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Correlation of Prostate Specific Antigen, Gleason Score and Bone Metastases in Bone Scan in Prostate Cancer Patient

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Abstract	Original Research Article

Introduction: For men prostate cancer is most commonly occurring cancer and it is responsible for fifth leading cause of death in whole world (3.8% of all deaths caused by cancer in men in 2018). For developed country prevalence rate is much higher however there are reports which revealed higher incidence of positive bone scan with low PSA in mass population screening in Asians as compared with western data. ***Aim of the Study:*** To identify correlation and incidence of bone metastases in prostate cancer patient with low Gleason scores (GS) and prostate specific antigen (PSA) levels. ***Material & Methods:*** This was a retrospective study of prostate cancer patients referring to Institute of Nuclear Medicine and Allied Sciences, Khulna, Bangladesh for bone scan form January 2020 to December 2020. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 22.0. ***Results:*** There were 58 patients with prostate cancer in January 2020 to December 2020 and 45 patients with the complete data. The patients were of age 53–89 years, with mean age of 68.41 ± 7.5 years. The incidence of osseous metastases proven by bone scan was found to be 1 out of 5(25.00%) for PSA level>20 ng/ml, (20-60 ng/ml); 9 out of 17 (52.94%) for PSA level (60–100) ng/ml; 10 out of 12(83.33%) and 100% for PSA >100 ng/ml. All patients (n = 11) with PSA >100ng/ml was having BM. ***Conclusion:*** There was high incidence of BM in diagnosed PC in our study (68.89%) compared to other studies; PSA and GS positively related to the incidence of BM; and there were still small number of patients had BM with low GS and PSA.

Keywords: Prostate cancer, Low PSA, Low GS - bone metastases, Bone scans.

INTRODUCTION

For men prostate cancer is most commonly occurring cancer and it is responsible for fifth leading cause of death in whole world (3.8% of all deaths caused by cancer in men in 2018). For developed country prevalence rate is much higher however there are reports which revealed higher incidence of positive bone scan with low PSA in mass population screening in Asians as compared with western data. Diagnosis of prostate cancer is based on elevated level of prostate specific antigen (PSA> 4 mg/dl) and tissue biopsy which is considered gold standard for confirmation of cancer[1, 2]. On Histopathology grading of prostate cancer by Gleason Score is a good predictor of the pace of disease. Patient with well differentiated tumors (Gleason Score 2 to 6) generally have a favorable prognosis while high grade tumors (Gleason Score 7 to 10) are associated with higher mortality [3]. The

Skeleton is the most common site for metastases from prostate cancer after lymph nodes and there is an incidence of 65%-75% of skeletal involvements in patients with advance disease [4]. Metastases are commonly found in axial skeletal due to enrich blood supply to the trabeculated bone and arrangement of venous plexus of vertebra [5]. Radionuclide Bone Scan (BS) is the most sensitive method (72-77%) to detect BM and currently is the investigation of choice [6]. Due to high osteoblastic activity within metastases from prostate cancer compared to other tumors means that Tc99m –MDP bone scan have traditionally shown good sensitivity though lack of specificity of bone scan is a major disadvantage [7]. Many studies had confirmed that incidence of BM correlated positively with staging of the tumor, PSA and Gleason Score (GS) [8]. However, there was still a lack of consensus, of the selection of criteria for bone scan in low risk patients, and PSA and GS cut-off value. Though, European Association of Urology (EAU), American Urological Urological Association (AUA) and American Joint Committee on Cancer (AJCC) had recommended similar indication for BS, which were: GS>7, PSA level>20 ng/mL and presence of bony symptoms, based on studies in western countries[9].

METHODOLOGY AND MATERIALS

This was a retrospective study of prostate cancer patients referring to Institute of Nuclear Medicine and Allied Sciences, Khulna, Bangladesh for bone scan form January 2020 to December 2020. All patients who were diagnosed prostate cancer either by prostatic biopsy or from histopathology after prostectomy were included in this study while Patient with other recognizable carcinoma was excluded. Data were collected from the medical records of the patients. Recorded data were PSA value at the time of bone scan, histopathological examination of prostate's tissue as Gleason Score and bone scan result as metastases. Statistical analysis: Continuous variables were expressed as mean with range and categorical variables as count with percentage. Groups were compared using Chi Square test (cross tabulation method) for categorical variables. P value less than 0.05 was considered statistically significant with 95% confidence interval. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 22.0.

RESULTS

There were 58 patients with prostate cancer in January 2020 to December 2020 and 45 patients with the complete data. The patients were of age 53–89 years, with mean age of 68.41 ± 7.5 years. The PSA levels were ranging from <20 to >100 ng/ml with mean

value of 60 ± 30.74 ng/ml. The mean biopsy Gleason score was 7.28 ± 1.7 (ranging from ≤6 to ≥8) [Table 1].Out of 45 patients, 31 patients (68.89%) had positive bone scan and 14 patients (31.11%) had negative bone scan as shown in Figure 2.The patients were stratified into four groups according to their PSA level: The first group of patients had PSA level ranging from <20 ng/ml (n = 5), the second group had PSA level ranging from 20 to 60 ng/ml (n = 17), the third group had PSA levels 60–100 ng/ml (n = 12), and the fourth group has PSA levels >100 (n = 11). The incidence of osseous metastases proven by bone scan was found to be 1 out of 5(25.00%) for PSA level>20 ng/ml (20-60 ng/ml); 9 out of 17 (52.94%) for PSA level (60–100) ng/ml; 10 out of 12(83.33%) and 100% for PSA >100 ng/ml. All patients (n = 11) with PSA >100 ng/ml were having BM. The mean age and PSA of these subgroups are described in Table 2.A significant correlation between serum PSA and positive BM was found with P < 0.005.
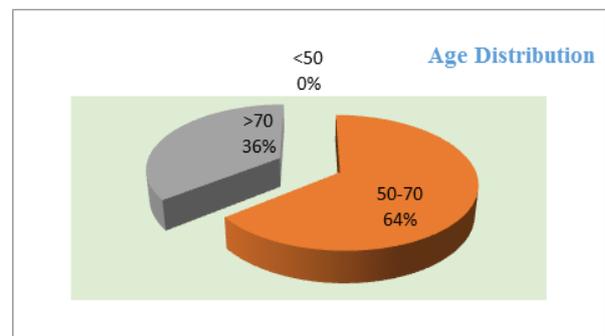

Fig-1: Age Distribution of the patients (N=45)

Table-1: Demographic characteristics (N=45)

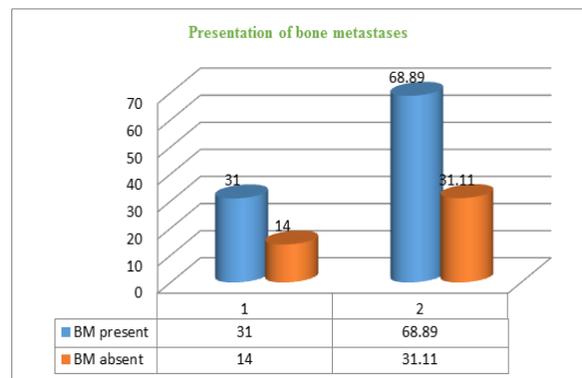| Characteristics	Mean±SD	N
PSA	60±30.74	45
GS	7.28±1.7	45
Age	68.41±7.5	45

Fig- 2: Presentation of bone metastases

Table-2: Correlation between PSA Value, BM and between GS and BM (N=45)

PSA	Patients	Mean age	Mean GS	Metastatic disease (%)	
				BM/Total PSA	%
<20	5	69.75±5.44	7±2.16	1/5	25.00
20-60	17	69.62±8.79	6.62±1.39	9/17	52.94
60-100	12	66.78±7.1	7.39±1.53	10/12	83.33
>100	11	69±7.6	7.54±1.91	11/11	100.00

*p<0.001; PSA: Prostate Specific Antigen; BM: Bone Metastasis; GS: Gleason Score
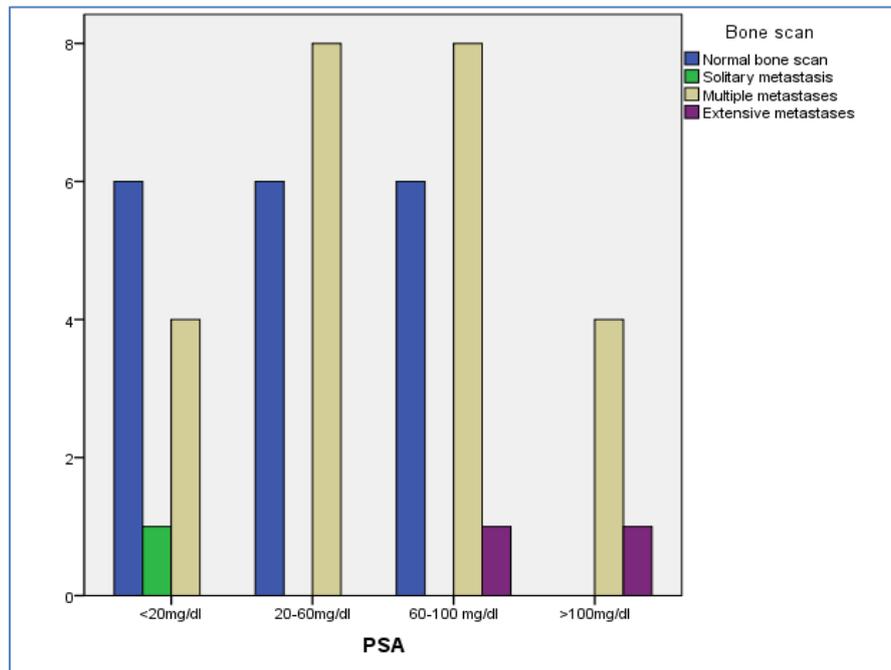
Fig-3: Correlation between PSA Value and BM

Table-3: Incidence of BM in Low PSA Patients in Asian Countries

Study	Number of Patients	PSA (ng/ml)	BM+	
			N	%
Ito et al. (2000)	303	<10	13/36	36.1
Yang et al. (2009)	77	<20	5/26	19.2
I Putu Gde Sanjaya et al.(2013)	358	<20	25/90	27.7
		<10	10/42	23.80
Amitsharma et al.(2017)	89	<20	10/42	21.73
Bhargava et al.(2018)	85	<20	11/31	35.48
Current study	45	**<20**	1/5	25.00

DISCUSSION

BM is one of the strongest negative prognostic factors for prostate cancer as it is not only compromises the survival outcome but also hampers quality of life in these patients. The serum PSA and biopsy Gleason score are the independent parameters defined by many studies which can predict the occurrence of BM. However, the optimal cut-off of PSA level for defining high-risk disease for staging bone scan has always been a matter of debate. Currently, the American Urological Association and the EAU do not recommend staging bone scan in patients with well-differentiated prostate cancer with PSA <20 ng/ml. This inference was made from the studies which included western cohort. Besides the incidence of BM in patients with low PSA <20 ng/ml is much higher in Asian men compared to western countries. It is thus certain that there is difference in intrinsic biological behavior of prostate cancer between different geographic origin, race, and ethnicity. The incidence of bone metastasis in prostate carcinoma in our study is significantly very high (68.89%) compared to western studies [6]. This could be partly attributed to the adoption of symptomatic screening method rather than population-based screening. However, the prevalence of BM in our study is comparable to other Asian studies (30%–60%).

However, age was not found to be a predictor for bone metastasis (P = 0.8) as reported in the literature. The prevalence of BM with higher Gleason score >7 was established (P = 0.002).The rate of positive bone metastases with lower serum PSA levels in our study is extremely higher than the United States and Canada (8.9%) [7]. However, our results are comparable to other Asian studies. Oesterling et al. were the first to demonstrate PSA as independent predictor of BM and concluded that bone scan can be omitted in patients with PSA <10 ng/ml [8]. Ito et al. have reported an incidence of 36% (13/36 patients) of bony metastasis with PSA ≤10 ng/ml in Japanese mass screening program [9]. Another study from China by Yang et al., the positive rate of bony metastases was 19.2% (5/26 patients) of patients with PSA <20 ng/ml [10]. Similar high rates were present in other Asian studies as Pakistan (12.6%), Indonesia (27.7%) and current study in Bangladesh (25.00%) [Table 3] [11-14].

Facts from these studies suggest that in Asian men, limiting the screening bone scan for PSA >20 ng/ml as per the western guidelines could lead to high number of patients with BM remain undetected. Especially in the Indian subcontinent, the majority of patients present with poorly differentiated histology, and high incidence of BM occurs even at low PSA. As in our study, if western guidelines were to be followed we could miss BM and under stage 25.00% patients with PSA <20 ng/ml. In our study for cut-off PSA >20 ng/ml, the incidence of osseous metastases proven by bone scan was found to be 1 out of 5(25.00%) for PSA level>20 ng/ml, (20-60 ng/ml); 9 out of 17 (52.94%) for PSA level (60–100) ng/ml; 10 out of 12(83.33%) and 100% for PSA >100 ng/ml. All patients (n = 11) with PSA >100 ng/ml were having BM. Hence, we recommend that the cut-off for staging bone scan should be relaxed to PSA <10 ng/ml in asymptomatic patients at least in Indian setting.

Limitations of the Study

This was a single center study with small sample size. Patient was selected irrespective of considering of newly diagnosed or already treated and based on last available PSA. Hence, it will be difficult to generalize in the whole community.

CONCLUSION AND RECOMMENDATIONS

There was high incidence of BM in diagnosed PC in our study (68.89%) compared to other studies; PSA and GS positively related to the incidence of BM; and there were still small number of patients had BM with low GS and PSA.

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