Relationships between serum PSA levels, Gleason scores and results of 68Ga-PSMAPET/CT in patients with recurrent prostate cancer

Yasemin Sanli1 · Serkan Kuyumcu1 · Oner Sanli2 · Fikret Buyukkaya3 · Ayça İribaş4 · Goksel Alcin1 · Emin Darendeiller4 · Yasemin Ozluk5 · Sevda Ozel Yildiz6 · Cüneyt Turkmen1

Received: 26 April 2017 / Accepted: 28 August 2017 © The Japanese Society of Nuclear Medicine 2017

Abstract

Aim To investigate the relationship between serum PSA level, Gleason score of PCa and the outcomes of Ga68-PSMA PET/CT in patients with recurrent PCa.

Methods A total of 109 consecutive patients (median age 71 years; range 48–89 years) who had PSA recurrence after RP and/or hormonotherapy and/or radiotherapy were included in this study. Local recurrences, lymph node metastasis (pelvic, abdominal and/or supradiaphragmatic), bone metastases (oligometastatic/multimetastatic) and other metastatic sites (lung, liver, brain, etc) were documented.

Results In 91 (83.4%) patients at least one lesion characteristic for PCa was detected by 68Ga-PSMA PET/CT. The median serum total PSA (tPSA) was 6.5 (0.2–640) ng/ml. There was a significant difference between 68Ga-PSMA PET/CT positive and negative patients in terms of serum total PSA value. No statistical significance was found between positive and negative 68Ga-PSMA PET/CT findings in terms of Gleason score. Local recurrence was detected in 56 patients, whereas lymph node metastases were demonstrated in 46 patients. Pelvic nodal disease was the most frequent presentation followed by abdominal and supradiaphragmatic nodal involvement. Bone metastases [oligometastasis, (n = 20); multimetastasis, (n = 35)] were also detected in 55 patients. In the ROC analysis for the study cohort, the optimal cut-off value of total serum PSA was determined as 0.67 ng/ml for distinguishing between positive and negative 68Ga-PSMA PET/CT images, with an area under curve of 0.952 (95% CI 0.911–0.993).

Conclusions 68Ga-PSMA PET/CT was found to be an effective tool for the detection of recurrent PCa. Even though no relationship was detected between the GS and 68Ga-PSMA PET/CT findings, serum total PSA values may be used for estimating the likelihood of positive 68Ga-PSMA PET/CT results.

Keywords 68Ga-PSMA · Recurrent prostate cancer · PSA value · Gleason score

Introduction

Prostate cancer (PCa) recurrences after curative intent are mostly detected with an increase in serum prostate specific antigen (PSA) levels. This happens in 20–30% of patients after radical prostatectomy (RP) and in up to 60% after radiotherapy [1, 2]. After confirmation of recurrence, some treatment alternatives such as salvage RP, radiotherapy or systemic therapy is initiated. On the other hand, primary hormonal treatment is the most efficient treatment alternative in the metastatic stage of the disease. It however, generally ends up with a castration resistant state within 18–24 months [3]. Meanwhile, there is some evidence that
local treatment of solitary or oligometastatic recurrence of PCa may enhance the effectiveness of current therapeutic strategies and benefit certain patients [4].

According to the Chemo-Hormonal Therapy vs. Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer (CHAARTED) study, the timing of chemotherapy was changed due to a significant overall survival advantage (14 months) in patients receiving docetaxel and androgen deprivation therapy (ADT) in comparison with ADT alone [5]. This trial also put into practice the concept of high volume or low volume disease according to the extension of the metastatic disease. High volume disease was defined as visceral metastasis and/or four or more bone metastasis with at least one beyond the pelvis. For either of these situations, it is mandatory to know the location and extent of the disease. Reliable imaging modalities aid in choosing the best treatment alternative that minimizes unnecessary treatments which may cause side effects and have a negative impact on quality of life.

Prostate specific membrane antigen (PSMA) is a type II membrane glycoprotein that is expressed by the prostate gland, salivary gland, renal proximal tubule and ileum but most highly expressed by prostate cancers. Recent studies have confirmed the location of the PSMA gene on chromosome 11p [6]. Ga68-PSMA PET/CT is an emerging imaging modality that has been reported to be associated with better outcomes in patients with recurrent PCa even at lower levels of serum PSA [7]. These results are generally attributed to PSMA overexpression in higher grade, metastasized, or castration resistant PCa cells and its transmembrane location.

For this reason, this imaging modality is becoming the standard of care for the surveillance of patients with recurrent disease.

Among the parameters that are used for the management of PCa, serum PSA level and Gleason score obtained either from TRUS biopsy or RP specimens are the most common tools used for the decision-making process. Accordingly, the aim of the present real life study is to investigate the relationship between serum PSA level, Gleason score of PCa and the outcomes of Ga68-PSMA PET/CT in patients with recurrent PCa.

### Materials and methods

#### Patient characteristics

68Ga-PSMA PET/CT scans of 198 PCa patients were retrospectively reviewed and 109 consecutive patients (median age 71 years; range 48–89 years) who had PSA recurrence after RP and/or hormonotherapy and/or radiotherapy were included in this study. All patients underwent at least one therapy protocol as summarized in Table 1. Median Gleason score was 7 (range 5–9). Verification of PCa metastasis with 68Ga-PSMA PET/CT scan was done on the basis of clinical evaluation considering the patient’s past history, clinical symptoms, Gleason score of PCa and the most recent serum total PSA values. In this study, lesions detected in 3 or fewer localized areas outside the prostate are accepted as suggestive for oligometastatic disease, whereas lesions identified in more than 3 locations were accepted as multimetastatic disease [8]. This retrospective study was approved by our institutional review board (61/2016). Additionally, written informed consent was obtained from all patients recruited to the present study.

#### Table 1  Treatment groups recruited to the present study

<table>
<thead>
<tr>
<th>Therapy</th>
<th>N</th>
<th>Mean PSA level ng/ml (min–max)</th>
<th>GS mean (min–max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical prostatectomy</td>
<td>25</td>
<td>7.8 (0.2–110)</td>
<td>7.32 (5–9)</td>
</tr>
<tr>
<td>Hormonal therapy</td>
<td>15</td>
<td>49.4 (2.5–437)</td>
<td>8.4 (7–9)</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>8</td>
<td>4.63 (2.0–15)</td>
<td>6.8 (6–8)</td>
</tr>
<tr>
<td>Hormonal therapy + radiotherapy</td>
<td>23</td>
<td>24.2 (0.29–168.5)</td>
<td>8.0 (7–9)</td>
</tr>
<tr>
<td>Radical prostatectomy + hormonal therapy</td>
<td>11</td>
<td>30.1 (0.26–437)</td>
<td>7.0 (5–9)</td>
</tr>
<tr>
<td>Radical prostatectomy + radiotherapy</td>
<td>6</td>
<td>1.8 (0.3–7.5)</td>
<td>7.3 (6–9)</td>
</tr>
<tr>
<td>Hormonal therapy + chemotherapy</td>
<td>3</td>
<td>265.7 (103.9–570.2)</td>
<td>6.6 (5–9)</td>
</tr>
<tr>
<td>Radical prostatectomy + hormonal therapy + radiotherapy</td>
<td>3</td>
<td>31.2 (1.1–89)</td>
<td>7.6 (7–9)</td>
</tr>
<tr>
<td>Radical prostatectomy + hormonal therapy + chemoradiotherapy</td>
<td>7</td>
<td>183.6 (12.8–640)</td>
<td>7.4 (5–9)</td>
</tr>
<tr>
<td>Hormonal therapy + chemoradiotherapy</td>
<td>5</td>
<td>117.5 (29.3–133.7)</td>
<td>7.6 (5–9)</td>
</tr>
<tr>
<td>Chemoradiotherapy</td>
<td>1</td>
<td>10.5</td>
<td>8</td>
</tr>
<tr>
<td>Radical prostatectomy + hormonal therapy + chemotherapy</td>
<td>1</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Radical prostatectomy + chemoradiotherapy</td>
<td>1</td>
<td>18</td>
<td>8</td>
</tr>
</tbody>
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Radiolabelling was carried out with a fully automated radiopharmaceutical synthesis device (Scintomics) based on a modular concept and good manufacturing practice-grade disposable cassettes and reagent kit (ABX). $^{68}$Ga-chloride was obtained by elution of a $^{68}$Ge/$^{68}$Ga generator (iThemba Labs, 1110 MBq reference activity) with 8 ml 0.6 N HCl solution. The $^{68}$Ga-chloride solution was added to 25 µg PSMA I&T (GMP quality) and pH adjusted to 4.5 with buffer solution. The resulting solution was heated to 95 °C for 20 min, diluted and cooled with saline and transferred to a C-18 reversed-phase cartridge for final product purification. $^{68}$Ga-PSMA was eluted with 1 ml ethanol/water (1:1) and diluted with 9 ml sterile-filtered saline solution. The resulting solution contained >500 MBq of $^{68}$Ga-PSMA with average radiochemical yields of >80% and <10% ethanol in physiological saline solution. Radiochemical purity of $^{68}$Ga-PSMA >95% was determined by HPLC. The $^{68}$Ga-PSMA complex solution was administered to patients via an intravenous bolus (range 1406–2035 MBq).

$^{68}$Ga-PSMA PET/CT was performed at 45–60 min after the intravenous injection of approximately 185 MBq of $^{68}$Ga-PSMA on a dedicated PET/CT scanner (Biograph TruePoint PET/CT; Siemens Healthcare). An iodine-based, water-soluble high-contrast agent was administered orally to all patients. CT images were acquired on a spiral 6-slice CT scanner, with a slice thickness of 4 mm. After the transmission scan, 3-dimensional PET images were acquired for 3 min per bed position for 6–8 bed positions. CT-based attenuation correction of the emission images was used. PET images were reconstructed by the iterative method using ordered-subset expectation maximization (two iterations and eight subsets) with a filter size of 5 mm. After completion of the PET acquisition, the reconstructed PET images, CT images, and fused images of matching pairs of PET and CT images were reviewed using the dedicated software (TrueD VE31A; Siemens).

Image analysis

All images were interpreted by 2 board-certified nuclear medicine physicians. Local recurrences, lymph node metastases (pelvic, abdominal and/or supradiaphragmatic), bone metastases (oligometastatic/multimetastatic) and other metastatic sites (lung, liver, pleural metastases, etc.) were documented. Visual interpretation was the main criterion for reaching the final diagnosis.

Statistical analysis

The performance of $^{68}$Ga-PSMA PET/CT in relation to the trigger PSA was assessed by receiver operating characteristics (ROC) curves generated by plotting sensitivity vs. 1-specificity. To compare serum PSA levels in patients with positive and negative $^{68}$Ga-PSMA PET/CT findings, Mann Whitney $U$ test was used. Meanwhile to compare $^{68}$Ga-PSMA PET/CT findings in terms of Gleason scores (5–6 vs. 7 vs. >8), Chi-square test was utilized. Statistical significance was assumed for $p$ values less than 0.05. Statistical analyses were performed using IBM SPSS statistics version 21.

Results

In 91 (83.4%) of 109 patients at least one lesion characteristic for PCa was detected in $^{68}$Ga-PSMA PET/CT. The median (min–max) serum total PSA (tPSA) was 6.5 (0.2–640) ng/ml. There was a significant difference between $^{68}$Ga-PSMA PET/CT positive [mean 48.05 ± 105.6; median (min–max) 9.14 (0.27–640 ng/ml)] and negative patients [mean 0.76 ± 1.0; median (min–max) 0.36 (0.2–4.4) ng/ml] in terms of serum total PSA value ($Z$ 6.043; $p < 0.001,$ Mann Whitney $U$ test).

Local recurrence was detected in 56 patients and lymph node (LN) metastases in 46 patients. Pelvic nodal disease was the most frequent presentation ($n = 38$) followed by abdominal ($n = 27$) and supradiaphragmatic ($n = 11$) nodal involvement. All LNs that demonstrated $^{68}$Ga-PSMA uptake were considered pathological. Bone metastases [oligometastasis, ($n = 20$); multimetastasis, ($n = 35$)] were also detected in 55 patients (Table 2).

In the present cohort, no isolated visceral metastasis was detected. Of patients with visceral metastasis, 8 patients had metastatic pulmonary nodules on CT images in which 4 were demonstrated to have $^{68}$Ga-PSMA uptake. Despite the fact that the remaining patients were also thought to have newly developed pulmonary metastasis based on their non-contrast CT images, they were scheduled for follow-up visits for their $^{68}$Ga-PSMA non-avid lesions because of their advanced characteristics.

<table>
<thead>
<tr>
<th>Table 2 Regions of lesions with $^{68}$Ga-PSMA uptake</th>
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<tr>
<td>Region</td>
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<tr>
<td>Local recurrence</td>
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<tr>
<td>Lymph node metastases</td>
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<tr>
<td>Pelvic</td>
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<tr>
<td>Abdominal</td>
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<td>Supra diafragmatic</td>
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<td>Bone metastases</td>
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<td>Oligometastases</td>
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<tr>
<td>Multimetastatic</td>
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<td>Other metastatic sites</td>
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disease stage (Fig. 1). On the other hand, one patient who demonstrated diffuse low $^{68}$Ga-PSMA uptake at the apical posterior segment of the upper lobe of the left lung was thought to have inflammatory changes and again scheduled for follow-up visits (Fig. 2). All metastatic lesions in the liver ($n=5$) demonstrated significant $^{68}$Ga-PSMA uptake. Meanwhile, $^{68}$Ga-PSMA uptake in 2 patients with meningioma was also false positively interpreted as brain metastases. However, one of these patients was already known to be under follow-up due to meningioma and 1-year follow-up with MRI excluded metastases in the other patient (Fig. 3). Another false positive $^{68}$Ga-PSMA avid lesion was a thyroid nodule that was histopathologically proven to be benign.

In the ROC analysis for the study cohort, the optimal cut-off value of total serum PSA was determined to be 0.67 ng/ml for distinguishing between positive and negative $^{68}$Ga-PSMA PET/CT images (Fig. 4a), with an area under curve (AUC) of 0.952 (95% CI 0.911–0.993). Cut-off values in terms of total serum PSA were also calculated separately for patients with isolated local recurrence in 20 patients (Fig. 4b), isolated lymph node metastases in 8 patients (Fig. 4c), and isolated bone metastases in 13 patients (Fig. 4d) using 18 patients with negative $^{68}$Ga-PSMA PET/CT findings. These results are shown in Table 3.

In this study, 25 patients had a history of RP as a primary treatment of PCa and experienced PSA recurrence (>0.2 ng/ml) after surgery (Table 1). The detection rates for positive PSA uptake were 20% (2 of 10 patients), 25% (1 of 4 patients), 100% (2 of 2 patients) and 100% (9 of 9) for serum PSA levels of 0.2 to <0.5 ng/ml, 0.5 to <1.0 ng/ml, 1 to <2 ng/ml and ≥2 ng/ml, respectively. From another point of view, 5 of 20 patients with isolated local recurrence detected with $^{68}$Ga-PSMA PET/CT have previously had RP. Of these, 1 (0.47 ng/ml), 2 and 2 patients had serum PSA levels of 0.2 to <0.5 ng/ml, 1 to <2 ng/ml and ≥2 ng/ml, respectively.

$^{68}$Ga-PSMA PET/CT findings were further evaluated according to the histopathologic findings on the basis of Gleason score. The median GSs of patients with positive and negative $^{68}$Ga-PSMA PET/CT findings were 8 and 7, respectively. Overall, in 76.9% (10/13) of patients with a Gleason score of 5–6, 78.5% (33/42) of patients with a Gleason score of 7 and 88.8% (48/54) of patients with a Gleason score equal to or greater than 8, $^{68}$Ga-PSMA PET/CT was found to be positive. No statistical significance was found

![Fig. 1](image1.png)

**Fig. 1** 70-year-old man (GS 7) who was treated prostate cancer with radiation therapy and underwent hormonal therapy. He had increased PSA values and the last PSA value was 25.5 ng/ml. Local recurrence, oligometastatic bone lesion were showed with increased $^{68}$Ga-PSMA uptake at PET/CT images, but we thought to have millimetric pulmonary metastasis which were not $^{68}$Ga-PSMA avid lesions.
between positive and negative $^{68}$Ga-PSMA PET/CT findings in terms of Gleason score ($\chi^2 = 2.285; p = 0.319$).

**Discussion**

Although choline-based PET/CT is widely used for the evaluation of recurrent PCa, some studies have reported a low sensitivity and specificity, especially at low PSA levels and high GSs with this imaging modality [9, 10]. For this reason $^{68}$Ga-PSMA PET/CT images could be a significant step forward in the diagnosis of recurrent disease; especially for targeted salvage treatments. The aim of the present study was to evaluate the role of $^{68}$Ga-PSMA PET/CT in a real life study with a heterogeneous group of patients having different treatment regimens; but using the most common parameters for the evaluation of PCa such as serum PSA value and GS.

Recently, several studies have investigated the role of $^{68}$Ga-PSMA PET/CT in patients with recurrent PCa. In the study by Ceci et al. [11] the role of $^{68}$Ga-PSMA PET/CT in 70 patients with recurrent PCa after radical therapy was investigated. The authors noted a significant difference between the patients with positive and negative $^{68}$Ga-PSMA PET/CT in terms of serum PSA levels (median 2.6 vs. 0.7 ng/ml) and PSA doubling time (median 4.74 vs. 8.95 months). Meanwhile, the authors noted that a PSA value of 0.83 ng/ml was the optimal cut-off value for distinguishing between positive and negative $^{68}$Ga-PSMA PET/CT with an AUC of 0.868. In addition, the authors had the lesion detection rate as 93% when the PSA cut-off value was chosen as >2 ng/ml. In another study, Eiber et al. found that the mean PSA level of patients with

**Fig. 2** 75-year-old man who had radical prostatectomy for 5 years ago. He had elevated PSA value and his pelvic MR images had no abnormal findings. PSA value was 0.48 ng/ml. He had sequel fibrotic changes on apical posterior segment of the upper lobe of the left lung at CT scan and diffuse low $^{68}$Ga-PSMA uptake at same location. That was thought to have inflammatory changes and again scheduled for follow-up visits.

**Fig. 3** 89-year-old man who underwent hormonal therapy after PCa diagnosed. His GS was 8 and after 1 year in hormonal therapy PSA value was increased. $^{68}$Ga-PSMA PET/CT images was obtained on PSA values 85 ng/ml. We showed $^{68}$Ga-PSMA avid lesions such as local recurrence, multiple bone metastases, supra and infradiaphragmatic lymph node metastases and right temporal lobe lesion into the brain. Brain lesion thought that suspicion of the $^{68}$Ga-PSMA avid metastasis and the past brain images such as CT and MR were investigated. That lesion was showed 5 years ago with brain MR images that interpreted as a meningioma at same localization.
positive findings was significantly higher than in patients with negative findings (4.78 ± 7.0 vs. 1.20 ± 1.0) on 68Ga-PSMA PET/CT. Similar to the former study, the authors found the detection efficacy of 68Ga-PSMA PET/CT to be 96.8% for a PSA value of ≥2 ng/ml [12]. Subsequently, Afshar-Oremiehet al. analyzed 319 patients with very low PSA values whom were referred to PSMA imaging after progressive disease was suspected with alternative imaging modalities such as CT or MR. They found that the median PSA value was 6.02 ng/ml in 264 patients who

**Fig. 4** a Optimal cut-off value of total serum PSA was determined as 0.67 ng/ml for distinguishing between positive and negative 68Ga-PSMA PET/CT images. b Optimal cut-off value of total serum PSA was determined as 1.23 ng/ml for distinguishing positive or negative local recurrence in patients with 68Ga-PSMA PET/CT images. c Optimal cut-off value of total serum PSA was determined as 0.68 ng/ml for distinguishing positive or negative lymph node metastases in patients with 68Ga-PSMA PET/CT images. d Optimal cut-off value of total serum PSA was determined as 2.35 ng/ml for distinguishing positive or negative bone metastases in patients with 68Ga-PSMA PET/CT images
In our study, we detected the optimal cut-off value of PSA as 0.67 ng/ml in the determination of positive and negative 68Ga-PSMA PET/CT findings. Despite our median serum total PSA value (9.14 ng/ml) being higher than the above-mentioned studies, our optimal cut-off values according to ROC analysis for distinguishing between positive and negative 68Ga-PSMA PET/CT were in line with those in other studies in the literature. Meanwhile, as mentioned in Table 3, we were also able to detect cut-off values for patients with isolated local recurrences as well as LN and bone metastasis in a separate way.

Current methods for assessing LNs in disease recurrence are limited. Although pelvic lymph node dissection is generally considered the most reliable procedure for assessing the presence of nodal invasion, this is generally useless in the recurrence setting [13, 14]. CT is commonly used for nodal staging; however it has a limited ability to predict lymph node invasion due to its low sensitivity for small-volume or micrometastatic disease [15]. Another limitation of CT is that the short-axis diameter of up to 80% of metastatic lymph nodes in PCa may be less than 7 mm [16, 17]. In our study, lymph node metastases were demonstrated in 46 patients. Pelvic lymph node metastases were seen in 38 patients, whereas abdominal and supradiaphragmatic lymph node metastases were seen in 27 and 11 patients, respectively. In the ROC analysis, the cut-off PSA value in patients with metastases limited to lymph nodes was 0.68 ng/ml. Despite this promising result, a recent study by Budaus et al. challenged the role of 68Ga-PSMA PET/CT for detecting LN metastasis in PCa. Briefly, the authors compared preoperative 68Ga-PSMA PET/CT LN findings with histologic work-up after RP performed for high risk PCa. They detected 33.3% of the patients as being true positive for LN metastasis, and 66.7% of the patients as false negative. Accordingly, they noted a low sensitivity (33.3%) and high specificity (100%) rate of 68Ga-PSMA PET/CT for detection of LN metastasis. Meanwhile, the median size of 68Ga-PSMA PET/CT-detected vs. undetected LN metastasis was 13.6 vs. 4.3 mm (p < 0.005). This outcome revealed that the size and tumor burden in LNs are important and even in the primary setting the value of 68Ga-PSMA PET/CT is still questionable.

Lung is the second organ involved after bone in patients with PCa and we had 4 patients with 68Ga-PSMA non-avid pulmonary nodules [19]. In this situation, differentiation between lung metastasis and primary lung cancer should be made for optimal patient survival. Recently, Pyka et al. reported the outcomes of 89 pulmonary lesions with 68Ga-PSMA uptake in 45 patients with PCa [20]. Of these lesions, 39 were proven as PCa, 37 were highly probable for PCa, and 7 and 2 to be lung cancer and tuberculosis, respectively. The authors found no significant difference in SUVmax values when lung cancer was compared with histologically proven PCa. This was attributed to the PSMA expression in tumor associated neovasculature in patients with primary lung cancer. Eventually, 68Ga-PSMA PET/CT is less valuable in lung, and a histological diagnosis should be made if the result will lead to modifications in the treatment regime.

On the other hand, 2 patients in our cohort had cranial meningioma lesions that showed increased 68Ga-PSMA uptake. Similar to the report by Chakraborty et al. who reported an increased 68Ga-PSMA uptake in a PCa patient with brain metastases, it has been also demonstrated that cranial meningiomas have an improved sensitivity of detection with 68Ga-DOTATOC when compared to CE-MRI [21, 22]. Thus, brain lesions with 68Ga-PSMA uptake may be meningioma instead of brain metastasis of PCa. Additionally, Kanthan et al. [23] reported a case of a PSMA-avid thyroid lesion, and subsequent tissue sampling confirmed the diagnosis of follicular thyroid adenoma similar to our case. It is important to be aware of this possibility to avoid scan misinterpretation. Tissue biopsy of PSMA-avid thyroid lesions should be considered to exclude a primary thyroid neoplasm.

It is known that PSMA expression increases with tumor aggressiveness, metastatic state and disease recurrence [24]. With recent improvements, GS has become the most important histological factor predicting the prognosis of patients undergoing radical treatment for PCa. In this group of patients, Eiber et al. [12] reported that Ga-PSMA PET/CT was positive in 86.7% (111/128) of patients with a GS ≤7 and in 96.8% (90/93) of patients with a GS ≥8 (p = 0.001). On the other hand, Ceci et al. did not find GS to be a predictive factor in multivariate analysis for positive Ga-PSMA PET/CT[11]. Similar to the latter study, we did not note any

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Cut-off values in terms of serum total PSA calculated separately for patients with local recurrence, lymph node metastases and bone metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (Recurrence +/-)</td>
</tr>
<tr>
<td>Overall study cohort</td>
<td>91/18</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>20/18</td>
</tr>
<tr>
<td>Lymph node metastases</td>
<td>8/18</td>
</tr>
<tr>
<td>Bone metastases</td>
<td>13/18</td>
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</table>

had pathological radiotracer uptake [7]. In our study, we detected the optimal cut-off value of PSA as 0.67 ng/ml in the determination of positive and negative 68Ga-PSMA PET/CT findings. Despite our median serum total PSA value (9.14 ng/ml) being higher than the above-mentioned studies, our optimal cut-off values according to ROC analysis for distinguishing between positive and negative 68Ga-PSMA PET/CT were in line with those in other studies in the literature. Meanwhile, as mentioned in Table 3, we were also able to detect cut-off values for patients with isolated local recurrences as well as LN and bone metastasis in a separate way.

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statistical difference between positive and negative 68Ga-PSMA PET/CT findings in terms of Gleason score. This outcome might be attributed to the limited number of patients in the latter and present study and should be investigated with studies including large number of patients.

The present study has some limitations. First, parameters on PSA kinetics such as PSA doubling time and PSA density were lacking due to the retrospective nature of the study. Meanwhile, since most of the patients were referred for Ga-PSMA PET/CT to our center, it was not possible to have information about the PSA kinetics of the study cohort. Second, it is not possible to know the histological nature of the positive images since none in the study cohort underwent any kind of surgery or biopsy. This admission is also valid for the use of conventional confirmatory imaging modalities, which might be used at least for oligometastatic lesions. Third, the present study is lacking data about the treatment related effects on PSA uptake, such as the use of ADT and follow-up. This situation is also valid for treatment outcomes of Ga-PSMA PET/CT-based lesions such as salvage RP or lymphadenectomy or early chemo-hormonal therapy. On the other hand, the major strength of the study is that it was done at a single center with significant experience in PET/CT and PSMA based PET/CT imaging.

Conclusion

Our data in the present study are consistent with those in previous studies in the literature on Ga-PSMA PET/CT as a promising diagnostic tool in recurrent PCa. Despite the lack of information on specific use of Ga-PSMA PET/CT in recurrent PCa in major guidelines, it has potential to be a standard in patients with recurrent PCA. Additionally, 68Ga-PSMA has the potential to lead to the development of PET-guided therapies that might have significant impact on the quality of life issues seen with current treatments. On the other hand, despite the fact that no relationship was detected between GS and 68Ga-PSMA PET/CT findings in our study, serum total PSA values may be used for predicting the likelihood of positive 68Ga-PSMA PET/CT results.

Funding None.

References


