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Evaluation of Treatment Response in Prostate Cancer Patients: Analysis of Ga-68 PSMA PET/CT Parameters According to PROMISE Criteria

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ABSTRACT

Aim: Gallium-68 (Ga-68) prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) is superior to conventional methods for detecting prostate cancer lesions. However, there is still no standardized tool to quantify treatment response. Using the PROMISE criteria, which standardize lesion selection and disease staging, we evaluated the prognostic significance of Ga-68 PSMA PET/CT imaging parameters.

Methods: Sixty-four patients who were referred for initial staging and for assessment of response using Ga-68 PSMA PET/CT were retrospectively included. For each primary tumor, lymph node metastasis, bone metastasis, and visceral metastasis, the highest PSMA expression was selected according to the PROMISE criteria. The quantitative PET/CT parameters (SUVmax, SUVmean, SUVpeak, TL-PSMA, and PSMA-TV) were calculated. Treatment response was then evaluated using PSMA PET progression criteria, which classify patients as progressors (exhibiting PSMA PET progression) or non-progressors. Receiver operating characteristic analysis was used to assess the predictive value of PET/CT parameters against biochemical response standards.

Results: A significant difference was observed between progressors and non-progressors. In non-progressors, SUVmax, SUVmean, and SUVpeak decreased significantly in the prostate, lymph nodes, and visceral metastases. When miTNM was compared with PET/CT, significant differences were observed only for miT. SUVmax, SUVmean, and SUVpeak in the prostate showed strong correlations with response, highlighting the importance of assessing intensity-based changes in primary lesions.

Conclusion: The PSMA PET progression criteria provide a robust framework for assessing response to therapy using Ga-68 PSMA PET/CT. miTNM staging is valuable for disease localization and extent, but our findings suggest it is less useful for monitoring response than for assessing changes in tumor intensity. We therefore recommend including PET parameters in routine response assessments.

Keywords: Ga-68 PSMA PET, treatment response, prostate cancer, PROMISE, miTNM

Introduction

Prostate cancer (PCa) is the second most common cancer among men worldwide and the fifth leading cause of cancer-related deaths [1,2]. Screening, early diagnosis, and follow-up are crucial for optimal outcomes. The prostate-specific antigen (PSA) test remains the primary tool for detection and monitoring [3]. Gallium-68 (Ga-68) prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) is increasingly used to detect

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recurrence or metastasis when PSA levels rise or when clinical suspicion of progression arises [4].

Although Ga-68 PSMA PET/CT is widely adopted in PCa management, evidence regarding its specific role in assessing treatment response remains scarce. Despite the expanding literature, data on standardized quantitative assessment remain scarce. Currently, there is no consensus on the optimal criteria for treatment response. To address this gap, the PROMISE criteria were developed specifically to guide lesion selection and disease staging, providing a standardized framework for interpreting Ga-68 PSMA PET/CT evaluations [5].

When selecting tumoral lesions on Ga-68 PSMA PET/CT, clinicians should follow the PROMISE criteria, which recommend using miPSMA expression scores and comparing them with those of the blood pool, liver, and parotid gland. The criteria also specify that miTNM classification, which helps clinicians and surgeons assess disease extent, should be performed at the time of diagnosis. PROMISE criteria also propose the PSMA PET progression (PPP) criteria for assessing treatment response in PCa [6-8]. Both the PSMA PET/CT consensus statements and PROMISE criteria call for research on the most appropriate quantitative parameters for Ga-68 PSMA PET/CT lesions [9]. Therefore, we aimed to investigate Ga-68 PSMA PET/CT parameters to evaluate treatment response in PCa by using lesion selection and staging according to the PROMISE criteria.

Methods

Patient Selection

This retrospective study was conducted in accordance with the Declaration of Helsinki and relevant ethical guidelines and was approved by the Clinical Research Ethics Committee of Mersin University, Mersin, Türkiye (date: 19.07.2023; meeting no: 15; decision no: 469). Of 708 patients with PCa who underwent Ga-68 PSMA PET/CT at the nuclear medicine department, 64 patients who had both staging and post-treatment response imaging between November 2018 and December 2022 were included retrospectively.

Clinicopathological data were collected from hospital records and patient files. These included age at diagnosis, survival status, ISUP scores, EAU risk groups, and treatments received. The interval between serum PSA tests and the corresponding Ga-68 PSMA PET/CT scans was kept within two weeks for both staging and response assessments.

PSA response definitions were as follows: complete response (serum PSA 0 ng/mL); biochemical progression (≥25% PSA increase); biochemical regression (≥50% PSA decrease); and stable disease (<25% increase or <50% decrease) [10,11]. These thresholds were adopted instead of the Prostate Cancer Working Group 3 (PCWG3) progression criteria [12]. PCWG3 was developed specifically for PSA-based progression assessment in metastatic castration-resistant prostate cancer (mCRPC) trials; however, because our cohort spanned a broader range of disease states and treatment modalities - including active surveillance and hormone-naive patients - a single mCRPC-specific criterion set was not considered directly applicable to the entire population.

Image Analysis

Ga-68 PSMA PET/CT images were reviewed by two nuclear medicine physicians on the Siemens syngo via PET/CT workstation. The interval between Ga-68 PSMA PET/CT scans was limited to 12 months. Lesions were selected based on miPSMA expression scores defined in the PROMISE framework and categorized as metastases in the prostate gland, lymph nodes, bone, or visceral organs. When multiple metastases were present in the same region, only the lesion with the largest size and highest uptake per PROMISE was considered. To evaluate treatment response using Ga-68 PSMA PET/CT images, the PPP criteria were applied [6,7]. As the PPP criteria define a binary progression outcome instead of discrete response categories, patients were classified as progressors (meeting the PPP-defined progression criteria) or non-progressors (not meeting the PPP-defined progression criteria). Staging was performed on the patients' initial and post-treatment images according to the miTNM staging system described in the PROMISE criteria. Changes between pre-treatment and post-treatment miTNM stages were classified separately for T, N, and M as follows: stable if the stage remained unchanged; progression if the stage advanced to a higher stage; and regression (response) if the stage declined to a lower stage.

Volumetric Analysis

Three-dimensional manual volumetric regions of interest (VOIs) were delineated for selected tumoral regions: the prostate gland, lymph nodes, bone, and visceral metastases. For each lesion, a 40% SUVmax threshold was used to define the VOIs and to calculate SUVmax, SUVmean, SUVpeak, and PSMA-TV. We calculated TL-PSMA by multiplying PSMA-TV by SUVmean. All parameters were measured both before and after treatment and were recorded separately.

Statistical Analysis

The primary endpoint of this study was to evaluate the ability of PET/CT parameters to predict treatment response using receiver operating characteristic (ROC) analysis. Data analysis was performed using SPSS software (version 22.0; IBM Corp., Armonk, NY, USA). Categorical comparisons were performed using chi-square tests. For continuous variables, differences between groups were analyzed using independent-samples t-tests, and pre- and post-treatment changes were assessed using paired-samples t-tests. Correlation analysis was conducted to assess relationships among continuous variables. A p value <0.05 was considered statistically significant.

Results

The pathological and clinical characteristics of the 64 patients are provided in Table 1. Serum PSA responses were compared with PET/CT-based treatment responses. Among patients with

Table 1. Descriptive characteristics of patients

Characteristics	Number (n)	Percentage (%)
GLEASON		
≤7	17	26.60
8	10	15.60
≥ 9	37	57.80
ISUP		
1	5	7.80
2	7	10.90
3	5	7.80
4	10	15.60
5	37	57.80
EAU Risk Classification		
Low-risk	2	3.10
Intermediate-risk	5	7.80
High-risk	57	89.10
Treatment options		
Hormonal therapy (monotherapy or combination)	53	82.8
Chemotherapy	8	12.50
Radiotherapy only	1	1.60
Active surveillance	2	3.10
Survival status		
Survivors	47	73.40
Non-survivors	17	26.60

EAU: European Association of Urology, ISUP: International Society of Urological Pathology

a complete serum PSA response, 1 patient (4.0%) showed PSMA PET progression. Among those with a partial serum PSA response, 3 (11.5%) exhibited PSMA PET progression. Among patients with a stable serum PSA response, 3 (42.9%) showed PSMA PET progression; among those with a progressive serum PSA response, 6 (100%) showed PSMA PET progression. There was a statistically significant difference between serum PSA response and PSMA PET progression status ($p<0.001$). However, no statistically significant differences were found between treatment response assessed by Ga-68 PSMA PET/CT and patients' ISUP scores or EAU risk classifications ($p=0.538$ and $p=0.367$, respectively).

Pre- and post-treatment Ga-68 PSMA PET/CT parameters were compared with PSMA PET evaluations. Changes in SUVmax, SUVmean, and SUVpeak for Δprostate, Δlymph node, and Δvisceral metastasis differed significantly according to treatment response assessed by Ga-68 PSMA PET/CT. SUV measurements associated with Δprostate, Δlymph node, and Δvisceral metastasis were higher among progressors. Other PET parameters did not show significant differences in response to Ga-68 PSMA PET/CT treatment ($p>0.05$).

To determine the predictive value of Ga-68 PSMA PET/CT parameters for response, ROC analysis was performed on changes in these parameters relative to PSMA PET progression status, determined in accordance with the PPP criteria (Figure 1). ROC analysis data for the prostate (Figure 1a), regional lymph node metastasis (Figure 1b), bone (Figure 1c), and visceral organ metastasis (Figure 1d) are presented in Table 2. Accordingly, the areas under the ROC curves (AUC) for prostate SUVmax, SUVmean, and SUVpeak measurements were found to be statistically significant ($p<0.05$). The AUCs for TL-PSMA and PSMA-TV measurements were not statistically significant ($p>0.05$). For regional lymph node and visceral organ metastases, the AUCs for SUVmax, SUVmean, SUVpeak, and TL-PSMA measurements were statistically significant ($p<0.05$). The AUCs for PSMA-TV measurements were not statistically significant ($p>0.05$). In bone metastases, the AUCs for SUVmax, SUVmean, SUVpeak, TL-PSMA, and PSMA-TV measurements were not statistically significant ($p>0.05$).

In our study, patients were classified as progressors or non-progressors based on Ga-68 PSMA PET/CT. Changes in pre- and post-therapy Ga-68 PSMA PET/CT parameters, as well as in serum PSA levels, were compared between the two groups. In patients who were progressors on Ga-68 PSMA PET/CT, no significant increase was observed between pre-treatment values of Ga-68 PSMA PET/CT parameters measured in the prostate, lymph nodes, bone, and visceral metastases and all post-treatment values ($p>0.05$). Similarly, the increase in serum PSA levels post-treatment compared with pre-treatment values was not significant ($p>0.05$). In the non-progressor group, among the PET parameters calculated from the prostate, lymph node, bone, and visceral metastases, only the treatment-secondary decrease in bone and visceral metastasis PSMA-TV values was not significant ($p>0.05$).

Patients were also staged according to the miTNM staging system, using both pre-treatment and post-treatment Ga-68 PSMA PET/CT. The distribution of patients by miTNM is presented in Table 3. Among the 12 patients in the M1c group prior to treatment, 7 had lung metastases, 1 had liver metastases, 2 had distant (supraclavicular) lymph node metastases, 1 had both lung and liver metastases, and 1 had penile metastases. Comparison of serum PSA responses with miTNM responses, based on patients' pre- and post-treatment miTNM data, showed that serum PSA response differed significantly by treatment response in miT ($p=0.007$). No significant correlation was found between serum PSA response and miN and miM treatment responses ($p>0.05$).

The comparison of Ga-68 PSMA PET/CT and miTNM treatment responses is presented in Table 4. While Ga-68 PSMA PET/CT progression status showed a significant difference according to miT, it did not show significant differences for miN or miM. Since there was only 1 patient in the progressive response group according to miT, the group was excluded from the analysis because the sample size was insufficient for statistical analysis. Also, the changes in Δprostate TL-PSMA and Δprostate PSMA-TV parameters according to miT were not significant; significant differences were found in the changes in other Δprostate SUV measurements ($p<0.001$).

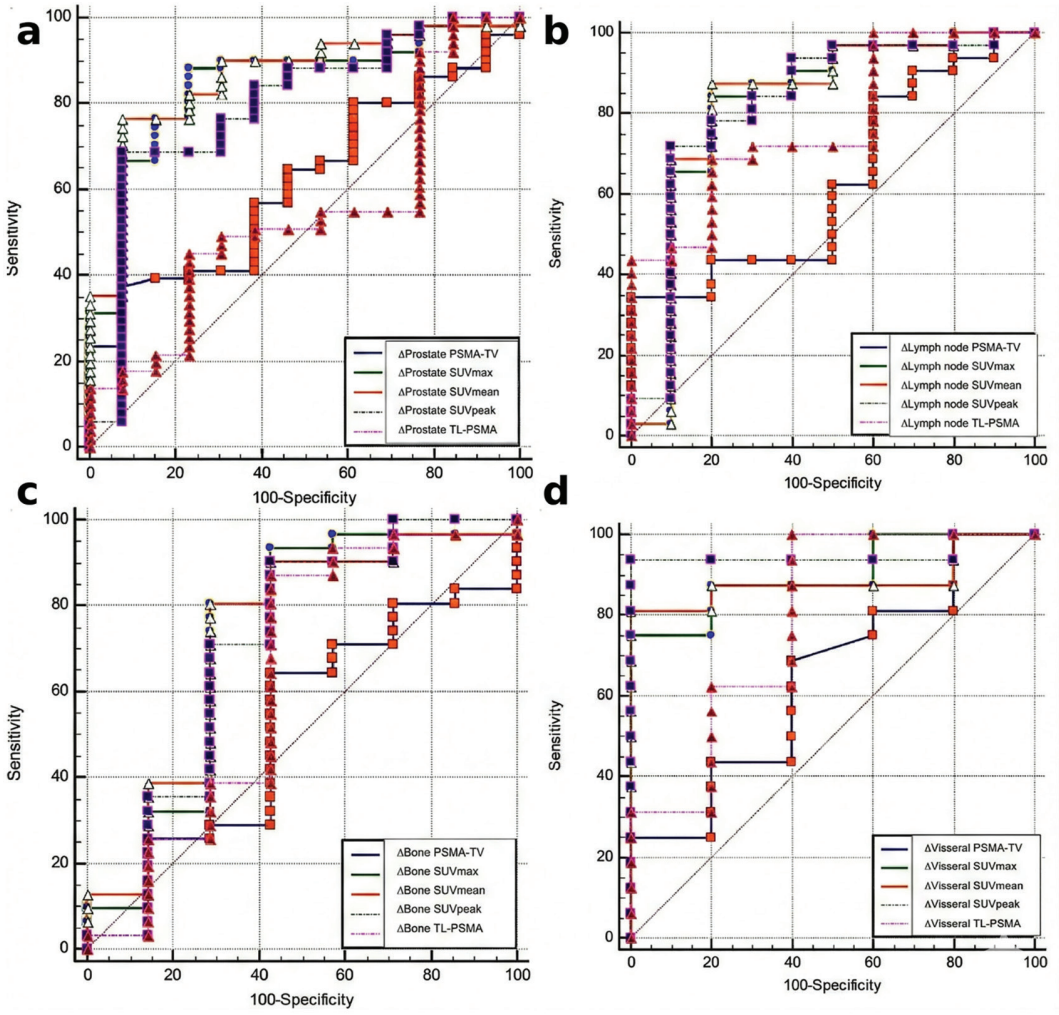


Figure 1. Receiver operating characteristic analyses of changes in gallium-68 prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/computed tomography (CT) parameters in predicting PSMA PET progression. Changes in PSMA PET/CT parameters: a) prostate, b) lymph nodes, c) bone metastases d) visceral metastases

Discussion

Since Ga-68 PSMA PET/CT is a molecular imaging method that demonstrates PSMA expression, there arose a need to develop response assessment criteria distinct from those used for F-18 FDG PET/CT, a metabolic imaging tool. To this end, PPP criteria were published. In a multicenter retrospective study by Gafita et al. [13], PSMA PET/CT response criteria were compared for evaluating treatment response in PCa; the PPP criteria were shown to be superior to RECIST 1.1 criteria in assessing response to 177Lu-PSMA radioligand therapy in patients with mCRPC.

The PROMISE criteria were developed to standardize the analysis of Ga-68 PSMA PET/CT images and the evaluation of disease extent, distribution, and PSMA expression. In our study, a statistically significant association was seen between PSMA PET progression status and serum PSA response ($p<0.001$). There was a statistically significant decrease in serum PSA levels from pre- to post-treatment in the non-progressor group compared with the progressor group, as assessed by Ga-68 PSMA PET/CT. Among patients with complete, partial, and stable PSA responses, 4.0%, 11.5%, and 42.9% showed PSMA PET progression, respectively. We attribute this discordance to potential heterogeneity in tumoral lesions' responses to treatment. In a study by Esen et al. [14], examining 345 serial Ga-68 PSMA PET/CT imaging of 96 patients, a significant level of concordance was found between PSMA PET response, as determined by the PPP criteria, and biochemical response, similar to our study. Lunger et al. [15] analyzed the relationship between serum PSA response and the adapted PCWG 3, aPERCIST, and the PPP criteria for assessing therapy response with Ga-68 PSMA PET/CT in patients receiving taxane-based chemotherapy and found that the PPP criteria had stronger prognostic value than other criteria.

In the published consensus report on response assessment with Ga-68 PSMA PET/CT in PCa, it was agreed that the timing of treatment response PET/CT should be at least 3 months after treatment, especially in patients receiving ADT, to avoid the flare

Table 2. ROC analysis of changes in Ga-68 PSMA PET/CT parameters for predicting treatment response

	PSMA-TV	SUVmax	SUVmean	SUVpeak	TL-PSMA
Prostate					
AUC (SE)	0.618 (0.08)	0.846 (0.06)	0.861 (0.06)	0.793 (0.08)	0.543 (0.09)
95% CI	0.488-0.736	0.734-0.924	0.752-0.935	0.674-0.884	0.414-0.668
p value	0.141	**<0.001**	**<0.001**	**<0.001**	0.637
Lymph node					
AUC (SE)	0.631 (0.10)	0.822 (0.10)	0.825 (0.10)	0.825 (0.09)	0.775 (0.08)
95% CI	0.469-0.775	0.673-0.923	0.677-0.925	0.677-0.925	0.620-0.889
p value	0.190	**0.001**	**<0.001**	**<0.001**	**<0.001**
Bone					
AUC (SE)	0.521 (0.13)	0.724 (0.14)	0.724 (0.13)	0.700 (0.14)	0.631 (0.15)
95% CI	0.353-0.685	0.555-0.856	0.555-0.856	0.530-0.838	0.460-0.782
p value	0.870	0.112	0.088	0.164	0.392
Visceral					
AUC (SE)	0.644 (0.15)	0.900 (0.07)	0.888 (0.07)	0.950 (0.05)	0.788 (0.15)
95% CI	0.408-0.837	0.690-0.987	0.674-0.982	0.758-0.999	0.556-0.933
p value	0.345	**<0.001**	**<0.001**	**<0.001**	**0.048**

AUC: Area under the curve, CI: Confidence interval, PSMA-TV: PSMA tumor volume, SE: Standard error, SUV: Standardized uptake value, TL-PSMA: Total lesion PSMA, Ga-68 PSMA PET/CT: Gallium-68 prostate-specific membrane antigen positron emission tomography/computed tomography

Table 3. Distribution of patients according to miTNM

	Pre-treatment	Post-treatment
	n (%)	n (%)
T stage		
T0	1 (1.6%)	6 (9.4%)
T1	1 (1.6%)	1 (1.6%)
T2	26 (40.6%)	35 (54.7%)
T3a	7 (10.9%)	3 (4.7%)
T3b	11 (17.2%)	5 (7.8%)
T4	18 (28.1%)	13 (20.3%)
Tr	—	1 (1.6%)
N stage		
N0	24 (37.5%)	35 (54.7%)
N1	40 (62.5%)	29 (45.3%)
M stage		
M0	23 (35.9%)	25 (39.1%)
M1a	3 (4.7%)	4 (6.2%)
M1b	26 (40.6%)	26 (40.6%)
M1c	12 (18.8%)	9 (14.1%)
Total	**64 (100%)**	**64 (100%)**

miTNM: Molecular imaging TNM, T: Tumor, N: Lymph node, M: Metastasis

phenomenon [9]. Since our imaging interval was longer than 3 months, acute flare-related changes are unlikely to account for the observed measurements. This interval, however, does not preclude a second and distinct source of bias: the sustained modulation of PSMA expression by the treatments themselves. The treatments administered in our cohort differ substantially in their mechanisms of action, and androgen-axis-directed agents, in particular, exert well-documented effects on PSMA expression that are independent of tumour burden. Emmett et al. [16] demonstrated in serial Ga-68 PSMA PET imaging that, within nine days of commencing androgen blockade, SUVmax decreased by a median of 30% in men with hormone-sensitive disease but increased by a median of 45% in men with castration-resistant disease, establishing a dichotomous and phenotype-dependent response of the PSMA signal to the same class of agent. Consistent with this, Vaz et al. [17] reported that short-term androgen deprivation upregulates PSMA expression whereas prolonged androgen deprivation reduces PSMA-ligand uptake. A reduction in SUV parameters observed after several months of androgen-axis-directed therapy may therefore reflect receptor-level downregulation rather than a genuine reduction in viable tumour burden; conversely, an increase in uptake in castration-resistant disease need not indicate progression. In our cohort, 53 of 64 patients (82.8%) received androgen-axis-directed therapy, alone or in combination, which limits the extent to which the observed changes in SUV parameters can be unambiguously attributed to an antitumour effect. This consideration applies to the interpretation of all quantitative PET parameters reported here and should temper any inference of a direct biological response. Similarly, the PROMISE criteria indicated the need for further research to determine which semi-quantitative parameter is the most appropriate tumor measurement, and this question remains unresolved in the current literature: a recent review of response evaluation in PCa concluded that, although both the PPP criteria and RECIP 1.0 carry prognostic value during PSMA-targeted radioligand therapy, response assessment remains considerably more complex under androgen-targeted agents because of variable treatment-induced changes in PSMA expression [18].

Table 4. miTNM treatment response assessment according to Ga-68 PSMA PET/CT

		Progressors	Non-progressors	Total	Statistics
		n (%)	n (%)	n (%)	p value
miT	Stable response	12 (92.3%)	29 (56.9%)	41 (64.1%)	**p=0.003***
	Treatment response	0 (0%)	22 (43.1%)	22 (34.4%)	
	Progressive response	1 (7.7%)	0 (0.0%)	1 (1.6%)	
miN	Stable response	11 (84.6%)	40 (78.4%)	51 (79.7%)	p=0.081*
	Treatment response	1 (7.7%)	11 (21.6%)	12 (18.8%)	
	Progressive response	1 (7.7%)	0 (0.0%)	1 (1.6%)	
miM	Stable response	11 (84.6%)	45 (88.2%)	56 (87.5%)	p=0.129*
	Treatment response	1 (7.7%)	6 (11.8%)	7 (10.9%)	
	Progressive response	1 (7.7%)	0 (0.0%)	1 (1.6%)	

*Chi-square.
Ga-68 PSMA PET/CT: Gallium-68 prostate specific membrane antigen positron emission tomography/computed tomography, miTNM: molecular imaging TNM

We found that ΔSUVmax, ΔSUVmean, and ΔSUVpeak values for prostate lesions, metastatic lymph nodes, and visceral metastases differed significantly by treatment response. According to the AUC in the ROC analysis performed to evaluate the predictivity of progression in prostate lesions, metastatic lymph nodes, and visceral metastases, ΔSUVmean (AUC=0.861) and ΔSUVmax (AUC=0.846) had excellent discriminative performance for prostate lesions, while ΔSUVpeak (AUC=0.793) had acceptable discriminative performance. ΔSUVmean, ΔSUVpeak, and ΔSUVmax values in regional metastatic lymph nodes and visceral metastases demonstrated excellent discriminative performance. Several publications in the literature investigate parameters similar to ours, employing different methods. In a multicenter study by Kendrick et al. [19], lesion-based semi-quantitative parameters were examined in 328 lesions from 138 patients with biochemical recurrence. They reported, in their analysis comparing patients with and without systemic progression, that SUVmean was the most significant prognostic parameter.

Schmuck et al. [20] investigated the statistical concordance between changes in PSA levels and Ga-68 PSMA PET/CT parameters to evaluate treatment response. In contrast to our study, their results showed that post-treatment changes in SUVmax and SUVmean were not statistically significant compared with changes in PSA levels. Contrary to our findings, a statistically significant relationship was observed between changes in TL-PSMA and PSMA-TV parameters and changes in PSA levels. A literature review by Adashek et al. [21] stated that inter- and intra-patient tumor heterogeneity may exist in cancers. They highlighted the difficulty of evaluating treatment response because of intra-patient tumor heterogeneity. In our study, contrary to the literature, TL-PSMA and PSMA-TV values in prostate lesions and bone metastases were not statistically significant predictors of treatment response.

In our study, the statistical significance of post-treatment changes in PSMA PET parameters was examined separately in the progressor and non-progressor groups using Ga-68 PSMA PET/CT imaging. In our progressor group of 13 patients, we observed that increases in pre- and post-treatment PSMA PET parameters and PSA levels in prostate lesions, metastatic lymph nodes, bone, and visceral metastases were not statistically significant. However, in our non-progressor group of 51 patients, we found that the decreases in pre- and post-treatment values were statistically significant for all parameters except PSMA-TV parameters in bone and visceral metastases. The EAU guideline states that the high-risk group may be associated with mortality and metastasis [22]. Although not statistically significant, the fact that all patients in the progressor group of our study were classified as high risk according to the EAU risk classification suggested that these patients' PCa had an aggressive course.

In a secondary analysis, the miTNM classification system was applied. Only the miT category demonstrated a significant association with PSA response (p=0.007). The Ga-68 PSMA PET/CT response showed a significant difference only in the miT category. In our study, 'stable' and 'treatment response', as categorized by the miT classification, showed statistically significant correlations with SUVmax, SUVmean, and SUVpeak. However, no statistically significant association was observed between treatment response in the miN and miM categories and Ga-68 PSMA PET/CT parameters. Furthermore, the PROMISE criteria state that miTNM staging should be performed to provide detailed information about the extent and localization of PCa. Although treatment response in the miT category showed statistical significance with PSMA PET progression status, based on our findings, we suggest that performing treatment response assessment with miTNM staging may not be appropriate; however, given the results of publications in the literature indicating that pre-treatment miTNM staging can predict disease progression, performing miTNM staging pre-treatment appears appropriate [23].

Study Limitations

This study has several limitations due to its retrospective design, including a relatively small sample size, which may limit the clarity of the outcomes. Furthermore, PSA served as the sole reference standard against which the predictive performance of Ga-68 PSMA PET/CT parameters was benchmarked. Our

cohort included several distinct treatment modalities, and the number of patients in each modality was insufficient to permit a formal stratified analysis by treatment type. Although the great majority of patients received androgen-axis-directed therapy, rendering the cohort relatively homogeneous with respect to the dominant mechanism of action, residual heterogeneity remains. To address this, future research should explore total-tumor-burden sampling approaches and incorporate imaging-based or clinical progression-free survival endpoints as reference standards to capture the full spectrum of metabolic and molecular variability.

Conclusion

In this study, we evaluated the predictive role of PSMA PET in patients with PCa, using the PPP criteria within the PROMISE framework. We suggest that the PPP criteria are preferable for routine clinical practice due to their ease of application. Also, miTNM classification appears most suitable for determining disease extent during initial staging. Therefore, prospective studies with larger patient cohorts are warranted to further validate these findings.

Ethics

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Mersin University, Mersin, Türkiye (date: 19.07.2023, meeting no: 15, decision no: 469).

Informed Consent: Retrospective study.

Footnotes

Presented in: This study was presented as an oral presentation at the 38th National Nuclear Medicine Congress, held in Belek, Antalya, Türkiye, on 1-5 April 2026.

Authorship Contributions

Surgical and Medical Practices: M.B., E.S., Concept: Z.S.S.B., P.P.Ö., Design: Z.S.S.B., P.P.Ö., Data Collection or Processing: Z.S.S.B., P.P.Ö., Z.P.K., Literature Search: Z.S.S.B., P.P.Ö., G.T., Writing: Z.S.S.B., P.P.Ö., G.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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