Bone Scintigraphy Metastatic Patterns in Patient with Prostate Cancer at Ocean Road Cancer Institute

Iramu RS*, Makungu HM and Lulu LS

ABSTRACT

Objectives: Prostate cancer is the second most common malignancy in the world next to lung cancer and it is the leading cause of morbidity and mortality among men. The most common metastatic site in prostate cancer is the bone. This study is aiming at finding the pattern and frequency of bone metastasis among prostate cancer patients at Ocean Road Cancer Institute, Tanzania.

Methods: This was a cross section retrospective hospital based descriptive study involving 139 patients with prostate cancer who were seen from June 2014 to June 2016 whose bone scan were reviewed.

Results: Bone metastases were found in 77 patients (55.4%) The prevalence was higher in the age group between 60 and 79 (56.3%) however there was no statistical significance between age and occurrence of bone metastasis. Patient who had high PSA level and Gleason score had more occurrence of skeletal metastasis.

Spine was the most common site for bone metastasis constituting 72 patients (51.8%) of all the patients followed by ribs metastasis (31.7%). Also it was shown that of the spine metastasis, lumbar spine was more frequent affected (48.2%) followed by thoracic and cervical spine (41.0% and 27.3% respectively)

Conclusion: The prevalence of skeletal metastasis in patients with Prostate cancer at Ocean Road Cancer Institute was high (55.4%). The prevalence was higher in patients with PSA level more than 20 and those with Gleason score of more than 7. Spine was the commonest site for metastasis and of the spine, metastasis lumbar spine metastasis was most frequent site.

Recommendations: It is recommended that bone scan should be done as baseline in patients with prostate cancer particularly those with PSA level more than 20ng/ml and Gleason score of more than seven.

Keywords
Prostate cancer, Prostate specific antigen, Gleason score, Skeletal metastasis.

Introduction
Prostate cancer is the fourth most common cancer worldwide among all sexes combined and the second most common malignancy among men [1]. In the US, it is the commonest non cutaneous malignancy among men and the second most common cause of cancer related morbidity and mortality among men in the western hemisphere [2]. The incidence of the prostate cancer varies considerably among different groups with highest incidences in Australia and lowest among south central Asia.

In Africa, limited data are available regarding prostate cancer, though the condition appears more prevalent among developed
countries when compared to less developed countries with the exception of South Africa, which was reported to have incidence of 61.8% [1]. In Tanzania, the prevalence of prostate cancer is 9.6% among all cancers and is ranked third among all cancers in prevalence [3]. Death related to prostate cancer is higher among less developed countries as compared to developed countries due to effective screening programs in the developed countries [1].

The most common site for metastases in prostate cancer is the bone with skeletal metastases detected in up to 90% of patients dying from the disease and 22% of the newly diagnosed patients [4,5].

Prostate specific antigen is an established prognostic marker that as shown correlation with bone scans positivity. A low risk of bone metastasis in bone scintigraphy is related to the low levels of PSA [6,7].

Gleason score system was developed to assess the level of differentiation of the prostate based on five pattern of cellular differentiation [8]. It is of prognostic importance and is an independent predictor of bone scan results [7,9-11].

In cancer of the prostate, the most frequent site for skeletal metastases is the spine and pelvis [12]. According to the study by Memon AG et al., the most frequently involved areas were thoracic spine 32%, shoulder joint 28% and sacroiliac joint 21%. The other areas involve were skull 16%, sacrum 15%, lumbar vertebra 14% and ilium 13%. Other sites included the mandible, femur, Sternum, cervical spine, iliac crest, scapula, hip joint and tibia [13].

Severe pain, pathological fracture, symptomatic hypercalcemia and cord compression are among the commonest complications associated with skeletal metastasis among prostate cancer patients with 50% of those having bone metastases dying within 30 to 35 months [4,5].

Bone scintigraphy is the most frequently used acceptable and standard method for detecting bone metastases with reported sensitivity of up to 95% in patients with PSA value of more than 20ng/ml [13,14]. Sensitivity of 72 to 77% was reported for planar bone scan in detection of bone metastases in adults and currently is the investigation of choice [15,16]. The high sensitivity of radionuclide bone scan in determining the presence and extent of metastatic disease makes it an extremely important tool in decision making, particularly because survival rate in patients with multiple distant osseous metastases from many tumors are worse than for those patients with localized disease [17]. Classically, these positive scans demonstrate markedly increased radiotracer uptake [18].

Bone metastases are present in up to 14% of patients at presentation and in 80 to 85 % of those who die of the disease and they therefore affect morbidity, reflect prognosis and significantly influence decision with regard to patient management [6,7,19]. The sensitivity of bone scan is higher than that of radiography [14].

Methodology
This study was a descriptive cross sectional retrospective hospital based study conducted at Ocean Road Cancer Institute (ORCI), Dar es salaam, Tanzania for six months on which data of patients who were seen from June 2014 to June 2016 were reviewed. The study included all histological confirmed prostate cancer patient referred to the nuclear medicine department of ORCI for bone scintigraphy during the study period.

Convenience sampling was used. Files of the patients were collected on the medical record, screened, those who had histological confirmed Prostate cancer were selected, and further evaluation was done to see PSA and Gleason score results. Then, their bone scans were reevaluated. Bone scan results were recorded as positive or negative for the presence of metastases in a structured questionnaire.

Data collection was done retrospectively through data collection tool which was filled by investigator and image evaluated. Data collected (Secondary data) included age, prostate specific antigen, Gleason score and absence or presence of bone metastasis.

Whole body scanning was performed 3 h after injection of 700MBq 99mTc methyl diphosphonate using a matrix size of 256×1024 at a scan speed of 15 cm min⁻¹ and an energy window of 20 % at 140 keV using a dual head Mediso Any Scan system. Images were processed and then displayed in anterior and posterior view for analysis. Reporting of bone scans was performed by the investigator under the supervision of a specialist radionuclide radiologist at the hospital so as to reduce observation bias and ensure quality.

Bone scan results were recorded as positive, equivocal or negative for the presence of metastases. In equivocal cases, a specialist nuclear medicine physician reviewed the initial bone scan. Any outstanding indeterminate cases were treated as equivocal. Standard criteria will be used in defining the abnormalities.

All bone scan images obtained were stored in a system memory and DVD’s. The reports were read by the investigator under the supervision of the specialist radionuclide radiologist so as to reduce bias in observations and ensure quality.

All filled questionnaires were daily checked for completeness and accuracy by the Investigator and then coded before entering the data into the computer. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 20 for Windows evaluation. Frequency distribution and cross tables were used to tabulate data. Variables were expressed in percentage and comparison between independent and Chi squire did dependent variables and Fishers test. P value of < 0.05 was considered statistically significant.
Ethical clearance was obtained from the Institutional Review board (IRB) of the Muhimbili University of Health and Allied Sciences and permission to conduct the study at Ocean Road using the medical records and imaging facility were obtained from the executive Director of ORCI through the Director of Academic unit of ORCI.

**Results**

139 patients with prostate cancer participated in this study. Participants ages ranges from 42-90 years with most of participants 103 (74.1%) in the 60-79 years’ category. The Mean Age was 68.34 years and standard deviation of 9.02. PSA levels of the patients ranges from 0 to 380 ng/ml with 53 (39%) having a PSA level of more than 20 nanogram. Mean PSA level was 39.89 ng/ml of the total patient 43 (30.9%) had GS of more than seven (Table 1).

**Table 1:** Demographic and basic characteristics of the studied population N=139.

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
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</thead>
<tbody>
<tr>
<td>Age group</td>
<td></td>
</tr>
<tr>
<td>40-59</td>
<td>21 (15.1%)</td>
</tr>
<tr>
<td>60-79</td>
<td>103 (74.1%)</td>
</tr>
<tr>
<td>80+</td>
<td>15 (10.8%)</td>
</tr>
<tr>
<td>Mean age</td>
<td>68.34</td>
</tr>
<tr>
<td>PSA level</td>
<td></td>
</tr>
<tr>
<td>&gt;20ng/ml</td>
<td>53 (38.1%)</td>
</tr>
<tr>
<td>Mean PSA level</td>
<td>39.89</td>
</tr>
<tr>
<td>Gleason score</td>
<td></td>
</tr>
<tr>
<td>&gt;7</td>
<td>43 (30.9%)</td>
</tr>
</tbody>
</table>

Seventy-seven patients (55.4%) out of 139 patients with Prostate cancer had bone metastasis. Patient with the age group 60-79 had higher prevalence of bone metastasis compared to the other groups however it was not statistically significant (p – 0.933) as shown in table 2 below.

**Table 2:** Prevalence of Bone Metastasis among patients with Prostate Cancer according to age group N=139.

<table>
<thead>
<tr>
<th>Metastasis</th>
<th>YES</th>
<th>NO</th>
<th>Total</th>
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<tbody>
<tr>
<td>40-59</td>
<td>11</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>60-79</td>
<td>58</td>
<td>45</td>
<td>103</td>
</tr>
<tr>
<td>80+</td>
<td>8</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td>62</td>
<td>139</td>
</tr>
</tbody>
</table>

Patients with PSA of more than 20 ng/ml had more bone metastasis 88.4% (47/53) as compared to those with PSA less than 10 and those of between10-20. The difference was statistically significant with a p-value of 0.0001. Also fifty-five patients (96.5%) of patients with Gleason score of more than seven had more bone metastasis as compared to those of less or equal to 7 (p-0.0001).

**Table 3:** Relationship between bone metastasis with PSA and Gleason score.

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>Total</th>
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<tbody>
<tr>
<td>PSA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 10ng/ml</td>
<td>8</td>
<td>52</td>
<td>60</td>
</tr>
<tr>
<td>10 to 20ng/ml</td>
<td>22</td>
<td>4</td>
<td>26</td>
</tr>
<tr>
<td>More than 20ng/ml</td>
<td>47</td>
<td>6</td>
<td>53</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td>62</td>
<td>139</td>
</tr>
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</table>

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<tbody>
<tr>
<td>GS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 7</td>
<td>4</td>
<td>37</td>
<td>41</td>
</tr>
<tr>
<td>7</td>
<td>18</td>
<td>23</td>
<td>41</td>
</tr>
<tr>
<td>More than 7</td>
<td>55</td>
<td>2</td>
<td>57</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td>62</td>
<td>139</td>
</tr>
</tbody>
</table>

Among all patients with prostate malignancy included in the study 72 (51.8%) presented with spine metastasis which was the most frequent followed by ribs metastasis that was present in 44 (31.7%) patients included in the study. Only 26 (18.7%) patient of these patients presented with metastasis to the upper limb which was the least affected area [P=0.0001].

Lumbar spine was the most frequent site for spine metastasis occurring in 67 (48.2%) patients, followed by thoracic spine metastasis 57 (41%) and the last was sacral metastasis which was present in 33 (23.7%) of all patients with prostate cancer included in the study. [P=0.0001], as shown in the table 6 and figure 2 below.

**Discussion**

The overall prevalence of bone metastasis as detected by bone scintigraphy was 55.4 % (77 out of 139 patients). This is in contrast to the study done by Lin KP et al. and Klatte et al. who showed in their researches that the prevalence of bone metastasis in patient to be 14% and 10% respectively [7,20]. Also, the prevalence of 8% and 14% in white and black Americans respectively was found in
a study done by Carlin BL et al. [21]. This could be explained by the fact that, most of the patient in this study came to the nuclear medicine in late stages after having metastatic symptoms contrary to the newly diagnosed patients included in the other studies.

The study showed there is an increase in the rate of positive bone scan with increased level of prostate specific antigen which was statistically significant seven [P=0.0001]. Only 5.1% of participants with PSA level of less than 10ng/ml had positive bone scan for metastasis in comparison with 34.6% in those with PSA of more than 20ng/ml. This is similar to the findings in research done by Pal RP et al that showed that there was a steady increase of rate of bone metastasis with an increase in the level of PSA and that PSA was an independent prognostic indicator for the positive bone scan [7].

Similar findings were depicted by Lin K et al showing in their study that low levels of prostate specific antigens were associated with low risk of bone metastasis when compared to high levels [8].

Low levels were shown to be associated with lower risk of bone metastasis and vice versa. Those with Gleason score of less than 7, only 2.9% had bone metastasis while those with more than 7, 28.1% had positive bone scan the findings similar to the study retrospective study by Ritenour et al which similar trend of increased rate of bone metastasis with an increase in Gleason score [23].

About fifty-two percent of all recruited patients in the study had spine metastasis, which proves to be the most common site for metastasis. This is similar to the study done by Memon AG et al and Vahid et al., who both showed that the spine was the most common site for skeletal metastasis in prostate cancer patients [14,15]. This predilection to the spine can be explain by the venous plexus drainage of the pelvic organ through the Batson plexus.

The lumbar spine was the most affected part of the spine followed by the thoracic spine, 48.2% and 41% respectively. This finding are similar to the study done by Lukas B et al which showed that lumbar spine metastasis was more common than thoracic metastasis and this was explained by the backward flow of metastatic deposits through the venous drainage from the prostate to the lumbar spine and then upwards as it was hypothesized by Batson [24]. On the other hand, Memon G et al. showed in their research that, thoracic vertebra was the most affected part of the spine contributing 42% of the studied patients with prostate carcinoma [14].

Acknowledgement
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