



# Retrospective correlation of $^{68}\text{Ga}$ -psma uptake with clinical parameters in prostate cancer patients undergoing definitive radiotherapy

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## Abstract

**Objective** The aim of the study is to investigate the correlation between the intensity of prostate-specific membrane antigen (PSMA) uptake in primary tumor and clinico-pathological characteristics of non-metastatic prostate cancer patients treated with definitive radiotherapy (RT).

**Methods** Using the clinical data of 201 prostate cancer patients who were referred for  $^{68}\text{Ga}$ -PSMA-positron emission tomography (PET/CT) for staging and RT planning, we analyzed the correlations among intermediate- or high-risk disease based on Gleason score (GS), prostate-specific antigen (PSA) level, D'Amico risk group classification, and maximum standardized uptake ( $\text{SUV}_{\text{max}}$ ) of primary tumor.

**Results** Primary tumor was visualized via  $^{68}\text{Ga}$ -PSMA-PET/CT scan in 192 patients (95.5%). The median  $\text{SUV}_{\text{max}}$  of primary tumor and metastatic lymph node were 13.2 (range 3.3–83.7) and 11.4 (range 3.6–64.5), respectively. A significant moderate correlation was observed between PSA level and median tumor  $\text{SUV}_{\text{max}}$  as measured by  $^{68}\text{Ga}$ -PSMA-PET/CT (Spearman = 0.425;  $p < 0.001$ ). Patients with serum PSA > 10 ng/mL, GS > 7, D'Amico high-risk group classification, and pelvic lymph node metastasis had significantly higher tracer uptake in primary tumor than their counterparts. The median  $\text{SUV}_{\text{max}}$  of primary tumor was highest in patients with GS 9. The primary tumor detection rates of  $^{68}\text{Ga}$ -PSMA-PET/CT were 83%, 92%, and 99% for patients with serum PSA ≤ 5.0 ng/mL (14 patients, 7%), PSA 5.1–10.0 ng/mL (45 patients, 22%), and PSA > 10 ng/mL (142 patients, 71%), respectively.

**Conclusions** We demonstrated a correlation between prostate tumor characteristics and PSMA tracer uptake. Patients with serum PSA > 10 ng/mL, GS > 7, D'Amico high-risk group classification, and pelvic lymph node metastasis had significantly higher SUV than their counterparts. In addition, the primary tumor detection rate was higher in patients with serum PSA > 10 ng/mL and GS > 7.

**Keywords** Prostate cancer · Positron emission tomography · Prostate-specific membrane antigen · Staging · Radiotherapy

## Introduction

Prostate cancer is the most frequently diagnosed cancer and the second most common cause of cancer-related deaths in men worldwide [1]. Several treatment options are available, including watchful waiting, hormonal treatment, radical surgery, and radiotherapy (RT); RT may be administered alone or in combination with hormonal therapy. However, definitive RT relies primarily on accurate clinical and radiological tumor staging based on clinical parameters, especially risk group classification. Currently, serum prostate-specific antigen (PSA), clinical T stage, and Gleason score (GS) are used to define prostate cancer risk groups [2]. PSA doubling time

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and PSA density are also used to predict disease outcome, but they are nonspecific in determining prognosis [3].

Histological evaluation of the prostate is required to predict a tumor's biological behavior. However, histopathological findings for prostatectomy and biopsy specimens do not always accurately reflect actual disease status [4, 5]. Discordance between clinical and pathological staging may be observed, and GS of biopsy and prostatectomy specimens may vary. Thus, the use of non-invasive methods to evaluate the entire prostate and the tumor biology before definitive prostate RT is a potentially promising alternative approach.

Gallium-68 ( $^{68}\text{Ga}$ )-labeled prostate-specific membrane antigen (PSMA) ligand, which is a cell surface glycoprotein highly expressed in prostate cancer cells, has emerged as a new promising PET tracer [6]. In primary staging of intermediate- to high-risk prostate cancer patients,  $^{68}\text{Ga}$ -PSMA-PET/CT has demonstrated greater sensitivity and specificity in nodal staging than conventional imaging modalities [7]. Preclinical studies have demonstrated that high PSMA expression is significantly correlated with high GS [8, 9]. A few studies have evaluated the correlation between PSMA uptake and tumor characteristics [10, 11]. However, these studies included a limited number of patients, who were treated with heterogeneous treatment modalities and had metastatic disease. Thus, we sought to investigate the correlation between intensity of PSMA uptake in primary tumor and the clinical and pathological characteristics in non-metastatic prostate cancer patients planned to be treated with definitive RT.

## Materials and methods

### Patient selection

Clinical data of 201 prostate cancer patients who were intended for treatment with definitive intensity-modulated RT between June 2014 and December 2017 were retrospectively analyzed. The inclusion criteria were as follows: referral for  $^{68}\text{Ga}$ -PSMA-PET/CT for staging and/or RT planning and intermediate- or high-risk disease according to the D'Amico staging system [2]. The exclusion criteria were as follows: patients who had received hormone therapy or chemotherapy before  $^{68}\text{Ga}$ -PSMA-PET/CT delivery and patients with radical prostatectomy or those previously treated with radical RT. Patients with clinical and radiological evidence of distant metastasis were also excluded. In all patients, prostate cancer was verified histologically with transrectal ultrasound (TRUS)-guided biopsy, and the GS results of TRUS biopsy served as the reference for the PET findings. Written informed consent was obtained from all patients.

### $^{68}\text{Ga}$ -PSMA-PET/CT Imaging

The patients were imaged using a dedicated PET/CT system (Discovery-STE 8, General Electric Medical System, Milwaukee, WI, USA). The median activity of intravenously injected  $^{68}\text{Ga}$ -PSMA was 150 MBq (range 78–199 MBq). During the distribution phase, the patients were asked to lie in the supine position in a quiet room. Combined image acquisition began 60 min after the  $^{68}\text{Ga}$ -PSMA injection. The patients were scanned on a flat-panel carbon fiber-based composite table. An unenhanced CT scan (5-mm-thick slice) of the base of the skull down to the inferior border of the pelvis was obtained using a standardized protocol (140 kV and 80 mA). Subsequently, a PET scan of the base of the skull down to the inferior border of the pelvis (6–7 bed positions, 3 min per bed position) was acquired in three-dimensional mode without repositioning the patient on the table. CT and PET images were obtained while each patient breathes shallowly. Attenuation was corrected using the CT images.

### Image analysis

PET/CT images were interpreted independently by two experienced nuclear medicine physicians, each with more than 15 years of clinical experience; these physicians were aware of all the available clinical data. Any disagreement was resolved by consensus. All transrectal-guided biopsies were performed before the  $^{68}\text{Ga}$ -PSMA-PET/CT scan. The site of the primary tumor within the prostate gland was known to the  $^{68}\text{Ga}$ -PSMA-PET/CT interpreters based on the TRUS biopsy result. Initially, they assessed whether the primary tumor was visually distinguishable from the surrounding prostate tissue. The tumor was judged positive when focal tracer uptake of the tumor was higher than that of the surrounding prostate tissue. For calculation of the maximum standardized uptake ( $\text{SUV}_{\text{max}}$ ) of the primary tumor, volumes of interest (VOIs) were drawn automatically with a manually adapted isocontour threshold centered on lesions with focally increased uptake; these lesions correspond to the tumor site verified by TRUS biopsy. In cases where the primary tumor could not be clearly identified from the PET images, the VOIs were placed over the area where the primary tumor was found based on the TRUS biopsy result. As regards lymph node evaluation, any focal uptake higher than the surrounding background activity that does not correspond to physiologic tracer accumulation was considered pathologic and suggestive of malignancy.

No quantitative cut-off for prostate cancer lesions has been defined to date. The  $\text{SUV}_{\text{max}}$  values of metastases

were calculated within VOIs placed over the sites of pathologic tracer accumulation corresponding to the tumor site. In addition,  $SUV_{max}$  values were measured in areas of normal prostate tissue with physiologic tracer uptake; these measurements were obtained from patients with available magnetic resonance imaging (MRI). Healthy prostate tissue was selected in correlation with MRI, and a VOI of  $1 \pm 0.06 \text{ cm}^3$  was chosen for normal prostate tissue.  $SUV_{max}$  was separately measured for the entire cohort and in patients with MRI. For image analysis,  $SUV_{max}$  was chosen because  $SUV_{mean}$  depends on the volume of interest drawn by the investigator, whereas  $SUV_{max}$  is operator-independent [12].

### Statistical analysis

Statistical analysis was performed using SPSS 20.0 software (SPSS for Windows, IBM Corp., Armonk, NY, USA). Descriptive analysis was performed by calculating the mean, standard deviation, range, and median. Correlations of GS, PSA, and D'Amico risk group classification with  $SUV_{max}$  of primary tumor were described descriptively and then evaluated using Mann–Whitney *U* test and Kruskal–Wallis test. Spearman correlation coefficient was used to assess the correlation between primary tumor  $SUV_{max}$  and serum PSA values. For multivariate analysis, the possible factors identified with univariate analysis were further entered into the logistic regression analysis to determine independent predictors of lymph node metastasis. Receiver operating characteristic (ROC) curves with respective areas under the curve [AUC] were generated for the prediction of cut-off values to differentiate high-risk patients and patients with high PSA values. A *p* value of  $< 0.05$  indicated statistical significance.

### Results

Patient and tumor characteristics are summarized in Table 1. Primary tumor was visualized in 192 patients (95.5%) in  $^{68}\text{Ga}$ -PSMA-PET/CT scan. Ninety-seven patients had GS 7 disease; of them, 47 (23.4%) had GS 3 + 4 disease, whereas 50 (24.9%) had GS 4 + 3 disease. The median  $SUV_{max}$  of primary tumor was 13.2 (range 3.3–83.7) (Fig. 1a), whereas that of normal prostate tissue was 1.7 (range 1.1–3.5).

In 72 patients (35.8%), a pathologic  $^{68}\text{Ga}$ -PSMA uptake corresponding to lymph node metastases was detected, with a median  $SUV_{max}$  of 11.4 (range 3.6–64.5) (Fig. 1b). The median  $SUV_{max}$  of tumors was higher in patients with lymph node metastases than in those without malignant lymph node involvement ( $25.0 \pm 21.3$  vs.  $14.7 \pm 10.6$ ,  $p < 0.001$ ) (Fig. 3d).

Clinical *T* stage, PSA, GS, and  $SUV_{max}$  of primary tumor were significantly associated with lymph node metastasis

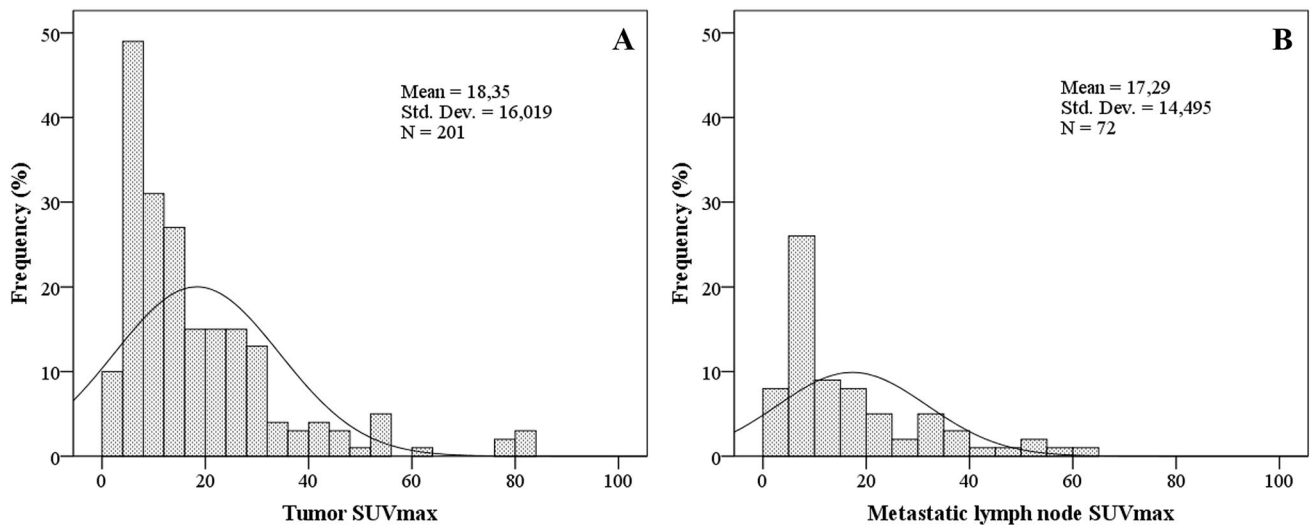
**Table 1** Patient and tumor characteristics

Characteristics	Patient number	%
Age (years), (median, range)	68 (45–85)	
PSA (ng/dL), (mean, range)	20.3 (2.1–301.0)	
Clinical tumor stage		
T2a	6	3.0
T2b	68	33.8
T2c	33	16.4
T3a	33	16.4
T3b	56	27.9
T4	5	2.4
Nodal stage		
N0	129	64.2
N1	72	35.8
Gleason score		
7	97	48.3
8	47	23.4
9	48	23.9
10	9	4.4
Risk group		
Intermediate	42	20.9
High	159	79.1
Hormonotherapy		
None	29	14.4
Neoadjuvant	149	74.1
Adjuvant	23	11.5

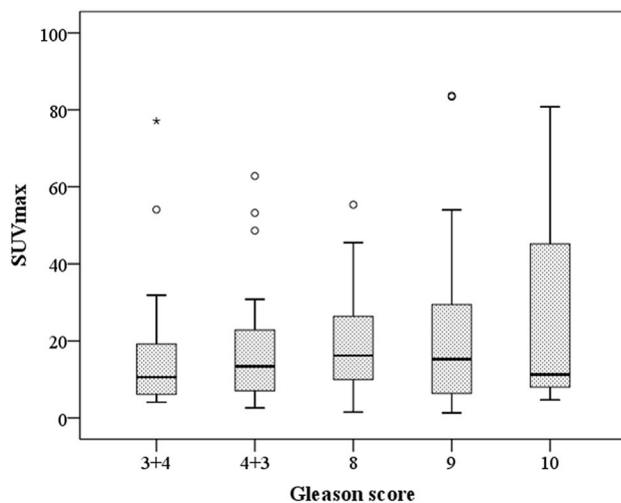
according to our univariate logistic regression analysis. In the multivariate regression analysis, a 1-unit change of clinical *T* stage, PSA, GS, or  $SUV_{max}$  was significantly correlated with lymph node metastasis, with an AUC of 0.677 (CI = 0.617–0.738) for PSA, 0.637 (CI = 0.573–0.701) for  $SUV_{max}$  of primary tumor, 0.713 (CI = 0.657–0.769) for clinical *T* stage, and 0.667 (CI = 0.607–0.728) for GS, not statistically different from each other.

### Correlation between GS and $SUV_{max}$

The correlation of GS scores with  $SUV_{max}$  of primary tumor is shown in Fig. 2, and detailed information on GS group is listed in Table 2. For the entire cohort, patients with  $GS > 7$  have significantly higher mean  $SUV_{max}$  values than those with GS 7 disease ( $20.9 \pm 18.0$  vs.  $15.6 \pm 13.1$ ;  $p = 0.02$ ) (Fig. 3b). For subgroup analysis, correlations of intraprostatic  $SUV_{max}$  with clinical parameters were determined using the data from multiparametric MRI, where  $SUV$  was measured from the lesions detected through MRI. In 99 patients (49.3%) with MRI,  $SUV_{max}$  was significantly higher in patients with GS 7 disease than in those with  $GS > 7$  disease ( $21.5 \pm 16.8$  vs.  $15.8 \pm 12.7$ ;  $p = 0.03$ ) (Table 3). The median  $SUV_{max}$



**Fig. 1** Histogram of the distribution of maximum standardized uptake (SUV<sub>max</sub>) of **a** primary tumor and **b** pelvic lymph nodes



**Fig. 2** Box plots of maximum standardized uptake (SUV<sub>max</sub>) of primary tumor according to Gleason score

**Table 2** Median and mean maximum standardized uptake (SUV<sub>max</sub>) of primary tumor according to Gleason scores

Gleason score	N	Median SUV <sub>max</sub> (range)	Mean SUV <sub>max</sub> ± SD
7	97	12.0 (2.6–77.1)	15.6 ± 13.1
8	47	16.2 (1.5–55.3)	19.3 ± 12.4
9	48	15.3 (1.3–83.7)	21.1 ± 19.4
10	9	11.3 (4.7–80.8)	28.2 ± 21.5

of primary tumor was highest in patients with GS 9. The median SUV<sub>max</sub> of the subgroups with GS 3 + 4 and 4 + 3 did not significantly differ (10.6 vs. 13.4;  $p = 0.18$ ).

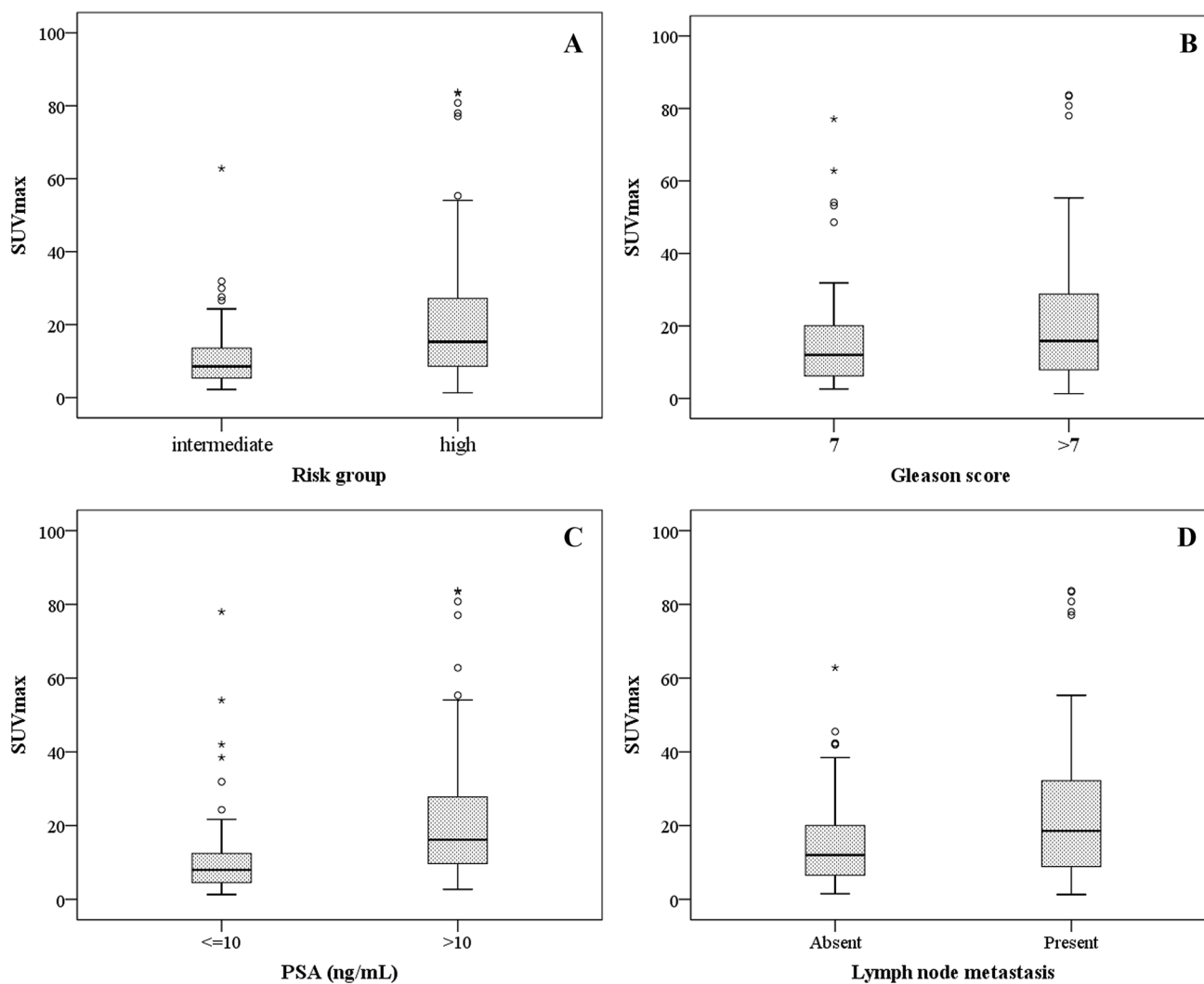
Of the nine patients without <sup>68</sup>Ga-PSMA uptake, six had GS 3 + 4 disease, one had GS 4 + 3 disease, and two had GS 5 + 4 disease.

### Correlation between PSA and SUV<sub>max</sub>

Correlation between PSA values and primary tumor SUV<sub>max</sub> is presented in Fig. 4. A significant moderate correlation was observed between PSA level and median tumor SUV<sub>max</sub> measured by <sup>68</sup>Ga-PSMA-PET/CT (Spearman = 0.425;  $p < 0.001$ ). PSMA tracer uptake was higher in patients with PSA ≥ 10 ng/mL than in those with PSA < 10 ng/mL, with a median SUV<sub>max</sub> of 16.2 (range 3.7–83.7) vs. 8.0 (range 3.3–78.0) ( $p < 0.001$ ), as shown in Fig. 3c.

The primary tumor detection rates of <sup>68</sup>Ga-PSMA-PET/CT were 83%, 92%, and 99% for patients with serum PSA ≤ 5.0 ng/mL (14 patients, 7%), PSA 5.1–10.0 ng/mL (45 patients, 22%), and PSA > 10 ng/mL (142 patients, 71%), respectively (Fig. 5a). Moreover, the pelvic lymph node detection rate of <sup>68</sup>Ga-PSMA-PET/CT was higher in patients with serum PSA > 10 ng/mL than in patients with serum PSA ≤ 5.0 ng/mL or with PSA 5.1–10.0 ng/mL (Fig. 5b). In ROC analysis, the area under the curve [13] was 0.646 ( $p < 0.001$ ; 95% confidence interval, 0.557–0.735), and the cut-off value of SUV<sub>max</sub> in the present study was determined to be 11.5 for differentiating patients with PSA > 10 ng/mL.

SUV<sub>max</sub> of primary tumor was significantly lower in intermediate-risk patients than in high-risk patients based on the D'Amico scale (11.9 ± 10.6 vs. 20.4 ± 16.9,  $p < 0.001$ )



**Fig. 3** Box plot of maximum standardized uptake ( $SUV_{max}$ ) of primary tumor according to **a** D’Amico risk group, **b** Gleason score (GS), **c** serum prostate-specific antigen (PSA) values, and **d** pelvic lymph node status

**Table 3** Correlation between maximum standardized uptake ( $SUV_{max}$ ) and Gleason score (GS) in the entire cohort and in patients with multiparametric MRI

Gleason score	Median $SUV_{max}$	Mean $SUV_{max} \pm SD$	<i>p</i>
Entire cohort ( <i>n</i> = 201)			
7	12.0	15.6 ± 13.1	0.02
> 7	18.0	20.9 ± 15.9	
Patients with multiparametric MRI ( <i>n</i> = 99)			
7	12.2	15.8 ± 12.7	0.03
> 7	18.6	21.5 ± 16.8	

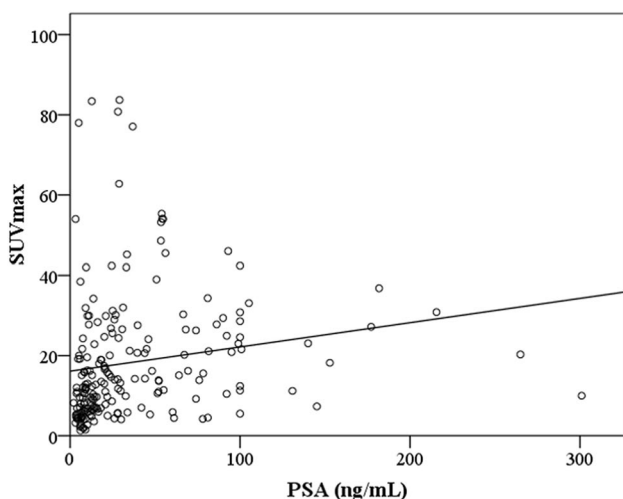
(Fig. 3a). The AUC was 0.726 (95% CI 0.647–0.805;  $p < 0.001$ ), and the cut-off value of  $SUV_{max}$  was 11.7 for differentiating high-risk patients.

## Discussion

In this study, we demonstrated a correlation between prostate tumor characteristics and  $^{68}\text{Ga}$ -PSMA tracer uptake. Patients with serum PSA > 10 ng/mL, GS > 7, D’Amico high-risk group classification, and pelvic lymph node metastasis had significantly higher tracer uptake in primary tumor than their counterparts. The primary tumor detection rate of  $^{68}\text{Ga}$ -PSMA-PET/CT was 95.5%, and tumor detection rates were higher in patients with serum PSA > 10 ng/mL and GS > 7.

Prostate cancer cells typically show increased PSMA expression, enabling targeted PET imaging with PSMA ligands; among these ligands,  $^{68}\text{Ga}$ -PSMA has demonstrated high affinity for PSMA [14, 15]. Besides prostate cancer cells, normal prostatic tissue also exhibits PSMA expression as proved by immunohistochemical studies





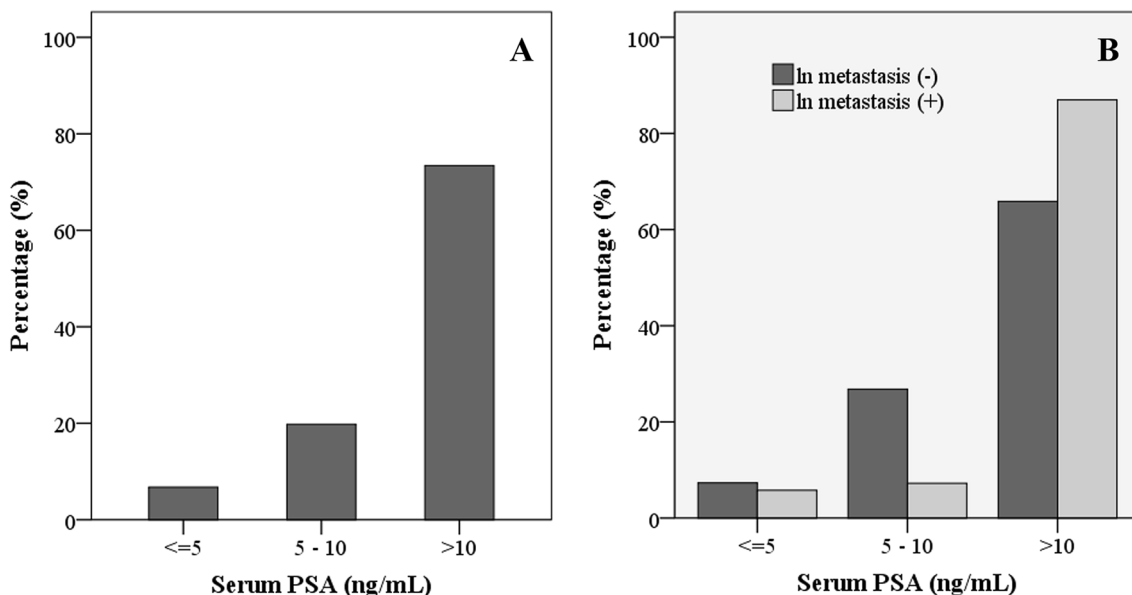
**Fig. 4** Scatter plot showing the correlation between serum prostate-specific antigen (PSA) values and maximum standardized uptake ( $SUV_{max}$ ) of primary tumor

[16, 17]. However, the intensity of tracer uptake is lower in benign prostate tissue than in malignant cells [10, 18], consistent with our current findings. Although increased tracer uptake in prostate cancer cells has been demonstrated, in some cases, minimal or no tracer uptake was observed despite a positive diagnosis of prostate cancer. Maurer et al. [7] reported that 8.4% of prostate tumors showed no increase or only a slight increase in tracer accumulation in 30 patients with intermediate- to high-risk prostate cancer staged with  $^{68}\text{Ga}$ -PSMA-PET/CT. In another study, Budäus et al. [19] reported that 7.1% of primary tumors were negative based

on  $^{68}\text{Ga}$ -PSMA-PET/CT images. Uprimny et al. [10] also found that 8.9% of primary tumors were not distinguished by  $^{68}\text{Ga}$ -PSMA-PET/CT. In the current study, the absence of tracer uptake in primary tumor showed a 4.5% incidence, which is lower than that reported in previous studies; this finding may be due to the exclusion of patients with GS 6 disease.

We investigated the correlation between PSMA uptake and several clinical and pathological parameters. Despite significant changes in the clinical and histologic diagnosis of prostate cancer, the Gleason grading system remains one of the most powerful prognostic predictors in prostate cancer. However, this system has undergone significant revisions and continues to have deficiencies that can potentially impact patient care. The correct diagnosis and grading of prostate cancer are crucial for a patient’s prognosis and therapeutic options. The 2005 and 2014 International Society of Urological Pathology grading consensus conferences have improved the overall Gleason grading system [20, 21]. However, this system continues to have limitations which a new prostate cancer grading system would improve upon.

Studies have demonstrated that patients with GS 6 and 7 display significantly lower PSMA accumulation than those with  $GS > 7$  [10, 11, 18]. In the current study, we analyzed  $SUV_{max}$  according to the GS. Although the clinical behavior of GS 3 + 4 and 4 + 3 differs, primary tumor  $SUV_{max}$  did not significantly differ. The median  $SUV_{max}$  values were highest in patients with GS 9, and no significant difference was observed between GS groups. Studies have shown that  $SUV_{max}$  is lower in GS 10 tumors than in GS 9 tumors—consistent with our findings—assuming that the lower



**Fig. 5** Detection rate of **a** primary tumor and **b** lymph node metastasis according to serum prostate-specific antigen (PSA) values

intraprostatic tracer uptake is caused by dedifferentiation of tumor cells in GS 10 prostate carcinomas [11, 18, 22]. We performed an additional analysis in patients with available multiparametric MRI to better define the tumor sites. Again, primary tumor  $SUV_{max}$  values significantly differed between patients with GS 7 and GS > 7.

Studies have demonstrated a correlation between PSA levels and PSMA tracer uptake, especially based on the biochemical evidence, in recurrent prostate cancer patients. [10, 18, 23–26]. Our results support this finding, as patients with higher PSA values had significantly higher primary  $SUV_{max}$ . Moreover, with increasing PSA values, the primary tumor detection rate of  $^{68}\text{Ga}$ -PSMA-PET/CT also increased. Primary tumor could not be visualized in only 1 of the 142 patients with PSA > 10 ng/mL, and the tumor detection rate in patients with PSA > 10 ng/mL was 99%. Similarly, Meyrick et al. [26] reported that primary tumor was not detected by  $^{68}\text{Ga}$ -PSMA-PET/CT in only 1 of the 35 patients with PSA > 10 ng/mL. Uprimny et al. [10] also found a significant difference in tracer uptake between patients with PSA < 10 ng/mL and those with PSA  $\geq$  10 ng/mL, consistent with our findings. Furthermore, the pelvic lymph node detection rate of  $^{68}\text{Ga}$ -PSMA-PET/CT was higher in patients with PSA > 10 ng/mL than in their counterparts.

Risk group identification is extremely important especially for definitive RT, because RT fields and doses and hormone therapy delivery are decided on according to risk. In the current study, we analyzed only intermediate- and high-risk patients according to the D'Amico classification [2], and found that mean  $SUV_{max}$  is significantly higher in tumors with high D'Amico risk classification than in tumors with intermediate-risk group classification. Furthermore, promising data show that  $^{68}\text{Ga}$ -PSMA-PET/CT demonstrates higher sensitivity and specificity for nodal staging compared with CT and other tracers [7, 27]. Investigating 90 patients, Uprimny et al. [10] found 82 lymph nodes with pathological tracer uptake in 26.7% of the patients, and the median  $SUV_{max}$  of primary tumor was significantly higher in patients with metastatic lymph nodes (18.7 vs. 9.7;  $p < 0.001$ ). In the current study, 72 patients (35.8%) had a pathologic  $^{68}\text{Ga}$ -PSMA uptake in lymph nodes, and the median  $SUV_{max}$  of tumors was higher in patients with lymph node metastases than in those without malignant lymph node involvement (25.0 vs. 14.7;  $p < 0.001$ ).

Histological evaluation of the prostate is required to predict a tumor's biological behavior. However, histological evaluation involves invasive biopsy procedures and is subject to sampling error. A discordance between clinical and pathological staging may be observed, and GS of biopsy and prostatectomy specimens may vary. The TRUS-guided 10–12 core biopsy is frequently used to diagnose prostate cancer [28]. Unfortunately, biopsy has relatively low sensitivity for high-grade cancer detection, with 25–30% of men with low-risk disease

being upgraded at confirmatory biopsy or radical prostatectomy [29]. Thus, our results must be interpreted with caution. To better define prostate tumor, we used multiparametric MRI in 99 patients. We also found a similar correlation between primary tumor  $SUV_{max}$  in the entire cohort and in patients with multiparametric MRI. Nevertheless,  $^{68}\text{Ga}$ -PSMA-PET/CT seems to be a promising diagnostic tool for the identification of malignant segments in the prostate. These findings are in accordance with the results of a study involving 30 high-risk prostate cancer patients who underwent  $^{68}\text{Ga}$ -PSMA-PET/CT imaging prior to radical prostatectomy. Budäus et al. [19] reported that in 92.9% of the patients, intraprostatic tumor foci were predicted correctly. Therefore, PSMA PET/CT may play an important role not only in detecting metastases but also in localizing tumor segments in the prostate. For definitive RT, identification of high malignant intraprostatic lesion is extremely helpful because of the high risk of local recurrence of these so-called dominant intraprostatic tumor lesions after local treatment [30, 31]. We previously demonstrated the dosimetric feasibility of simultaneous-integrated boost radiation dose for intraprostatic lesion based on an MRI-guided definition of dominant intraprostatic tumor lesions [32]. It has recently been shown that delineation of target volume and dominant intraprostatic tumor lesions is also feasible with  $^{68}\text{Ga}$ -PSMA-PET/CT [33]. Because of some benefits of PET compared with MRI, irradiation planning based on PSMA-PET/CT would be of great interest.

Our study is not without inherent limitations because of its retrospective nature and the associated selection biases. Moreover, we could not perform histological verification of primary tumor and lymph nodes; thus, we could not exclude the PSMA-PET false-positive areas. Despite the high specificity in lymph nodes, the reported sensitivity of  $^{68}\text{Ga}$ -PSMA-PET/CT is only 60%–70% due to lower detection rates of small lymph node metastasis, necessitating caution when interpreting negative scans. In addition,  $^{68}\text{Ga}$ -PSMA-PET/CT is not accepted as a routine imaging modality for prostate cancer staging. Because the conclusion of the present study is premature, validation of this study through other large-scale studies are required to interpret these findings in clinical practice. Despite these inherent limitations, this study is important due to the relatively high patient number and the homogeneous patient population, wherein we analyzed only the non-metastatic treatment-naïve patients undergoing definitive RT and excluded patients with relapse after local treatment.

## Conclusion

$^{68}\text{Ga}$ -PSMA-PET/CT was introduced for primary tumor staging of prostate cancer, and various studies have demonstrated that primary tumors may display different PSMA

uptake intensities. Patients with serum PSA > 10 ng/mL, GS > 7, D'Amico high-risk group classification, and pelvic lymph node metastasis had significantly higher SUV than their counterparts. The primary tumor detection rate of <sup>68</sup>Ga-PSMA-PET/CT was 95.5%, and tumor detection rates were higher in patients with serum PSA > 10 ng/mL and GS > 7. Hence, our data can be used as a basis for further prospective studies.

**Funding** None.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflicts of interest.

**Ethical approval** All the procedures in studies involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Baskent University Institutional Review Board (Project no: KA19/45) and was supported by the Baskent University Research Fund.

**Informed consent** Informed consent was obtained from all participants included in the study.

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