project: Assessment of Bone Scintigraphy Results and Its Clinical Indications and Determinants in Prostate Cancer Patients at CHU Bab El Oued, Algiers, Algeria

Examiner 1 Name _____ Signature _____ Date _____

Examiner 2 Name _____ Signature _____ Date _____

Advisor Name _____ Signature _____ Date _____

Advisor Name _____ Signature _____ Date _____