

# PREDICTIVE VALUE OF SERUM PROSTATE SPECIFIC ANTIGEN IN DETECTING BONE METASTASIS IN PROSTATE CANCER

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## ABSTRACT

**Objective:** We determine the utility of Prostate Specific Antigen (PSA) for predicting the presence of skeletal metastasis on Bone Scan (BS) in prostate cancer patients. **Material & Methods:** Retrospective analysis of medical records of 70 consecutive prostate cancer patients subjected to bone scan during the last 2 years was done. 5 cases were excluded due to the following reasons: Serum PSA not available, hormonal or other therapy given prior to serum PSA measurement, and/or Bone Scan, and symptomatic for bone metastasis. In remaining 65 cases, PSA value and bone scan were evaluated. **Results:** BS was found to be positive in 20/65 (31%) and negative in 45(69%) patients. 24 (37%) had serum PSA>100 ng/ml, 25 (38.5%) had PSA of 20 - 100 ng/ml and only 16 (24.5%) had PSA< 20 ng/ml. **Conclusion:** 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 asymptomatic in this group of patients would translate into a significant cost - saving and reduction in their psychological and physical burden.

**Keywords:** Prostate specific antigen, bone scan, prostate cancer.

## ABSTRAK

**Tujuan:** Menentukan kegunaan Prostate Specific Antigen (PSA) untuk memprediksi adanya metastasis tulang pada Bone Scan (BS) pasien kanker prostat. **Bahan & Cara:** Telah dilakukan analisis retrospektif terhadap rekam medis dari 70 pasien kanker prostat yang menjalani BS selama 2 tahun terakhir. 5 kasus ditiadakan karena alasan berikut: PSA serum tidak tersedia, hormonal atau terapi lain yang diberikan sebelum pengukuran serum PSA, dan/atau BS, dan gejala metastasis tulang. Dalam 65 kasus tersisa, nilai PSA dan BS dievaluasi. **Hasil:** BS ditemukan positif pada 20/65 (31%) dan negatif pada 45 (69%) pasien. 24 (37%) memiliki PSA serum>100 ng /ml, 25 (38.5%) memiliki PSA 20-100 ng/ml dan hanya 16 (24.5%) memiliki PSA<20 ng/ml. **Simpulan:** Serum PSA<20 ng/ml memiliki nilai prediktif yang tinggi untuk mencegah kemungkinan terjadinya metastasis tulang. Data kami sesuai dengan hasil studi sebelumnya bahwa BS dilakukan jika PSA >20 ng/ml. Dengan menggunakan batasan ini, investigasi yang tidak perlu dapat dihindari. Pencegahan BS asimtomatik pada kelompok pasien ini akan menghemat biaya yang signifikan dan mengurangi beban psikologis dan fisik mereka.

**Kata Kunci:** Prostate specific antigen, bone scane, kanker prostat.

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## INTRODUCTION

Prostate cancer is the most common cancer in men and is responsible for 19% of all newly diagnosed male cancers.<sup>1</sup> Serum prostate-specific antigen (PSA)-based screening is helpful in early diagnosis and staging of prostate cancer.<sup>2-3</sup> Prostate cancer tends to metastasize to bone. On presentation,

up to 14% of patients have bone metastasis.<sup>4</sup> Radionuclide bone scanning being the most sensitive method plays an important role in detecting bone metastasis in prostate cancer.<sup>5-6</sup> Because of the high incidence of bone metastases, bone scan (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 states 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.<sup>7</sup> However, BS should be considered only if the result is likely to have a strong impact on the management plan. This puts a 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 patients with prostate cancer.<sup>8-10</sup> 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.<sup>9,11-16</sup>

Furthermore, tumor grade and clinical tumor stage along with serum PSA have also been successfully used to predict the presence of bone metastasis.<sup>11,15-18</sup> However, some studies suggest that an appropriate PSA cut-off for these patients may be 15 ng/mL or higher.<sup>10,19-22</sup> Irrespective of tumor stage and grade.

## OBJECTIVE

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.

## MATERIAL & METHODS

A retrospective analysis of medical records of 70 consecutive prostate cancer patients subjected to bone scintigraphy during the last 2 years was done. Five 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 65 cases, PSA value and BS were evaluated.

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

## RESULTS

BS was found to be positive in 20/65 (31%) and negative in 45 (69%) patients. 24 (37%) had serum PSA > 100 ng/ml, 25 (38.5%) had PSA of 20 - 100 ng/ml and only 16 (24.5%) had PSA < 20 ng/ml. The BS positivity with relation to PSA levels has been depicted in table 1.

## DISCUSSION

BS is routinely performed to confirm or exclude bone metastasis in patients with prostate cancer with serum PSA value  $\geq$  20 ng/ml. The rationale behind this is to avoid unnecessary investigations in patients with carcinoma of the prostate who are unlikely to harbor metastatic disease. However, BS is 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.<sup>9-17</sup>

In the present study, 110/113 (97.4%) with a serum PSA  $\leq$  20 ng/ml did not have bone metastasis while only the 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 have been reported in previous studies with a high negative predictive value (NPV).<sup>9-16,19-22</sup>

However, in these studies, the NPV at given PSA thresholds varies considerably. A higher percentage of positive BS at equivalent PSA thresholds has been reported in studies with a higher percentage of locally advanced prostate cancer.<sup>8,10,18</sup>

A high proportion of patients (80%) with locally invasive cancer were associated with a low

**Table 1.** Bone scans results and prostate specific antigen values.

PSA levels	Bone scan		
	Positive (n 24)	Negative (n 41)	RR
> 100 ng/ml (24)	10	14	2.2
20-100 ng/ml (25)	7	18	1.5
< 20 mg ng/ml	3	13	

\* Chi -square P = 0.020 .

NPV for serum PSA  $\leq 20$  ng/ml for predicting positivity on BS.<sup>18</sup> Similarly, patients with clinically locally advanced tumors revealed higher NPV for serum PSA  $\leq 20$  ng/ml. The 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. 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.<sup>23</sup> In our study, all the patients with serum PSA  $< 20$  ng/ml and positive BS were symptomatic for bone metastasis. Bruwer et al. reported that BSs could not be excluded in patients with prostate cancer based on a low serum PSA, but this was based on results from a population with tumor characteristics significantly different from most other studies.<sup>18</sup> Our results strengthen previous reports in the literature that state that a PSA of  $\leq 20$  ng/ml is an appropriate cut-off for BS investigation in prostate cancer asymptomatic for bone metastasis.<sup>7,21</sup> However, a careful review of these studies indicate significant differences in the study populations and selection bias and hence PSA threshold cut-off.

## CONCLUSION

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 asymptomatic in this group of patients would translate into a significant cost - saving and reduction in their psychological and physical burden.

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