ORIGINAL RESEARCH

The Correlation of Gleason Score and Prostate Specific Antigen in Predicting the Presence of Bone Metastasis in Patients with Prostate Adenocarcinoma: A Retrospective Descriptive Study

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Introduction

Cancer is the leading cause of disease and death worldwide and among all cancers, prostate cancer (PCA) is the second most frequently diagnosed cancer of men after lung cancer. Despite the low incidence of prostate cancer, there is a rapid increase of prostate cancer's incidence and mortality in Asian countries due to a more westernized lifestyle and high proportion of advanced stage prostate cancer.

The European Association of Urology (EAU), American Urological Association (AUA) and National Comprehensive Cancer Network (NCCN) had recommended similar indications for bone scan: GS>7, PSA level>20 ng/mL and presence of bone symptoms, based on studies in Western countries.

According to a study done by Al-Ghazo, et al. doing a bone scan can be omitted in patients with a PSA level of ≤ 20 ng/mL and Gleason score < 8 in which the authors suggest that by considering the Gleason score and PSA, a larger proportion of patients with prostate cancer could avoid a staging bone scan. Another study done by Rhoden et.al concluded that PSA serum concentration over 20 ng/mL was a more accurate cutting point than PSA serum concentration over 10 ng/mL to predict the presence of metastasis in the bone scan.

Interestingly, there were several studies in Asian countries such as Japan, China, and Pakistan, which revealed incidence of bone metastasis (BM) in prostate cancer patients, despite of low PSA and GS. Several studies in Asia found similar findings. Somehow there was a higher incidence of BM in low PSA and GS in the Asian population, even though there was lower incidence of prostate cancer. According to a study done by Sanjaya, et al. there was still a small percentage of patients with bone metastasis even when low values of PSA (PSA<10 ng/mL) and GS (GS≤6) were applied. This study also revealed that there was high incidence of BM in newly diagnosed PCA in the study compared to other studies and that PSA and GS positively related to the incidence of BM in which there was still a small number of patients having BM with low GS and PSA.

The prevalence of prostate cancer is increasing. Currently, the diagnostic tools for prostate cancer

are digital rectal examination (DRE) and serum prostate-specific antigen (PSA) test. To establish the diagnosis of prostate adenocarcinoma, a Transrectal Ultrasound-guided Prostate Needle Biopsy is warranted. The combination of both DRE and PSA testing leads to a greater detection of prostate cancer through TRUS-PNB. The high sensitivity and low specificity of PSA testing in the diagnosis of prostate cancer are problems in clinical practice if done alone due to the influence of prostate volume and other factors such as infection and manipulation. Even with this disadvantage, however, PSA measurement is still used in clinical practice. A higher PSA level may relate to a greater likelihood of positive tissue diagnosis, a higher Gleason score, and a greater likelihood of bone metastasis.

Bone is the most common metastasic site of prostate cancer and the first site to be metastasized by the cancer cells, preceding the lung and liver.[5] Bone metastasis occurred in up to 14% of cases at presentation and around 80% in advanced stage. Bone Scan (BS) is the most sensitive method to detect BM and currently is the investigation of choice in spite of its high rate of false positives resulting from degenerative changes, inflammation, Paget disease, and trauma. There needs to be only a 10% change in bone mineral turnover to be detected by bone scan.

The aims of this study were to identify and correlate the incidence of bone metastasis in low PSA and Gleason score in prostate cancer patients in Veterans Memorial Medical Center and to evaluate or reassess the recommendation of a prostate cancer patient selection to undergo bone scan according to the current guidelines.

Its objective was to evaluate or reassess the recommendation of a prostate cancer patient selection to undergo bone scan according to the current guidelines.

Materials and Methods

Patients diagnosed with Prostate Adenocarcinoma from 2010-2016 were included in the study. Each patient's Gleason score, PSA, and bone scan results were gathered from each patient's hospital chart or from the records of the Department of Nuclear Medicine which handles the previously mentioned diagnostic examinations.

Serum PSA was measured using the sandwich electrochemiluminescent immunoassay technique. The PSA value in the study was divided into 3 categories: <10 ng/mL, 10.1 to 20.1 ng/mL, and >20.1 ng/mL. Prostate tissue for histopathological examination was obtained from Trans-Rectal Ultrasound Prostate Needle Biopsy, Trans-Urethral Resection of Prostate and Open surgery. Histological examination was graded according to the Gleason's grading. The histopathologic findings based on GS were divided into 3 categories: GS≤6, GS=7 and GS 8-10 which is validated from the NCCN guidelines placing the patients into the appropriate risk group. Bone scans were done using the radiopharmaceutical agent Tc 99m methylenendiphosphonate and then the image was captured using a gamma camera. The bone scan result was divided into patients with BM and patients without BM. Statistical analysis was done using a Chi-square test of difference between 2 categorical variables.

Results

A total of 209 patients with prostate cancer in January 2013 to January 2015 were included in this study. Patients were divided according to PSA value and GS and correlation of each parameter with the presence or absence of bone metastases were plotted on a bar graph.

Table 1 and Graph 1 revealed no significant difference between Negative and Positive BM when grouped according to PSA. The graph shows that patients with a PSA level of >10 have a higher percentage of having bone metastases. Table 2 and Graph 2 also revealed no significant difference between negative and positive BM when grouped according to GS. The graph shows that there is almost an equal chance of manifesting BM with a low or high Gleason score. Table 3 revealed that there is an incidence of 1.9% to manifest BM in spite of having a low PSA value and low Gleason score.

Table 1. Comparison of PSA value and presence of bone metastasis.

		BM		Total	P-value	Interpretation
		Negative	Positive			
PSA	Less than 10	116	5	121		
	10 to 20	51	8	59	0.054	Not Significant
	Above 20	12	2	14		

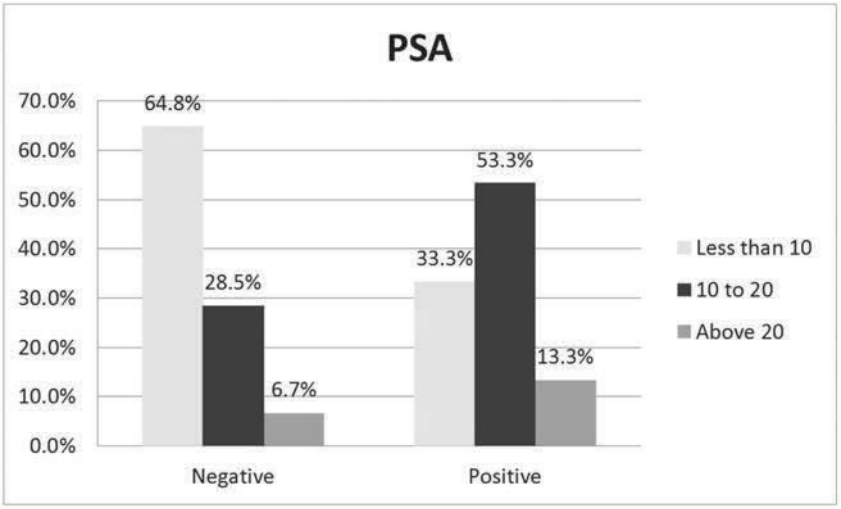

Figure 1.Comparison of PSA value and presence of bone metastasis.

Table 2. Comparison of Gleason score and presence of bone metastasis.

		BM		Total	P-value	Interpretation
		Negative	Positive			
GS	6 and below	43	7	50		
	7	66	2	68	0.083	Not Significant
	8 to 10	84	7	91		

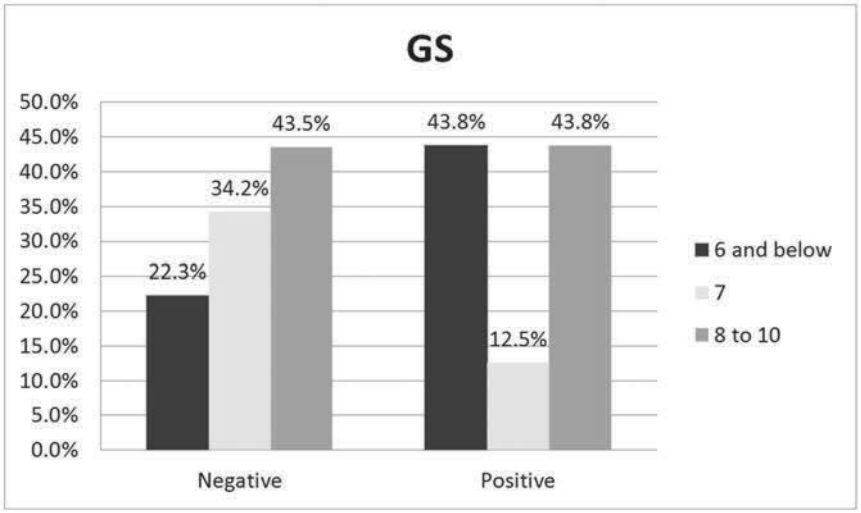

Figure 2. Comparison of Gleason score and presence of bone metastasis.

Table 3. Correlation of PSA and Gleason score with presence of bone metastases.

	PSA Less than 10			PSA 10 to 20			PSA above 20		
	GS Less than 6	GS 7	GS 8 to 9	GS Less than 6	GS 7	GS 8 to 9	GS Less than 6	GS 7	GS 8 to 9
Negative	29 (13.8%)	39 (18.5%)	48 (22.8%)	11 (5.2%)	17 (8%)	23 (10.9%)	1 (0.4%)	4 (1.9%)	7 (3.3%)
Positive	4 (1.9%)	0 (0%)	1 (0.4%)	3 (1.4%)	0 (0%)	5 (2.3%)	0 (0%)	1 (0.4%)	1 (0.4%)
Grand Total	33 (15.7%)	39 (18.5%)	49 (23.3%)	14 (6.6%)	17 (8%)	28 (13.3%)	1 (0.4%)	5 (2.3%)	8 (3.8%)

Discussion

The incidence of bone metastases was noted to be high in the groups whose PSA: >20.1 ng/ml and GS: 8-10. The results are consistent with the current NCCN/EAU/AUA guidelines which states that a bone scan can be omitted if the patient's PSA: <20 ng/ml and GS: <8 which would be cost-effective to the patient. The dilemma was that of the diagnosis of bone metastasis would have been missed in 13 patient if the current guidelines. Asian countries such as Pakistan, Japan, China, and Indonesia have done studies which recommend the lowering of the threshold of PSA level in deciding whether to do a bone scan or not because an incidence of as high as 30% revealed the presence of bone metastases in patients with a PSA: <10 mg/ml.

In conclusion, the present lowering of the study indicated that a small percentage of patients who still manifested with bone metastases in spite of having a low PSA value and a low GS. If the current guidelines were applied, these cases would be missed and the possibility of having bone metastases in more than one site would be increased upon work up of these patients.

Recommendation

Based on this study, the authors recommend including a bone scan in the work up of newly diagnosed patients with prostate cancer, despite the PSA level being less than 10 mg/ml or the Gleason score being less than 8. The limiting factor in including a baseline bone scan in the initial work up would be its cost-effectiveness, especially in third-world countries.

References

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