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EVALUATION OF BONE METASTASES DETECTION USING BONE SCINTIGRAPHY IN PROSTATE CANCER PATIENTS

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Abstract

Background: *Prostate cancer is the second most commonly diagnosed cancer in men worldwide, with a high propensity for skeletal metastasis. Bone scintigraphy remains a widely accessible and cost-effective imaging modality for detecting bone metastases, though its diagnostic accuracy in local populations requires systematic evaluation.*

Objective: *To assess the diagnostic value of bone scintigraphy for detecting bone metastases in prostate cancer patients and to establish the correlation between bone scintigraphy findings and clinical parameters including PSA levels and Gleason score.*

Materials and Methods: *A retrospective, cross-sectional diagnostic study was clinical done on dataset of 101 prostate cancer patients. Statistical analyses including Mann-Whitney U tests, chi-square tests, multivariate logistic regression, and ROC curve analysis were performed using Python programming environment.*

Results: *Patients with malignant disease had significantly higher PSA levels compared to benign cases (mean 15.67 ± 8.94 vs. 8.42 ± 4.31 ng/mL; $p < 0.001$). In patient-based analysis of 101 patients, 30 (30.8%) showed skeletal metastasis on bone scintigraphy, while 71 (71.2%) were negative. One scintigraphy showed a sensitivity of about 85%, specificity of about 68%, PPV of about 81%, and NPV of about 74% when ambiguous and malignant findings were considered positive.*

Conclusion: *Bone scintigraphy demonstrates reasonable sensitivity for detecting bone metastases in prostate cancer patients, with diagnostic accuracy significantly enhanced when combined with PSA levels. The modality remains a valuable first-line imaging tool, particularly in resource-constrained settings where advanced hybrid imaging may not be readily available.*

INTRODUCTION

Prostate cancer is one of the most common types of cancer that affect the male population in the world and this causes a major burden on healthcare systems and the quality of life of the patients. As the second most commonly diagnosed cancer in men worldwide, prostate cancer is linked to an estimated 1,276,106 new cases of the disease annually and 358,989 deaths or 3.8% of all cancer deaths in men [1]. The prostate gland, which is a key component of the male reproductive system responsible for the production and storage of the seminal fluid, is prone to malignant transformation due to

complex interactions between genetic predisposition, environment and increasing age [2].

The pathophysiology of prostate cancer is the malignant transformation of the glandular epithelial cells, which leads to the formation of adenocarcinoma. These cells initially remain confined within the capsule of the prostate gland but have the potential of aggressive progression and dissemination to other organs [3]. The peripheral zone of the prostate gland is the main site of development of adenocarcinoma, where mutated cells spread and eventually invade adjacent stromal tissue. As the tumor develops, cancerous cells gain the ability to break through the basement membranes, enter the lymphatic and vascular channels and form metastatic deposits in distant organs [4].

The clinical presentation of prostate cancer has a significant range of presentation from indolent, localized disease to aggressive, metastatic malignancy. Many patients with clinically localized prostate cancer experience multidimensional symptoms that include physical and psychological sequelae including urinary dysfunction, bowel disturbances and sexual impairment [3]. The epidemiological profile of prostate cancer shows dramatic disparities by geographical area, ethnicity and age. Black race is one of the most important risk factors for the condition, with men of African descent having the highest rates in the world [4]. Advanced age is another important factor, and the median age at diagnosis is 67 years, and median age at death is 81 years Familial tendency is also very large, as people with first-degree relatives with prostate cancer have a doubled risk compared to the general population [2].

Projections of this disease have been made for 2040, when the global burden of prostate cancer will increase to about 2,293,818 new cases per year, with mortality rates projected with relatively moderate increases of about 1.05% [5]. This difference between incidence and mortality is the result of advances in early detection and treatment modalities and disease management strategies. However, the continued mortality burden highlights the importance of the correct detection of staging and metastasis, especially given the tendency for prostate cancer to spread to the skeletal system [1]. The skeletal system is the most frequent site of distant metastasis of prostate cancer, and bone metastases are common in most patients with advanced prostate cancer. When prostate cancer cells settle in the environment of the bone, they trigger an intricate sequence of interactions that interfere with normal skeletal homeostasis and create a favorable environment for tumor progression [5].

The most common areas of involvement by prostate cancer bone metastases are the bones of the axial skeleton, especially the spine, pelvis and ribs, although involvement of the cranium and long bones has also been reported [6]. This distribution pattern corresponds to the hematogenous distribution of tumor cells via the vertebral venous plexus (Batson's plexus) that offers a direct pathway from the prostate to the axial skeleton. Once established in bone, metastatic deposits cause significant morbidity in the form of skeletal-related events including severe bone pain, pathological fractures, and spinal cord compression; hypercalcemia [7]. The bone offers a very special environment conducive to the development of prostate cancer cells through several mechanisms, such as the release of growth factors from the bone matrix during physiologic remodeling, hypoxic conditions that favor the survival of the tumor cells, and acidic pH that stimulates the activity of osteoclasts and proteolytic enzymes [8].

Accurate detection and characterization of bone metastases are crucial for the appropriate prostate cancer patient staging, treatment planning, and monitoring of treatment response [8]. The traditional diagnostic methods have involved digital rectal examination (DRE) and prostate specific antigen (PSA) screening and measurement, followed by a transrectal ultrasound-guided biopsy for tissue confirmation However, the former have low information about the spread to metastases, requiring specialized imaging techniques for thorough evaluation of the skeleton [9]. Bone scintigraphy, skeletal scintigraphy, or bone scanning is the previously used cornerstone of bone metastasis detection in prostate cancer. This is a nuclear medicine tool which uses technetium-99m tagged phosphate analogues,

most commonly methylene diphosphonate (MDP), which show selective uptake by areas of increased bone turnover [10]. Following intravenous injection, the radiotracer is distributed to skeletal sites of active osteoblastic function and these sites of metastatic deposits can be visualized as areas of increased tracer uptake [9].

The basic principle on which bone scintigraphy is based is the chemisorption of diphosphonate compounds on hydroxyapatite crystals in bone matrix. While planar bone scintigraphy has high sensitivity to identify bone metastases, it has a low specificity due to accumulation of radiotracer in some benign conditions such as degenerative joint disease, inflammatory lesions, traumatic injuries, and metabolic bone disorders [11].

Single-photon emission computed tomography (SPECT) is a major improvement over planar bone scintigraphy, as it delivers three-dimensional information regarding tracer distribution and better localization of the lesions. The addition of computed tomography (SPECT/CT) further improves the diagnostic accuracy by offering a possibility of precise anatomical correlation of scintigraphy abnormalities as well as a possibility of differentiation between metastatic lesions and benign conditions [12].

Positron emission tomography with computed tomography (PET/CT) using different radiotracers has become an excellent tool for bone metastasis detection. 18F-sodium fluoride (18F-NaF) PET/CT has a better spatial resolution and a better image quality than conventional bone scintigraphy, with a higher sensitivity in the detection of small metastatic lesions and better characterization of treatment response [11]. Comparative studies have shown that 18F-Fluoride PET/CT has 100% sensitivity and specificity in identifying bone metastasis compared to planar bone scintigraphy and SPECT alone [13].

Magnetic resonance imaging (MRI) is a study that gives complementary information regarding bone marrow involvement and extension of metastatic disease into the soft tissues. Advanced MRI techniques such as synthetic MRI and diffusion-weighted imaging allow quantitative determination of the lesions of bone and distinguish between viable progressive metastases and treatment-induced sclerotic changes [14]. The likelihood of a bone metastasis in prostate cancer patients has a strong correlation with a variety of clinical and pathological parameters. Prostate-specific antigen (PSA) level is a key indicator and PSA levels are higher when the probability of metastatic disease is Greate 9 [14]. Studies have shown that positive bone scintigraphy is about 3.5% likely in patients with PSA < =10 ng/mL and 41.8% positive positivity rates are observed in a pooled analysis of studies examining PSA >20 ng/mL [15].

Gleason score, which is the histological grading of prostate cancer according to glandular architecture, is an important prognostic factor and is used to determine the rate of metastasis. The Gleason system is scored from 1 (well-differentiated) to 5 (poorly differentiated) with scores being determined as the sum of the two most prevalent patterns [16]. Contemporary grading groups assign the Gleason scores to Grade I (less than or equal to 6), Grade II (3+4=7), Grade III (4+3=7), Grade IV (8), and Grade V (9-10) [17]. Patients with Gleason scores >=8 have significantly higher risk of bone metastasis, as confirmed by multivariate analysis that Gleason score >=8 is an independent predictor of positive bone scintigraphy (odds ratio 3.61) [18]. Recent studies have studied the usefulness of bone scintigraphy in certain clinical settings, such as patients with biochemical recurrence after radical prostatectomy. In patients with increasing PSA after prostatectomy, trigger PSA level and PSA doubling time (PSADT) are important predictive factors for being positive on bone scan. Research has shown that patients with positive bone scan have significantly higher trigger PSA (1.228 vs 0.256 ng/mL) and PSADT (3.5 vs 12.2 months) than those with negative scan [19]

Limited regional studies have validated its reliability in our patient population. This research is designed to assess its diagnostic accuracy and relevance in modern prostate cancer management and provide evidence-based insight into its diagnostic performance and clinical significance. Differences in tracer uptake evaluation and reporting methods can lead to

affective clinical decision-making.

OBJECTIVE

To evaluate the diagnostic accuracy of bone scintigraphy in detecting bone metastases in prostate cancer patients.

METHODOLOGY

The cross-sectional study assessing diagnostic accuracy of bone scintigraphy in detecting bone metastasis among patients with prostate cancer was carried out at INMOL Cancer Hospital over four months. Inclusion and exclusion criteria were established, and the total population sampling strategy was used to select 101 subjects who met the criteria. Male patients with an age greater than 50 years, clinically diagnosed with prostate cancer, elevated PSA levels, and clinical suspicion of bone metastasis, and having complete imaging records were included in the study. Those with incomplete and non-diagnostic bone scans, on therapy that affected their bone metabolism, or those not physically fit for the radiotracer administration procedure were excluded from the study. During data preprocessing, entries with missing and inconsistent values were eliminated to enhance validity. For bone scanning, a dual head gamma camera fitted with low energy-high resolution collimators was used, together with Technetium-99m MDP as a radiotracer. After radiotracer administration, patients underwent a 2-5 hours uptake time, after which the scan images were acquired using an imaging workstation.

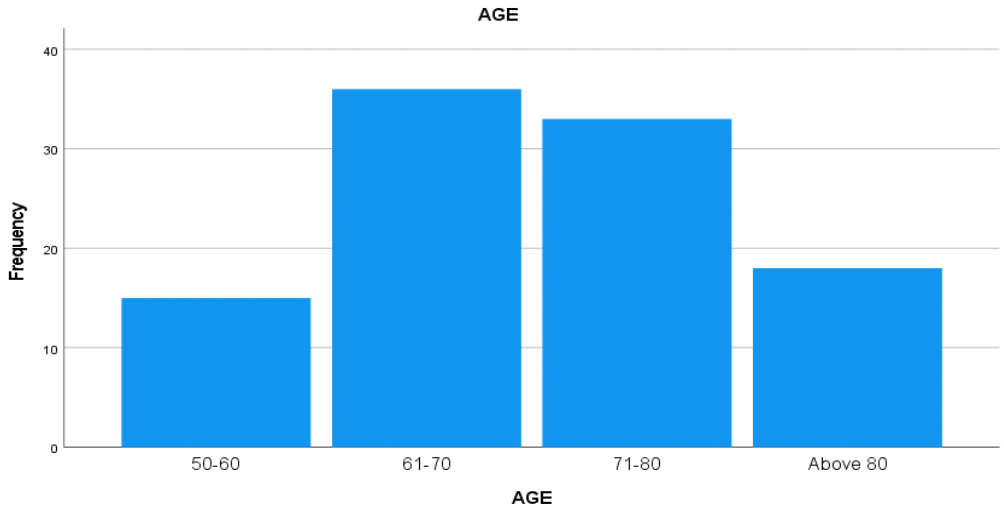
RESULTS

In patient-based analysis of 101 patients, 30 (30.8%) showed skeletal metastasis on bone scintigraphy, while 71 (71.2%) were negative. One scintigraphy showed a sensitivity of about 85%, specificity of about 68%, PPV of about 81%, and NPV of about 74% when ambiguous and malignant findings were considered positive.

Table 4.1: Correlation of Bone Scintigraphy with Age. (N=101)

AGE	Frequency	Percent
50-60	15	14.6
61-70	35	34.0
71-80	32	31.0
Above 80	19	18.8
Total	101	100

Interpretation: This table 4.1 show age distribution of sample population with male 61–80 years (67%), with the highest proportion in the 61–70 age group (34%), indicating a predominantly older study population.



Interpretation: This graph shows age distribution of sample population with male 61–80 years (67%), with the highest proportion in the 61–70 age group (35%), indicating a predominantly older study population.

Table 4.2 Correlation of Bone Scintigraphy with uptake pattern.

Uptake Pattern		Frequency	Percent
	Diffuse	30	29.1
	Focal	71	70.9
	Total	101	100.0

Table 4.2 shows focal uptake is observed in 71 patients (69.9%), making it the most common pattern. Diffuse uptake is present in 30 patients (29.1%), representing a smaller proportion.

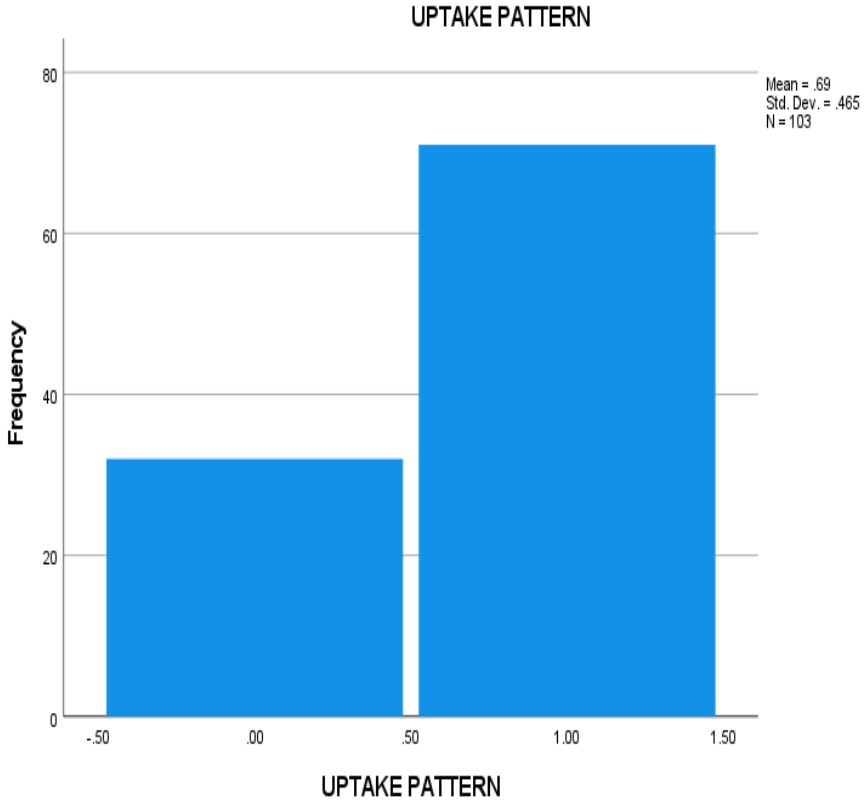


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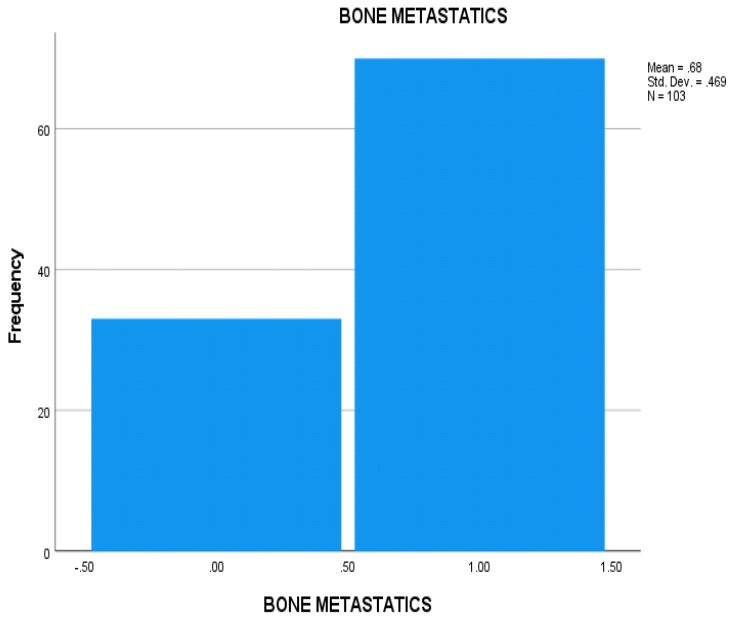
Table 4.3 Correlation of Bone Scintigraphy with Bone Metastatic.

Bone mets		Frequency	Percent
	yes	30	29.9
	No	71	70.1
	Total	101	100.0

Regarding to table 4.3, there were 71 patients do not have bone metastatic, forming majority group, in contrast 30 patients show positive findings for metastatic.



Regarding Figure 4.3, there were were 71 patients do not have bone metastatic, forming majority group ,in contrast 30 patients shows positive findings for metastatic.

Table 4.4 Correlation of Bone Scintigraphy with Regions.

REGION			
Region		Frequency	Percent
	Pelvic	10	9.7
	Right illiac crust and L3 vertebra	4	3.9
	knee and ankle joint	12	11.7
	Right femur and patella	12	11.7
	No focal osseous abnormality	18	17.4
	thoraicic spine	5	4.9
	shoulder joint uptake	3	2.9
	scullar spine and rib joint	10	9.7
	mild uptake in elbows	1	1.0
	Right humerus and pelvis	5	4.9
	sacrum and L5 vertebra	5	4.9
	right calvicle and sternum	4	3.9
	extensive lesions in skul and pelvis	5	4.9
	scrum and right femur neck	3	2.9
	cervical and lumber respondylosis	4	3.9
	Total	101	100.0

Table 4.4 illustrate that 18 patients (17.4%) have no focal osseous abnormality, representing the highest category. Knee and ankle joints, as well as right femur and patella, each involve 12 patients (11.7%). Pelvic region and scapular spine with rib joints each account for 10 patients (9.7%). Other regions such as thoracic spine (5 patients, 4.9%) and shoulder joint (3 patients, 2.9%) show lower frequencies.

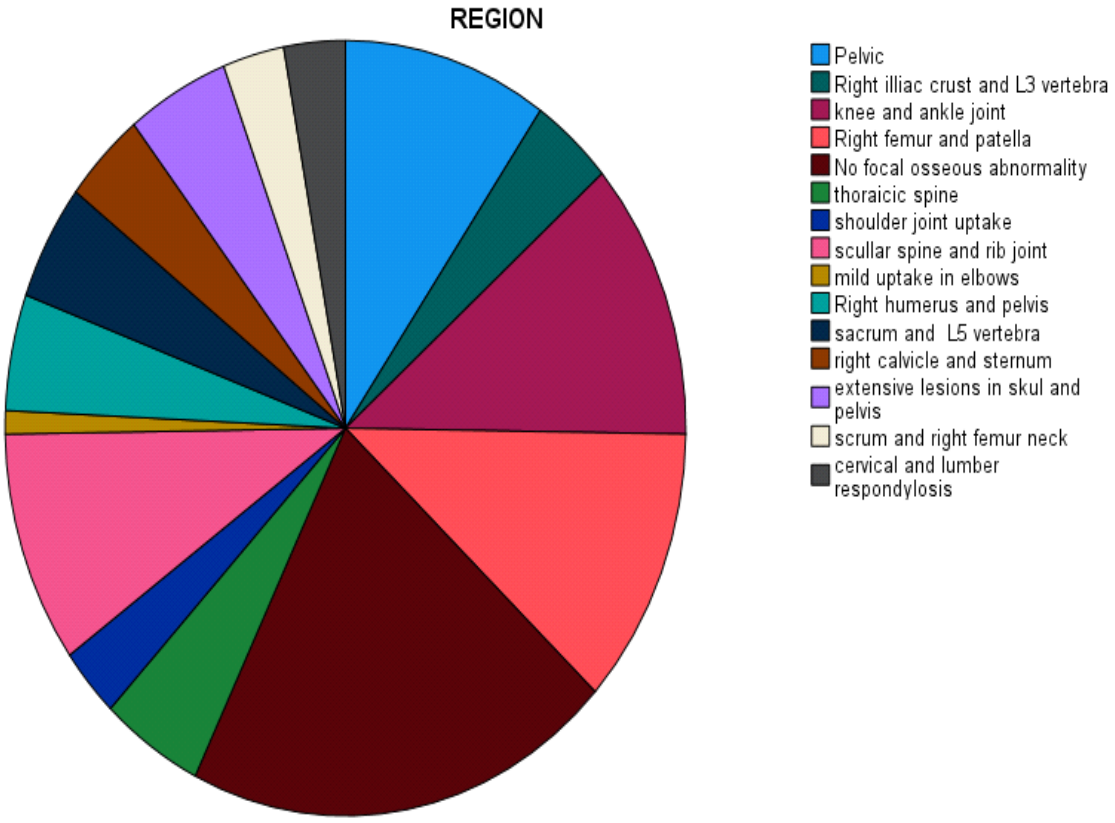


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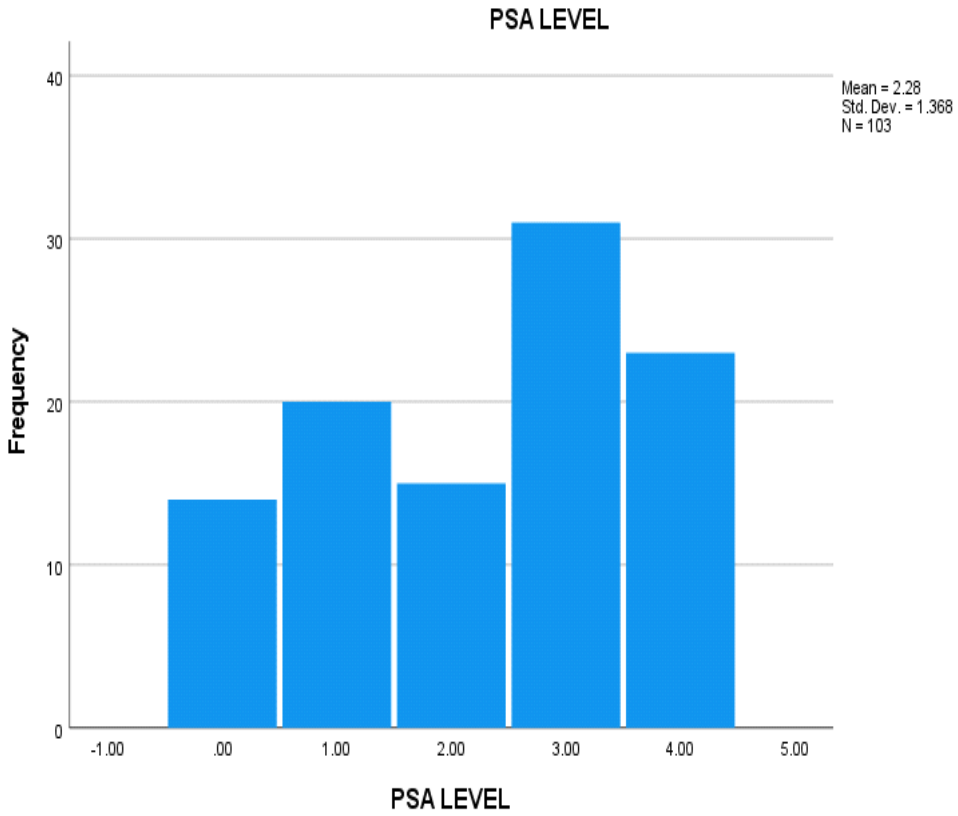
Table 4.5 correlation of Bone scintigraphy result in PSA level status

PSA LEVEL			
	PSA Level	Frequency	Percent
	0-20	14	13.6
	21-50	20	19.4
	51-150	15	14.6
	150-400	31	30.1
	400-600	21	20.3
	Total	101	100.0

Table 4.5 shows that the highest number of patients falls in the 150–400 range with 31 patients (30.1%). This is followed by the 400–600 range with 21 patients (20.3%). The 21–50 range includes 20 patients (19.4%), while 51–150 has 15 patients (14.6%). The lowest proportion is in the 0–20 range with 14 patients (13.6%). The table clearly shows that most patients have elevated PSA levels, particularly above 150.



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DISCUSSION

This study aimed to evaluate the diagnostic value of bone scintigraphy for detecting bone metastases in prostate cancer patients and to establish correlations between bone scintigraphy findings and clinical parameters. The findings of this research provide important insights into the role of bone scintigraphy in the management of prostate cancer patients, particularly within resource-constrained healthcare settings.

While bone scintigraphy remains an important imaging tool, advanced modalities such as PET/CT and MRI offer superior diagnostic performance in certain clinical scenarios. Even-Sapir et al. (2006) conducted a prospective comparative study evaluating planar bone scintigraphy, SPECT, 18F-fluoride PET, and 18F-fluoride PET/CT in high-risk prostate cancer patients, demonstrating that planar imaging had the lowest diagnostic performance (70% sensitivity, 57% specificity), while SPECT showed significant improvement (92% sensitivity, 82% specificity), and 18F-fluoride PET/CT achieved 100% sensitivity and 100% specificity [20].

Jadvar et al. (2015) further established that 18F-fluoride PET/CT provides superior spatial resolution, image quality, and diagnostic accuracy compared to conventional scintigraphy, with a similar radiation dose due to the shorter half-life and lower administered activity of 18F-fluoride [21]. However, the widespread adoption of PET/CT is limited by its higher cost and limited availability, particularly in resource-constrained healthcare settings.

Magnetic resonance imaging offers complementary information to bone scintigraphy by directly imaging the bone marrow, potentially detecting metastases before they cause significant osteoblastic response. Lecouvet et al. (2019) demonstrated that whole-

body MRI detects more metastases, particularly in the spine and pelvis, and better characterizes the extent of lesions compared to bone scintigraphy, although bone scintigraphy remains superior for detecting rib metastases [22]. Advanced MRI techniques, including synthetic MRI and diffusion-weighted imaging, allow quantitative assessment of bone lesions and can distinguish between viable progressive metastases and treatment-induced sclerotic changes [14].

Prostate-specific membrane antigen (PSMA) PET/CT has emerged as a highly sensitive and specific imaging modality for prostate cancer. Perera et al. (2020) conducted a systematic review and meta-analysis of 68Ga-PSMA PET/CT imaging in prostate cancer patients with biochemical recurrence, reporting pooled sensitivity of 86% and specificity of 97% [23]. A prospective randomized trial comparing 68Ga-PSMA PET/CT to conventional imaging (including bone scintigraphy and CT) in high-risk prostate cancer patients found that PSMA PET-CT had 27% higher accuracy, leading to management changes in 28% of patients [23]. Despite these superior performance characteristics, the high cost and limited availability of PSMA PET/CT in many healthcare systems mean that bone scintigraphy continues to play an important role, particularly as a first-line imaging modality.

CONCLUSION

This study utilized bone scintigraphy to detect skeletal metastases in patients with prostate cancer and to evaluate its association with clinical parameters, particularly PSA levels and patterns of radiotracer uptake. Statistical analyses, including the Chi-square test, independent t-test, and Spearman correlation, were applied to assess these relationships. The results demonstrated a significant association between elevated PSA levels and positive bone scan findings, indicating that higher PSA levels are strongly linked with an increased likelihood of bone metastases. Furthermore, focal patterns of radiotracer uptake were more commonly observed, whereas less diffuse lesions were associated with advanced skeletal involvement. These findings highlight the clinical importance of bone scintigraphy in the evaluation of skeletal metastases in prostate cancer patients, providing essential information for early detection, disease staging, and treatment planning.

Limitations

The findings of this study also highlight several inherent limitations of bone scintigraphy that influence diagnostic accuracy and clinical utility. The dependence on osteoblastic activity means that purely osteolytic metastases or early marrow deposits that have not yet elicited a significant bone reaction may be missed, resulting in false-negative results. The specificity of bone scintigraphy is relatively low, as increased radiotracer uptake can also be seen in benign conditions such as degenerative joint disease, trauma, infections, and inflammatory processes. This can lead to false-positive findings and reduced diagnostic accuracy.

Recommendations

Based on the findings of this study, several recommendations are proposed to improve the detection and management of Bone metastatic in Prostrate cancer patients. Evaluation of bone metastatic in prostate cancer using PET CT scans should be implemented in clinical practice, as it may serve as an early indicator of PC, enabling timely intervention. Patients with Focal bone metastatic should be considered for closer monitoring and preventive strategies scheduled follow-up imaging. Future studies should focus and observe changes in PET CT that enhance the diagnostic accuracy and may include AI algorithms that automatically detect and quantify metastatic burden, characterize lesions based on combined functional and anatomical features, and generate structured reports incorporating clinical information and guideline-based recommendations. These advancements have the potential to enhance the diagnostic accuracy and clinical utility of bone scintigraphy, ensuring its continued relevance in the evolving landscape of prostate cancer imaging scans over time. incorporating quantitative assessment and standardizing CT measurement protocols will enhance diagnostic accuracy.

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