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Original Article

Correlation of Ga-68 PSMA PET/CT Positivity with Gleason Scores and Serum PSA Levels in Initial Staging of Prostate Adenocarcinoma, and the Contribution of PET/CT Imaging to Patient Management

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ABSTRACT

Aim: Prostate cancer is the second most frequently diagnosed malignancy and the fifth leading cause of cancer-related mortality worldwide. Accurate staging at diagnosis is crucial for guiding treatment decisions. However, conventional imaging methods have limited sensitivity, especially for detecting early metastatic disease. Gallium-68 (Ga-68) prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT), a molecular imaging modality targeting PSMA, provides high sensitivity and specificity by visualizing PSMA expression in both primary and metastatic lesions. This study aimed to evaluate the correlation of serum prostate-specific antigen (PSA) levels and Gleason grade groups with primary lesion standardized uptake value maximum (SUV_{max}), and to assess the predictive value of PSMA expression for extraprostatic involvement in patients undergoing initial staging for prostate adenocarcinoma.

Methods: This retrospective study included 37 patients with biopsy-proven prostate adenocarcinoma who underwent Ga-68 PSMA PET/CT for initial staging. Correlations between primary tumor SUV_{max}, serum PSA levels, and Gleason grade groups were analyzed. The predictive value of SUV_{max} for extraprostatic metastases was assessed. Additionally, associations between PSA, Gleason grade groups, and the presence of lymph node or bone metastases were evaluated. In 33 patients, Ga-68 PSMA PET/CT findings were compared with concurrent bone scintigraphy. A subgroup underwent dual-phase PET/CT imaging to assess changes in delayed SUV_{max} in relation to PSA and Gleason grade groups.

Results: SUV_{max} of the primary tumor showed significant positive correlations with PSA levels ($p<0.001$) and Gleason grade groups ($p=0.005$). Gleason grade group was significantly associated with lymph node metastasis ($p=0.04$), but not with bone metastasis. A SUV_{max} threshold of 8.97 predicted extraprostatic disease with 81.25% sensitivity and 66.67% specificity. No significant association was found between PSA levels and lymphatic or osseous metastases. PSMA PET/CT outperformed bone scintigraphy in 76% of cases with suspected skeletal lesions. Although dual-phase imaging revealed no additional lesions, delayed SUV_{max} values remained significantly correlated with PSA and Gleason grade groups ($p=0.002$ and $p=0.013$, respectively).

Conclusion: Ga-68 PSMA PET/CT demonstrates high diagnostic performance in the staging of prostate adenocarcinoma and correlates significantly with key prognostic factors. It offers superior accuracy compared to bone scintigraphy and may guide personalized management strategies. While dual-phase imaging adds limited incremental value, it may be beneficial in selected cases. Further prospective studies are warranted to validate these findings.

Keywords: Clinical oncology, gallium-68, oncology, positron emission tomography computed tomography, prostate cancer, prostatic neoplasms

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Introduction

Prostate cancer is one of the most frequently diagnosed malignancies and remains a significant cause of morbidity and mortality among men worldwide. According to GLOBOCAN 2018 data, it is the second most common cancer and the fifth leading cause of cancer-related deaths in men globally [1]. Both the European Association of Urology (EAU) and the National Comprehensive Cancer Network emphasize the necessity of accurate risk stratification and staging for optimal treatment planning [2].

In intermediate- and high-risk patients, multiparametric magnetic resonance imaging (mpMRI), computed tomography (CT), and bone scintigraphy are traditionally used for initial staging. However, these conventional imaging techniques show significant limitations, particularly in identifying lymph node involvement and early metastatic spread. The 2024 EAU guidelines now recommend the use of prostate-specific membrane antigen (PSMA) positron emission tomography/CT (PET/CT) as the preferred imaging modality for staging high-risk and selected intermediate-risk prostate cancer cases, owing to its superior diagnostic performance in detecting both nodal and distant metastases [2].

A meta-analysis by Hövels et al. [3] reported that CT and MRI exhibit relatively low sensitivity (approximately 42%) for lymph node staging, despite showing reasonable specificity (around 82%). In contrast, gallium-68 (Ga-68) PSMA PET/CT, a molecular imaging modality targeting PSMA, has emerged as a highly sensitive and specific tool for detecting both locoregional and systemic spread of disease. The proPSMA randomized trial further confirmed that Ga-68 PSMA PET/CT demonstrates significantly higher diagnostic accuracy (92% vs. 65%) than conventional imaging and leads to more frequent and impactful management changes [4].

Given this context, the present study aims to assess the clinical utility of Ga-68 PSMA PET/CT in the initial staging of biopsy-proven intermediate- to high-risk prostate cancer. Specifically, we evaluate the correlations between PSMA PET/CT findings and key prognostic markers, including serum prostate-specific antigen (PSA) levels, Gleason Grade Groups, and metastatic involvement. Furthermore, the potential added value of dual-phase PET/CT imaging in a selected subgroup of patients is also investigated.

Methods

This retrospective study included 37 patients with biopsy-confirmed prostate adenocarcinoma who underwent Ga-68 PSMA PET/CT for initial staging. Ethical approval was received from the University of Health Sciences Türkiye, Dr. Abdurrahman Yurtaslan Ankara Oncology Education and Research Institute Institutional Review Board (approval no: 9, date: 01.06.2017). Demographic data, histopathological characteristics (Gleason score/Grade Group), serum PSA levels (measured within one month prior to imaging), clinical and radiological findings, and treatment details were retrieved from the hospital information system.

Ga-68 PSMA- Inhibitor & Therapy (I&T) was synthesized using a scintomics gallium radiopharmaceuticals module with a germanium-68/Ga-68 (Ge-68/Ga-68) generator (iThemba Labs, South Africa) and reagents from ABX (Germany). Radiolabeling efficiency and radiochemical purity were assessed using radio-thin layer chromatography and radio- high performance liquid chromatography, with a final purity of ≥95%.

All patients received 1.8-2.2 MBq/kg of Ga-68 PSMA-I&T via intravenous injection. Oral hydration with 1-1.5 liters of water containing contrast agent was administered approximately 30 minutes prior to injection. PET/CT imaging was performed approximately 60 minutes post-injection using a Siemens Biograph TruePoint 6 PET/CT scanner, covering the area from the vertex to mid-thigh. When the initial scan showed equivocal pelvic findings, typically due to urinary bladder tracer activity obscuring the prostate bed or subcentimetric nodal uptake, a 120-min delayed pelvic acquisition was obtained to improve lesion conspicuity.

Low-dose CT scans were acquired for attenuation correction and anatomical localization. PET/CT images were reconstructed in axial, coronal, and sagittal planes using a Siemens Leonardo workstation. Two experienced nuclear medicine physicians performed image interpretation. Lesions showing focal or heterogeneous uptake distinguishable from physiological background were evaluated in correlation with CT. Volumes of interest (VOIs) were semi-automatically delineated based on standardized uptake value (SUV) thresholds and manually adjusted to exclude adjacent normal tissues. The SUV maximum (SUV_{max}) was recorded for each VOI.

The SUV_{max} of the primary prostate lesion was measured on early-phase PET/CT images. The presence of lymph node and bone metastases was also assessed. In 33 patients, bone scintigraphy was performed within one week of PET/CT, and findings were compared for concordance.

A subgroup of patients underwent dual-phase Ga-68 PSMA PET/CT with delayed-phase images acquired at 120 minutes post-injection. SUV_{max} values from early and delayed phases were compared, and their correlations with serum PSA levels and Gleason Grade groups were analyzed.

All statistical analyses were conducted using IBM Statistical Package for the Social Sciences statistics version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as number (n), percentage (%), mean ± standard deviation ($\bar{x}$±SD), or median with interquartile range, as appropriate. The distribution of continuous variables was evaluated using the Shapiro-Wilk test and Q-Q plots.

For correlation analyses, Pearson's correlation coefficient was used for normally distributed variables, while Spearman's rank correlation was applied for non-normally distributed data. Independent samples t-test and Mann-Whitney U test were used to compare two groups, depending on the distribution. One-way ANOVA or Kruskal-Wallis tests were used for comparisons among more than two groups. Categorical variables were analyzed using Pearson's chi-square or Fisher's exact test, as appropriate.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of SUV_{max} in predicting extraprostatic disease (lymph node and/or bone metastases). The optimal cut-off value was determined using the Youden index, and corresponding sensitivity and specificity values were calculated. A p value <0.05 was considered statistically significant.

Results

A total of 37 patients who underwent Ga-68 PSMA PET/CT for primary staging due to elevated serum PSA levels and/or suspicious radiologic or scintigraphic findings were retrospectively evaluated. The mean age was 65.6 years (range: 44-84). According to biopsy results, Gleason Grade group distribution was as follows: 3 patients (8.1%) in group 1, 10 (27.0%) in group 2, 4 (10.8%) in group 3, 8 (21.6%) in group 4, and 12 (32.4%) in group 5. The mean ± SD serum PSA level was 29.88±34.40 ng/mL.

In all patients, Ga-68 PSMA PET/CT demonstrated focal or heterogeneous an increase in PSMA uptake in the prostate gland, corresponding to the primary tumor. The mean SUV_{max} of the primary lesions was 11.84±8.14 (range: 3.64-35.61) (Table 1). A statistically significant positive correlation was found between SUV_{max} and serum PSA levels (p<0.001, r=0.572), as well as between SUV_{max} and Gleason Grade group (p=0.005, r=0.449) (Table 2).

Lymph Node Metastases

Lymph node involvement consistent with prostate cancer metastasis was identified in 15 of 37 patients (40.5%), with localization confined to the pelvic region in 10 patients and involving both pelvic and extrapelvic regions in 5. One patient exhibited lymphadenopathy with low PSMA expression and atypical imaging features; further workup confirmed a diagnosis of chronic lymphocytic leukemia/lymphoma.

Among patients with nodal metastases, three had Gleason Grade group 2, six had group 4, and six had group 5 disease. A statistically significant association was found between Gleason Grade group and nodal metastasis (p=0.04). However, no significant relationship was observed between Gleason Grade group and the distribution pattern of nodal disease (pelvic vs. pelvic + extrapelvic) (p=0.16). Additionally, PSA levels were not significantly associated with nodal metastasis (p=0.19). The smallest PSMA-avid lymph node measured 5 mm in diameter.

Following the study, we were able to assess the surgical outcomes of 6 patients who underwent radical prostatectomy and lymph node dissection. Among these, lymph node metastasis was histopathologically confirmed in 2 patients, who showed lymph node involvement on PET/CT. In the remaining 4 patients, no lymph node involvement was observed on PET/CT, and histopathological examination also ruled out metastasis. In these 6 patients, PET/CT findings were in complete concordance with histopathological results; however, the sample size was relatively small for a robust comparative analysis.

Bone Metastases and Scintigraphy Comparison

Bone metastases were detected in 7 patients (18.9%), with a mean SUV_{max} of 10.61±6.77. In 4 additional patients (10.8%), sclerotic bone lesions were observed on CT without corresponding PSMA uptake. These lesions were deemed indeterminate, given that certain intensely sclerotic metastases may be PSMA-negative. Further evaluation via other imaging modalities or follow-up was recommended. No significant correlation was found between the presence of bone metastases and Gleason grade or PSA levels.

Thirty-three patients underwent concurrent bone scintigraphy. Among these, 6 patients (18%) showed no scintigraphic evidence of metastases, 2 (6%) showed definite metastases, and 25 (76%) had indeterminate findings. PSMA PET/CT was concordant with bone scintigraphy in only 8 cases (24%), specifically in patients with either negative or definitively positive scans.

In the subgroup with indeterminate scintigraphy (n=25), 20 patients (80%) had no PSMA-avid lesions, attributed to benign causes such as degenerative changes. In the remaining 5 patients (20%), PSMA-avid lesions confirmed metastatic involvement, thereby clarifying the diagnosis.

Table 1. Patient characteristics and imaging findings

Parameter	Value
Gleason Grade group (Gleason score)	
- 1 (3+3)	3 patients (8.1%)
- 2 (3+4)	10 patients (27%)
- 3 (4+3)	4 patients (10.8%)
- 4 (4+4, 3+5, 5+3)	8 patients (21.6%)
- 5 (4+5, 5+4, 5+5)	12 patients (32.4%)
Age (years)	65.62±8.12
Serum PSA (ng/mL)	29.88±34.40
Gleason Grade group (median)	4 (z: 2-5)
- primary lesion	11.84±8.14
- bone metastasis	10.61±6.77
- lymph node metastasis	6.25 (3.64-9.16)

*Data are presented as median (interquartile range) or mean ± standard deviation. Percentages may not total 100% because of rounding.
PSA: Prostate-specific antigen, SUV_{max}: Standardized uptake value maximum

Table 2. Statistically significant correlations and metastatic findings

Parameter	Value
Total number of patients	37
Patients with lymph node metastases	15 (40.5%)
Patients with bone metastases	7 (18.9%)
Correlation: PSA vs. of primary tumor	r=0.572, p<0.001
Correlation: Gleason Grade group vs.	r=0.449, p=0.005
Correlation: Gleason Grade group vs. LN metastasis	p=0.04, Cramér's V=0.51

PSA: Prostate-specific antigen, : Standardized uptake value maximum, LN: Lymph Node

Correlation with SUV_{max} and Disease Extent

Among all patients, 16 (43.2%) were found to have extraprostatic disease (nodal and/or bone metastases). A statistically significant correlation was observed between primary tumor SUV_{max} and the presence of metastasis (p=0.04). ROC curve analysis identified a cut-off SUV_{max} value of 8.97 for predicting extraprostatic involvement, with a sensitivity of 81.3% and specificity of 66.7% (Figure 1, Table 3). In the remaining 21 patients, no extraprostatic spread was detected, and these patients underwent curative treatments accordingly. Patients with advanced disease were managed with systemic therapies. Below, Case 1 and Case 2 are presented as two patient examples, highlighting the importance of Ga-68 PSMA PET/CT in treatment planning (Case 1, 2)

Dual-Phase Imaging

Dual-phase PSMA PET/CT imaging was performed in 27 patients to evaluate pelvic lymph nodes with subcentimetric size or equivocal uptake. No additional lesions were identified on delayed images. However, PSMA-avid lymph nodes were better visualized on delayed scans.

When comparing SUV_{max} between early and delayed phases, delayed SUV_{max} remained significantly correlated with PSA levels (p=0.002) and Gleason Grade group (p=0.013), similar to early-phase values. Although dual-phase imaging did not reveal additional lesions, it provided improved lesion conspicuity in selected cases and may be helpful in patients with high PSA levels or equivocal findings on standard imaging.

Discussion

This retrospective study assessed 37 patients with biopsy-proven intermediate- to high-risk prostate adenocarcinoma who underwent Ga-68 PSMA PET/CT for initial staging. The aim was to evaluate the correlation between imaging findings and key clinical parameters including PSA levels, Gleason Grade group, and presence of metastasis.

Based on previous studies in the literature, Silver et al. [5] demonstrated that PSMA expression is absent in benign prostatic epithelium and significantly elevated in high-grade prostate carcinomas, highlighting its potential as a molecular target for imaging and therapy. Building upon this, Perner et al. [6] reported a strong correlation between PSMA overexpression and adverse pathological features such as poor differentiation, tumor progression, and biochemical recurrence, further supporting its prognostic relevance. Fendler et al. [7] evaluated the accuracy of 68Ga-PSMA PET/CT in localizing intraprostatic tumor lesions and reported significantly higher SUV_{max} values in histopathologically confirmed tumor-positive segments compared to negative ones (mean 11.8 vs. 4.9; p<0.001), with a high positive predictive value (97%) and notable accuracy in the study. Consistent with these findings, our study demonstrated that all 37 patients exhibited visually discernible PSMA uptake in the primary prostate tumor, regardless of Gleason score or PSA level, further supporting the reliability of 68Ga-PSMA PET/CT in identifying the intraprostatic tumor site with high sensitivity, even in early-stage or multifocal disease presentations.

In our study, a statistically significant positive correlation was observed between the SUV_{max} of the primary tumor and both serum PSA levels (p<0.001) and Gleason Grade group (p=0.005). The mean SUV_{max} of the primary lesion was 11.84±8.14. These findings underscore the potential utility of SUV_{max} as a non-invasive surrogate biomarker reflecting tumor aggressiveness. Similarly, Kwan et al. [8] demonstrated that intraprostatic SUV_{max} values derived from Ga-68 PSMA PET/CT strongly correlated with International Society of Urological Pathology Grade groups, particularly in identifying Grade group 5 lesions. A SUV_{max} threshold >10 was associated with a 2.3-fold increased risk for high-grade disease, reinforcing its diagnostic value for risk stratification. Also, Uprimny et al. [9] reported significantly higher SUV_{max} values in primary tumors of patients with elevated PSA and higher Gleason scores, supporting the use of SUV_{max} values in initial staging and prognostication.

In a retrospective study by Zhou et al. [10], ^{68}Ga-PSMA PET/CT demonstrated superior detection rates compared to mpMRI in high-risk prostate cancer (97.0% vs. 87.9%, p< 0.05). Conversely, mpMRI showed higher sensitivity in low- and

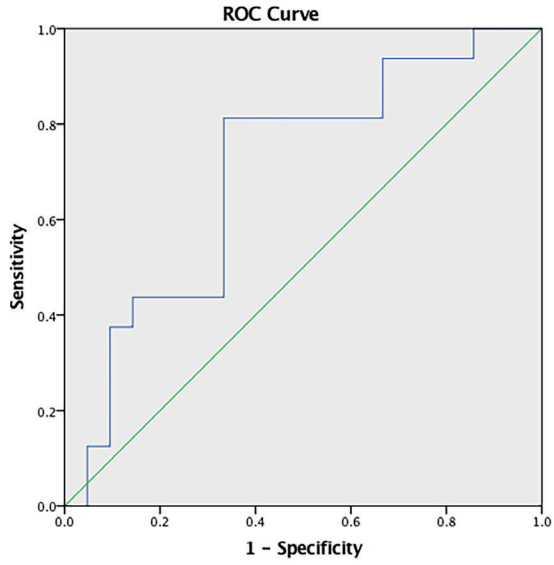
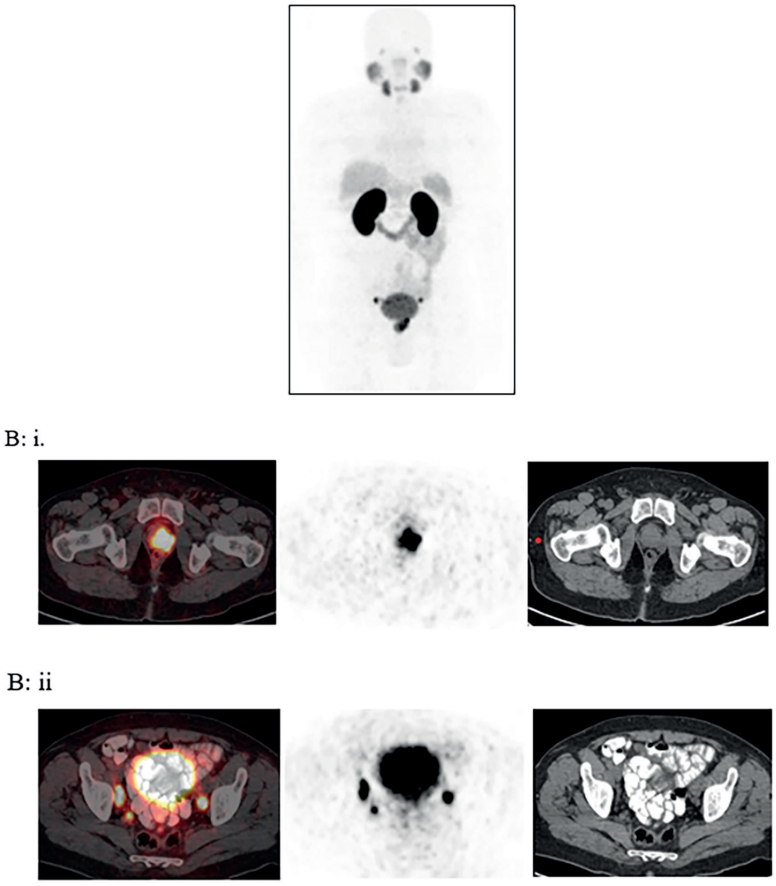


Figure 1. ROC Analysis ROC curve demonstrating the relationship between of the primary lesion and extraprostatic spread (lymph node and/or bone metastases)
ROC: Receiver operating characteristic, SUV_{max}: Standardized uptake value maximum

Table 3. Optimal cut-off for predicting extraprostatic disease

Parameter	AUC (95% CI)	Optimal cut-off	Sensitivity % (95% CI)	Specificity % (95% CI)	p value
	0.70 (0.53-0.87)	8.97	81.3 (57.0-93.4)	66.7 (45.4-82.8)	0.04

AUC: Area under the curve, : Standardized uptake value maximum, CI: Confidence interval



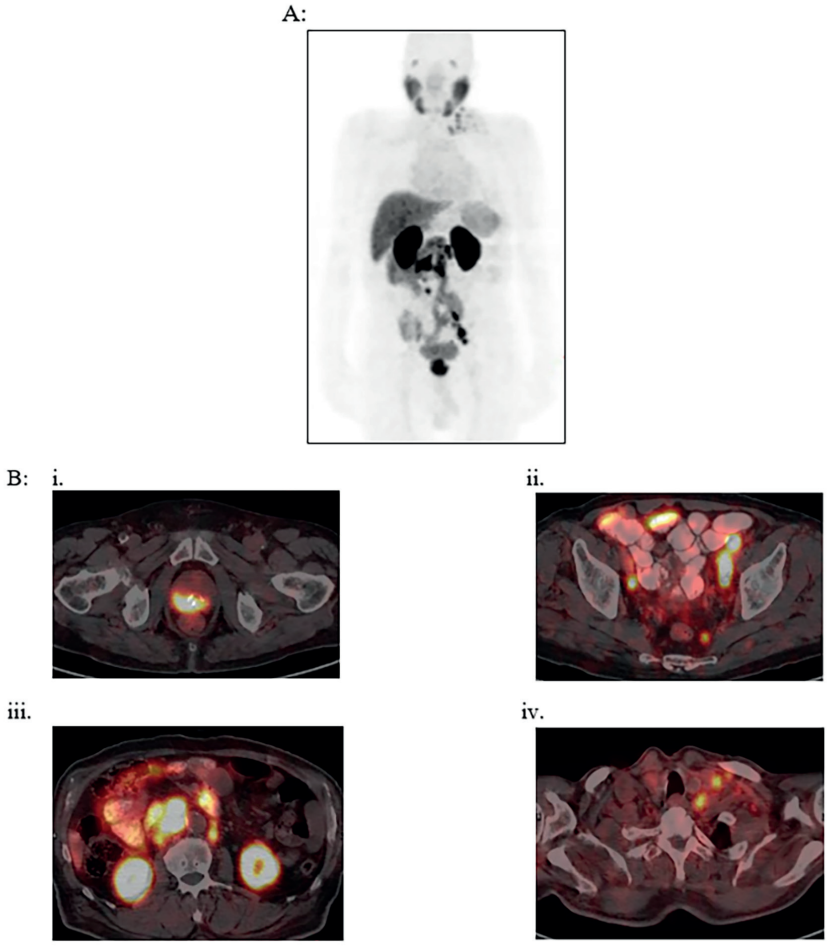
Case 1. A fifty-five-year-old male patient was diagnosed with prostate adenocarcinoma (Gleason Grade group 5; Gleason score 5+5) based on TRUS-guided biopsy. Due to elevated PSA level (19.07 ng/mL) and suspicious pelvic lymph nodes detected on MRI, the patient was referred for Ga-68 PSMA PET/CT for disease staging.
Figure A shows the MIP image demonstrating intense PSMA uptake in the prostate gland and pelvic lymph nodes.
Figure B(i) displays axial PET/CT images of the primary prostate tumor with a maximum SUV of 29.55.
Figure B(ii) shows bilateral external iliac and obturator lymph nodes with pathological PSMA uptake; the smallest node measured 5 mm (range: 5-15 mm).
Following PET/CT, the patient underwent radical prostatectomy and pelvic lymph node dissection. Histopathological evaluation confirmed lymph node metastases. Postoperative pelvic radiotherapy was administered. At 9 months post-treatment, the patient is disease-free with undetectable PSA levels (<0.003 ng/mL).
ROC: Receiver operating characteristic, : Standardized uptake value maximum, TRUS: Transrectal ultrasound, PSA: Prostate-specific antigen, MRI: Magnetic resonance imaging, Ga-68: Gallium-68, PSMA: Prostate-specific membrane antigen, PET/CT: Positron emission tomography/computed tomography, MIP: Maximum intensity projection

intermediate-risk cases (85.7% vs. 60.0%, p<0.05), particularly in younger patients and those with lower PSA levels. Notably, PSMA PET/CT positivity in lower-risk groups was more likely in patients aged ≥62.5 years and with PSA ≥9.4 ng/mL. These findings highlight the complementary roles of PSMA PET/CT and mpMRI across different risk categories. Although some prior studies have reported variability in the correlation between PET parameters and histopathological grades, our data support a robust association between PSMA expression level (SUV_{max}) and tumor differentiation. Nevertheless, further validation in prospective multicenter cohorts is warranted.

The proPSMA trial by Hofman et al. [4] showed that PSMA PET/CT outperformed conventional imaging in detecting nodal and distant metastases, with an accuracy of 92%, sensitivity of 85%, and specificity of 98%, compared to 65%, 38%, and 91%, respectively, for conventional imaging. Additionally, a meta-analysis by Hövels et al. [3] demonstrated limited sensitivity for both CT (42%) and MRI (39%) in detecting nodal involvement, despite relatively high specificity (~82%), highlighting the diagnostic gap that molecular imaging can address [3].

In a retrospective study of 50 intermediate- to high-risk prostate cancer patients, Spena et al. [11] evaluated Ga-68 PSMA PET/CT in patients undergoing radical prostatectomy and extended pelvic lymph node dissection, reporting a specificity of 88.1% but limited sensitivity of 25% for nodal metastasis. Furthermore, they noted a positive correlation between the SUV_{max} of the primary lesion and baseline PSA levels and tumor burden, suggesting its dual role in local and systemic assessment [11].

In a multicentre study, Öbek et al. [12] evaluated the diagnostic performance of ^{68}Ga-PSMA PET/CT for primary lymph node



Case 2. A seventy-four-year-old male patient was diagnosed with prostate adenocarcinoma, Gleason Grade group 4 (Gleason score 5+3), based on TRUS-guided biopsy. Due to elevated serum PSA levels (168 ng/mL), a Ga-68 PSMA PET/CT scan was performed for staging purposes.
A: MIP image showing increased tracer uptake in the prostate gland, as well as in abdominopelvic and left supra-infraclavicular lymph nodes.
B: PET/CT images demonstrating pathological PSMA uptake in the primary tumor within the prostate gland (i), and in metastatic lymph nodes in the pelvic (ii), abdominal (iii), and left supra-/infraclavicular (iv) regions.
The diagnosis of metastasis in the supraclavicular lymph nodes was histopathologically confirmed. The patient was diagnosed with metastatic prostate carcinoma with widespread lymph node involvement, and hormone therapy was initiated.
Ga-68: Gallium-68, PSMA: Prostate-specific membrane antigen, PET/CT: Positron emission tomography/computed tomography, MIP: Maximum intensity projection, TRUS: Transrectal ultrasound, PSA: Prostate-specific antigen

staging in high- and very high-risk prostate cancer. PSMA PET/CT demonstrated higher specificity (86%) and accuracy (76%) than conventional imaging, with improved values in patients undergoing extensive lymphadenectomy (accuracy: 81%). Kappa analysis showed better concordance with histopathology compared to morphological imaging, (0.41 vs. 0.18) and supports PSMA PET/CT as a superior non-invasive tool, although extended surgical dissection remains the gold standard for nodal staging [12].

Corona-Montes et al. [13] assessed the accuracy of ^{68}Ga-PSMA PET/CT for primary lymph node staging in high-risk prostate cancer using extended pelvic lymphadenectomy as the reference. In a small cohort of 17 patients, PSMA PET/CT demonstrated high specificity (92.3%) and negative predictive value (92.3%), with an overall diagnostic accuracy of 88.2%. Although sensitivity was lower (75%), the findings support the potential of PSMA PET/CT to reliably exclude nodal metastases preoperatively, suggesting it may help avoid unnecessary lymphadenectomy in selected patients [13].

In a large multicenter phase 3 trial, Hope et al. [14] assessed the diagnostic performance of ^{68}Ga-PSMA-11 PET/CT for detecting pelvic lymph node metastases in intermediate- to high-risk prostate cancer. Among 277 patients who underwent radical prostatectomy with lymph node dissection, PSMA PET/CT demonstrated high specificity (95%) but limited sensitivity (40%) for pelvic nodal disease. Despite its high negative predictive value (81%), the relatively low sensitivity highlights its limitations in detecting small-volume metastases, reinforcing that a negative PSMA PET result should not preclude pelvic lymph node dissection in surgical candidates [14].

Jochumsen and Bouchelouche [15] provided an updated overview of PSMA PET/CT for primary staging of prostate

cancer, highlighting its superior sensitivity and specificity for metastatic detection compared to conventional imaging. When combined with multiparametric MRI, PSMA PET/CT enhances assessment of extracapsular extension and seminal vesicle invasion, and may serve as a second-line modality in patients with inconclusive MRI or negative biopsies. Notably, PSMA PET/CT alters clinical management in approximately 25% of cases. However, its impact on long-term outcomes remains uncertain, underscoring the need for prospective validation.

In our study, lymph node metastases were detected in 40.5% of patients and were significantly associated with Gleason Grade group (p=0.04). Among the 37 patients included in our primary staging cohort, lymph node metastases were detected in 15 individuals. Of these, ten had metastatic involvement limited to the pelvic region, whereas five patients exhibited both pelvic and extrapelvic nodal metastases. The identification of extrapelvic spread led to significant modifications in treatment planning. The smallest lymph node demonstrating PSMA uptake measured 5 mm in short-axis diameter (range: 5-20 mm). Notably, the majority of these lymph nodes were below the threshold for pathological enlargement, rendering them unlikely to be identified with conventional radiological modalities. These findings highlight the added diagnostic value of PSMA PET/CT in detecting subclinical nodal metastases that may be missed on anatomical imaging alone.

In our study, bone metastases were identified in seven patients. Among patients who underwent concurrent conventional bone scintigraphy and Ga-68 PSMA PET/CT, PSMA PET/CT successfully characterized suspicious lesions in 76% of cases initially considered equivocal for metastasis on scintigraphy. This imaging modality demonstrated a significant clinical impact by contributing to more accurate disease staging and informing subsequent modifications in therapeutic management. Zhao et al. [16] conducted a meta-analysis comparing PSMA PET/CT with conventional bone scintigraphy and demonstrated superior sensitivity (98% vs. 83%) and specificity (97% vs. 68%) for PSMA PET/CT in detecting osseous involvement. Mainta et al. [17] reported that combining PSMA-RADS and PROMISE criteria in interpretation significantly reduced equivocal bone lesions and increased diagnostic accuracy, particularly in the pelvis and ribs, underscoring the value of structured reporting systems.

Some sclerotic lesions in our cohort showed no PSMA uptake and were deemed benign, highlighting the potential for false negatives. This is in line with findings by Afshar-Oromieh et al., [18] who found that although PSMA PET/CT achieves excellent tumor-to-background ratios and high lesion detectability (up to 100% in patients with PSA >2.2 ng/mL), variants such as dedifferentiated or neuroendocrine tumors may demonstrate low uptake. In our study, Ga-68 PSMA PET/CT resolved indeterminate findings in 76% of patients who also underwent bone scintigraphy, further supporting its clinical advantage.

In our cohort, an SUV_{max} cutoff of 8.97 yielded 81.3% sensitivity and 66.7% specificity for predicting extraprostatic extension. These results are comparable to those of Koerber et al., [19] who reported a threshold of 11.9 with sensitivity and specificity values of 76% and 58.4%, respectively, indicating that SUV_{max} may help stratify local invasion risk preoperatively.

Dual-phase imaging was performed in 27 patients. A significant correlation was again observed between delayed-phase SUV_{max} values and both PSA (p=0.002), and Gleason Grade group (p=0.013), although no additional lesions were identified. Derlin et al. [20] demonstrated that delayed imaging following diuretic administration can enhance lesion visualization in the prostate region by minimizing urinary tracer interference, particularly aiding pelvic lymph node assessment. Intraprostatic uptake patterns in our cohort ranged from heterogeneous to focally intense. This has previously been described by Afshar-Oromieh et al., [18] who reported strong tumor contrast and progressive lesion conspicuity in delayed imaging phases. Thus, while our findings suggest limited added diagnostic value in this population, tailored imaging protocols may offer benefits in specific clinical scenarios.

Tsechelidis and Vrachimis [21] highlighted in their review, that PSMA PET/CT detects more extensive disease than conventional modalities, and may significantly impact clinical management, with the potential to upstage more than 50% of patients initially classified as M0. Their conclusions support its growing role as a new standard in the staging of high-risk prostate cancer [21].Von Stauffenberg et al. [22] highlighted the transformative role of PSMA-PET in prostate cancer imaging, with superior sensitivity and specificity over conventional modalities. Its clinical utility spans initial staging of intermediate- to high-risk cases, detection of biochemical recurrence, and evaluation of metastatic disease. The use of targeted radiotracers enables detection of small-volume metastases, facilitating both diagnostic precision and personalized therapeutic strategies such as radioligand therapy. While its integration into guidelines has improved care pathways, prospective outcome data remain limited [22].

In our study, PSMA PET/CT was superior to bone scintigraphy in skeletal evaluation, particularly in cases with indeterminate findings, and demonstrated the ability to detect subcentimetric lymph node metastases undetectable by conventional imaging. Although dual-phase imaging did not yield additional lesions, delayed-phase SUV_{max} values remained consistent with early-phase measurements and may provide added value in selected clinical scenarios.

Given its capacity to provide both anatomical and functional information, PSMA PET/CT contributes meaningfully to initial staging, treatment planning, and prognostic assessment. Our findings support its incorporation into clinical algorithms for individualized management of prostate cancer patients. This study is limited by its retrospective nature, small sample size, and partial histopathological verification. Nonetheless, the findings offer valuable insights for hypothesis generation and warrant further prospective validation. Further large-scale prospective studies are warranted to refine the prognostic thresholds for optimal clinical decision-making.

Study Limitations

This study has several limitations. First, its retrospective design may have introduced selection bias and limited the

completeness of clinical data. Second, the relatively small sample size (n=37) may reduce the statistical power and limit the generalizability of the results. Third, histopathological confirmation of lymph node metastases was available in only a limited number of patients, potentially affecting the assessment of imaging accuracy. Lastly, the number of patients who underwent dual-phase imaging was low, making it difficult to draw definitive conclusions about the added value of delayed-phase acquisition. Further prospective, multicenter studies with larger cohorts and histopathological validation are needed to confirm these findings.

Conclusion

Ga-68 PSMA PET/CT demonstrates high diagnostic accuracy in the staging of intermediate to high-risk prostate cancer and shows significant correlation with key clinical and pathological prognostic markers, including serum PSA levels and Gleason Grade group. The SUV_{max} of the primary tumor was significantly associated with both the presence of extraprostatic disease and overall tumor aggressiveness, highlighting its potential as a non-invasive imaging biomarker for risk stratification.

Ethics

Ethics Committee Approval: Ethical approval was received from the University of Health Sciences Türkiye, Dr. Abdurrahman Yurtaslan Ankara Oncology Education and Research Institute Institutional Review Board (approval no: 9, date: 01.06.2017).

Informed Consent: This retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: İ.Ö., G.U., B.B.D., S.D.Ş., H.E., A.K.F., H.B., Concept: İ.Ö., G.U., B.B.D., S.D.Ş., H.B., Design: İ.Ö., G.U., B.B.D., H.B., Data Collection or Processing: İ.Ö., G.U., B.B.D., S.D.Ş., H.E., A.K.F., Analysis or Interpretation: İ.Ö., G.U., B.B.D., S.D.Ş., H.E., A.K.F., Literature Search: İ.Ö., G.U., H.B., Writing: İ.Ö.

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