Original Article

Predictive value of serum prostate specific antigen in detecting bone metastasis in prostate cancer patients using bone scintigraphy

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ABSTRACT

Introduction: Radionuclide bone scan (BS) used to be the investigation of choice for detecting osseous metastases in prostate cancer. Now, with the availability serum prostate specific antigen (PSA) testing, clinicians do have a timely, cost-effective method to determine those patients who are highly unlikely to have osseous metastases. We determine the utility of PSA for predicting the presence of skeletal metastasis on BSs in prostate cancer patients. **Materials and Methods:** Retrospective analysis of medical records of 322 consecutive prostate cancers patients subjected to BS during the last 3 years was done. 52 cases were excluded due to following reasons: Serum PSA not available, hormonal or other therapy given prior to serum PSA measurement, and/or BS, and symptomatic for bone metastasis. In remaining 270 cases, PSA value and BS were evaluated. BS was performed with Tc99m methylene diphosphonate (MDP) as per the standard protocol. **Results:** BS was found to be positive in 153/270 (56%) and negative in 117 (46%) patients. Of the 153 positive cases, 108 (70%) had serum PSA > 100 ng/ml, 42 (28%) had PSA of 20-100 ng/ml and only 3 (2%) had PSA < 20 ng/ml. All the patients with PSA > 100 ng/ml had multiple skeletal metastasis. Of the 117 negative cases, 110 (94%) had a PSA < 20 ng/ml, 5 had between 20 and 100 ng/ml and only 2 (1.8%) had PSA > 100 ng/ml. Of the 113 patients with serum PSA < 20 ng/ml, 110 (97.4%) did not show any bony metastasis. 150/157 (95.5%) patients with PSA > 20 ng/ml had bone metastasis. Using this criterion, 110 (40.7%) scans would have been omitted. **Conclusions:** Serum PSA < 20 ng/ml have high predictive value in ruling out skeletal metastasis. Our data are in corroboration with results from previous studies that BS should be performed only if PSA > 20 ng/ml. Using this cut-off, unnecessary investigation can be avoided. Avoiding BS in this group of patients would translate into a significant cost-saving and reduction in their psychological and physical burden.

Keywords: Bone scan, prostate Ca, prostate specific antigen, Tc99m-methylene diphosphonate

INTRODUCTION

Prostate cancer is the most common cancer in men and is responsible for 19% of all newly diagnosed male cancers.[1] Serum prostate specific antigen (PSA)-based screening is helpful in early diagnosis and staging of prostate cancer.[2,3] Prostate cancer has a tendency to metastasize to bone. On presentation, up to 14% of patients have bone metastasis.[4] Radionuclide bone scanning being the most sensitive method plays an important role in detecting bone metastasis in prostate cancer.[5,6] Because of the high incidence of bone metastases, bone scans (BS) are routinely performed to detect bone metastases and/or to assess the response of a patient's known metastatic bone disease to chemotherapy. Recent European Association of Urology guidelines state that a BS may not be indicated in asymptomatic patients with well or moderately differentiated prostate cancer presenting with a serum PSA < 20 ng/ml.[7] However, BS should be considered only if the result is likely to have a strong impact on the management plan. This puts strong emphasis on the need to suitably identify those patients who do not require unnecessary investigations.

Serum PSA has been reported to be the single most useful predictor of metastasis detected on radionuclide scanning in

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patients with prostate cancer.[8-10] Previous studies have suggested a serum PSA of more than 10 ng/ml as an appropriate cut-off for consideration of BS in such patients.[9,11-16] Furthermore, tumor grade and clinical tumor stage along with serum PSA have also been successfully used to predict the presence of bone metastasis.[11,15-18] However, some studies suggest that an appropriate PSA cut-off for these patients may be 15 ng/mL or higher,[10,19-22] irrespective of tumor stage and grade. In this retrospective study, we tried to find out the cut-off value of PSA and its utility to predict the presence of skeletal metastasis on BS in prostate cancer patients.

MATERIALS AND METHODS

A retrospective analysis of medical records of 322 consecutive prostate cancers patients subjected to bone scintigraphy during the last 3 years was done. Fifty-two cases were excluded due to one or more of the following reasons: Serum PSA not available, hormonal or other therapy given prior to serum PSA measurement, and/or BS. In the remaining 270 cases, PSA value and BS were evaluated.

Bone scintigraphy was performed 3 h after intravenous injection of 20 mCi of Tc99m methylene diphosphate. Whole body imaging was obtained under a large field of view gamma camera (Siemens, E.cam, Erlangen, Germany) coupled with high resolution collimator. Spot views were obtained wherever deemed necessary. The photopeak was centered at 140 keV with a 20% window. The scans were interpreted by two experienced nuclear medicine physicians.

PSA was measured by chemiluminescent immunoassay method in all the patients. Normal levels of the laboratory were 0-4 ng/ml.

RESULTS

Of the 270 patients (mean age 65 years; range 55-94 years) for analysis, BS was positive in 153 (57%) patients and negative in 117 (43%) patients. Of those 153 positive cases, 108 (70%) had serum PSA > 100 ng/ml, 42 (28%) had PSA levels between 20 and 100 ng/ml, and only 3 (1.8%) had PSA < 20 ng/ml. All those with PSA > 100 ng/ml had multiple skeletal metastasis (super scan pattern). Of the remaining 117 negative cases, 110 (94%) had a PSA < 20 ng/ml, five had between 20 and 100 ng/ml and 2 had PSA > 100 ng/ml. 110/113 (97.4%) of the cases with serum PSA < 20 ng/ml did not have metastasis. 150/157 (95.5%) with PSA > 20 ng/ml had bone metastasis. Using this criterion, 110 (40.7%) scans would have been omitted. The BS positivity with relation to PSA levels has been depicted in Table 1. Figures 1 and 2 represent normal bone scan in a patient with serum PSA level of 3 ng/ml and wide spread metastases in a patient with serum PSA level of 52 ng/ml, respectively.

DISCUSSION

BS is routinely performed to confirm or exclude bone metastasis in patients with prostate cancer with serum PSA value ≥ 20 ng/ml. The rationale behind this is to

Table 1: Bone scans results and prostate specific antigen values

PSA levels	Bone scan	
	Positive (*n*=153)	Negative (*n*=117)
>100 ng/ml (*n*=110)	108	02
20-100 ng/ml (*n*=47)	42	05
<20 ng/ml (*n*=113)	03	110

PSA: Prostate specific antigen

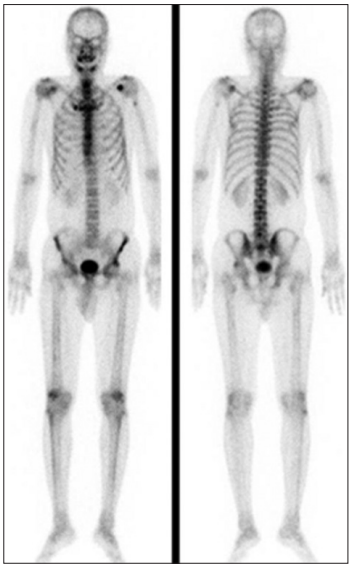

Figure 1: Tc99m-MDP whole body bone scintigraphy in anterior and posterior projections showing normal physiological tracer uptake in entire skeleton. Prostate specific antigen level was 3 ng/ml

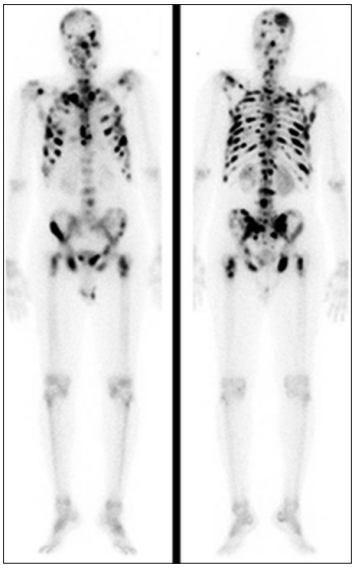

Figure 2: Tc99m-MDP whole body bone scintigraphy in anterior and posterior views showing widespread skeletal metastasis (super scan pattern). Prostate specific antigen level was 52 ng/ml

avoid unnecessary investigations in patients with carcinoma of the prostate who are unlikely to harbor metastatic disease. However, BS are not only time consuming but also expensive. In this retrospective study, we tried to determine the cut-off value of PSA for performing a BS in patients with prostate cancer and no symptoms of bone metastasis. Our data is in corroboration with previously published studies demonstrating the close relationship between serum PSA level and BS positivity.[9-17] In the present study, 110/113 (97.4%) with a serum PSA ≤ 20 ng/mL did not have bone metastasis while only remaining three patients had a positive BS of the cases with serum PSA < 20 ng/ml. However, if the threshold PSA value was increased to values more than 20.0 ng/ml, bone metastasis could not be sufficiently excluded. PSA thresholds to determine the requirement of a BS has been reported in previous studies with a high negative predictive value (NPV).[9-16,19-22] However, in these studies, the NPV at given PSA thresholds varies considerably. A higher percentage of positive BS at equivalent PSA thresholds have been reported in studies with a higher percentage of locally advanced prostate cancer.[8,10,18] A high proportion of patients (80%) with locally invasive cancer were associated with a low NPV for serum PSA ≤ 20 ng/ml for predicting positivity on BS.[18] Similarly, patients with clinically locally advanced tumors revealed higher NPV for serum PSA ≤ 20 ng/ml. Advanced clinical tumor stage has been reported to correlate with BS positivity for metastasis and therefore may account for some of these variations in NPV from study to study.

Many reports have questioned the role of omitting BS investigations in patients with low serum PSA. Although Wolff, *et al.*,[23] reported that 10/237 patients with PSA < 20 ng/ml had positive BS for metastasis; their study did not exclude patients symptomatic for bone metastasis. In our study, all the patients with serum PSA < 20 ng/ml and positive BS were symptomatic for bone metastasis. Bruwer, *et al.*,[18] reported that BSs could not be excluded in patients with prostate cancer on the basis of a low serum PSA, but this was on the basis of results from a population with tumor characteristics significantly different to most other studies. Our results strengthen previous reports in the literature that state that a PSA of ≤ 20 ng/ml is an appropriate cut-off for BS investigation in prostate cancer asymptomatic for bone metastasis.[7,21] However, careful review of these studies indicate significant differences in the study populations and selection bias and hence PSA threshold cut-off.

In conclusion, the results of our study suggest that radionuclide BS in a patient with prostate cancer with serum PSA ≤ 20.0 ng/ml and clinically asymptomatic for bone metastasis is unlikely to yield any positive information and may be omitted. In patients with a serum PSA > 20.0 ng/ml or those with symptoms suggestive of bone metastasis regardless of PSA value, a BS is amply justified.

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