Original Article

Bone Mineral Density in Patients with Metastatic Prostate Cancer with or without Androgen Deprivation Therapy

Imran Hyder, Anum Hafeez and Muhammad Waqas

ABSTRACT

Objective: To evaluate the bone mineral density in patients of malignant prostate cancer with and without use of androgen deprivation therapy.

Study Design: Case control study

Place and Duration of Study: This study was conducted at the Urology department of Nishtar Hospital, Multan from April 2021 to March 2022.

Materials and Methods: A total of 50 patients with malignant prostate cancer were enrolled in study. Patients were categorized on basis of their use of ADT (case or control). Bone mineral density of patients was measured by using bone densitometry. SPSS version 24 was used for data entry and analysis. P value ≥0.05 was considered as significant.

Results: The parameters of bone mineral density (BMD) in ADT and controls patients were almost equal and no statistically significant difference was found, (p>0.050). It was seen that 32.0% patients had normal BMD, 44.0% had osteopenia and 24.0% osteoporosis in ADT patients. Whereas, 36.0% patients had normal BMD, 44.0% had osteopenia and 20.0% osteoporosis in control patients, (p=0.928).

Conclusion: Men with prostate cancer in older age have significant bone loss, start of androgen deprivation therapy can cause more decrease in bone mineral density (BMD). Patients on treatment of ADT should have baseline bone mineral densitometry and checked periodically for assessment of possible osteoporosis and fracture risk. Use of bisphosphonate is much costly that cannot be started blindly until recommendations are proven.

Key Words: Metastatic Prostate cancer, ADT, BMD, T score, Bisphosphonate

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INTRODUCTION

In adults of age above 50 years prostate cancer is the most common malignancy, which is responsible for increased rate of mortality when it in advance stage[1]. Bones are the common sites where prostate cancer exclusively metastasizes. In metastatic stage it can cause spinal cord compression, fractures, degenerative disorders and severe pain[2]. Various debates and discussions has been published and about its treatment at early and late stage. Huggins and Hodges described the use of androgen manipulation in prostate cancer and this therapy is still in use and treatment of choice even in advance stages of carcinoma[3].

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But the use of these agents may cause bone fragility and osteoporosis especially in immune-compromised or old age patients[4]. Male with prostate cancer are at greater risk of side effects in both either in disease or treatment forms. Some hormones are essential for formation and development of bones like testosterone and estrogen, but in aging men these hormones starts decreasing gradually and after some time significant bone mineral density occurred[5]. Third decade of life is the peak time for bone mass occurrence but after that BMD starts losing with rate of 1% per year[6].

Term BMD is the measurement of bone mineralization that can be measures by different ways and represented in form of T-score and Z-score[7]. T score is the below average standard deviation of peak bone density in healthy young adults and z-score is standard deviation of below and average person of same gender, race and age[8]. During estrogen deprivation therapy it was recommended to evaluate serial bone densitometry for early detection of osteoporosis and associated fractures[9]. Another drug biophosphonates is in practice for the treatment of disease that can cause bone weakening features like osteopenia, osteoporosis and osteosarcoma. Its intravenous use is also known in myeloma of CA breast[10].

This study is designed to measure the changes in bone mineral density in patients of prostate cancer either using ADT or not and also evaluate the use of bisphosphonate in patients of prostate cancer at metastatic stage.

MATERIALS AND METHODS

Study was conducted at Urology department of Nishtar hospital, Multan from April 2021 to March 2022 in duration of one year. Study was approved by hospital committee of academic affairs after passing the defense. Patient's consent regarding the study purpose and inclusion was obtained. Non probability consecutive sampling technique was used. Patients of metastatic prostate cancer having age 60-80 years were included in the study and enrolled in two groups on basis of their treatment plan. In one group 25 patients were enrolled who are using androgen deprivation therapy and in other group 25 patients were enrolled who are not using ADT. Patients who are taking radiation, chemotherapy, warfarin, thyroxin, methrotrexate, corticosteroid, post organ transplant therapy, antipsychotic or anticonvulsant, chronic heparin, long term lithium were excluded from the study.

Prostate cancer was proven radiologically as well as histopathologically from in patient and out patients department Bone mineral density (BMD) was measure and T-score was recorded. SPSS version 24 was used for data entry and analysis. Numerical variables like age, duration ADT, duration of illness and T score were calculated and presented in form of mean ± SD. Categorical variables like osteopenia, osteoporosis and normal BMD were calculated and presented as frequency and percentages. T-test was applied to see association among numerical variables and chi-square test was applied to see association among categorical variables. P value less than or equal to 0.05 was taken as significant.

RESULTS

Overall, 50 patients were included in this study and enrolled in two groups. In case (ADT) group patients were using androgen deprivation therapy and in control group patients were not using ADT. The demographic and baseline characteristics like age, BMI, duration of illness, histopathology, and duration of ADT were shown in table I. The differences were statistically insignificant, (p>0.050). (Table. I).

The parameters of bone mineral density (BMD) in ADT and controls patients were almost equal and no statistically significant difference was found, (p>0.050). (Table. II).

It was seen that 8 (32.0%) patients had normal BMD, 11 (44.0%) had osteopenia and 6 (24.0%) osteoporosis in ADT patients. Whereas, 9 (36.0%) patients had normal BMD, 11 (44.0%) had osteopenia and 5 (20.0%) osteoporosis in control patients, (p=0.928). (Figure. I).

Table No.1: Demographic and Baseline Characteristics of the Study Groups

Characteristic	ADT N (%)	Controls N (%)	p-value
Age (years)	70.16±1.72	70.01±2.02	0.765
BMI (kg/m^2)	31.25±3.56	30.41±2.65	0.526
Duration of illness (years)	3.20±1.89	3.08±1.22	0.791
Histopathology	9 (36.0)	13 (52.0)	0.256
Duration of ADT (years)	2.44±0.71	-	-

Table No.2: Bone Mineral Density Parameters of the Study Groups

Parameter	ADT N (%)	Controls N (%)	p-value
L2-L4 (g/cm^2)	1.60±0.11	1.58±0.08	0.497
Femoral neck (g/cm^2)	0.84±0.12	0.77±0.11	0.056
One-third distal radius (g/cm^2)	0.91±0.22	0.82±0.25	0.178
Ultra distal forearm (g/cm^2)	0.38±0.21	0.48±0.25	0.165
Total body (g/cm^2)	1.83±0.11	1.82±0.08	0.799

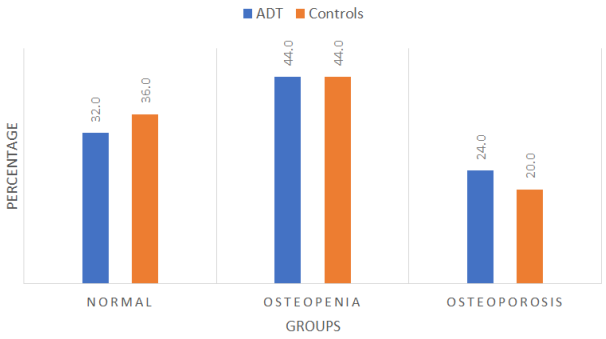

Figure No.1: Percentage of BDM Levels

DISCUSSION

Prostate cancer is most common type of cancer affecting 2 to 3% of men every year with bones as usual site of metastasis and causing significant skeletal morbidity. In metastatic cases primary treatment modality is hormone therapy which is either LH-releasing agonists or orchidectomy[11]. ADT have positive role in tumor growth suppression, but certain types of side effects are also associated e.g osteoporotic ADT effects on bone health and normal physiology. ADT along with old age and prostate cancer itself is a contributing risk factor and predictor[12].

In our study osteoporosis was found in 24% of patients with ADT and 20% in controls but results were insignificant p=0.928. A study was conducted by Malik MTBet al[13] and reported that BMD is affected by

prostate cancer and its treatment with ADT, osteoporosis was observed in 52% of patients and 27% patients in controls. In another study Smith et al[14] reported 4 to 13% decrease in BMD with use of ADT in patients of prostate cancer and older age.

In our study mean duration of ADT was 2.44±0.71 and after osteoporosis and osteopenia was observed in such cases. Wilcox et al[15] also concluded similar results BMD and prostate cancer. A total of 76 patients with median duration of ADT were evaluated and 50% of men observed with osteoporosis. A study was conducted by Husain et al[16] in 2003 and reported 42% of men with prostate cancer diagnosed as osteoporosis and 37% as osteoporotic before start of ADT therapy and osteoporosis was observed in 24% of patients in controls.

In 2005 Greenspanet al[17] reported identical results about study findings in prostate cancer who are taking ADT. A significant reduction of mean T-score 2.0 ± 0.6 was observed in such patients who are using chronic ADT. It was also concluded that 5-10 fold decrease in BMD occur with use of ADT at multiple bone sites along with generalized musculoskeletal weakness. Nishiyamaet al[18] also observed significant decrease in BMD after start of ADT, P-value < 0.023. Significant decrease in mean T-score was also described in this study.

Bisphosphonates is an effective agent used in hypercalcemia after malignancy, bone cancer, osteopenia and osteoporosis but its clear cut benefits were not demonstrated yet, that's why its use is controversial in prostate cancer[19]. In some cases of prostate cancer that is metastasized in skeleton osteomalacia was observed on histologic and indirect biochemical grounds. Use of bisphosphonate in such cases results in increase of osteomalacia due to osteoblastic activity over bone resorption[20].

CONCLUSION

Men with prostate cancer in older age have significant bone loss, start of androgen deprivation therapy can cause more decrease in bone mineral density (BMD). Patients on treatment of ADT should have baseline bone mineral densitometry and checked periodically for assessment of possible osteoporosis and fracture risk. Use of bisphosphonate is much costly that cannot be started blindly until recommendations are proven.

Author's Contribution:

Concept & Design of Study:	Imran Hyder
Drafting:	Anum Hafeez, Muhammad Waqas
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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