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Original Article

Standardised Uptake Value in Organ Confined Prostate Cancer in 68-Ga- Prostate-Specific Membrane Antigen Positron Emission Tomography-Computed Tomography Scan and its Correlation with Prostate Specific Antigen Level and Gleason Score

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Abstract

Introduction: A positron emission tomography (PET) scan and a computed tomography (CT) scan are an integral part of oncological imaging and other modalities such as magnetic resonance imaging, CT or bone scintigraphy have some limitations in staging the workup of prostate carcinoma. Combined with tissue-specific markers like prostate-specific membrane antigen (PSMA), positron emitter-based functional imaging results have improved. Our study aimed to determine the Standardised Uptake Value (SUVmax) in prostate adenocarcinoma that is confined to the organ in Ga-68-PSMA PET-CT scans and how it correlates with prostate-specific antigen (PSA) levels and Gleason score (GS). **Materials and Methods:** This cross-sectional study was conducted at Sindh Institute of Urology and Transplantation (SIUT), Karachi, and includes subjects referred for a Ga68-PSMA PET-CT scan from September 2017 to January 2022. Histopathologic-proven adenocarcinoma prostate patients with organ-confined disease and PSA levels obtained within 6 weeks before the PSMA-PET-CT scan were included in the study. PET-CT images were semi-quantitatively analysed by measuring SUVmax and the result was interpreted using statistical software SPSS version 22.0. **Results:** A total of 154 patients were analysed. The mean age of patients was 66.57 ± 8.86 years. The GS of all patients ranges from 6 to 10. The mean and median PSA levels were 32.33 ng/mL (range: 0.004–306.00) and 14.20 ng/mL, respectively. The mean SUVmax of all prostatic lesions was 14.67 ± 12.58 and the median value was 10.76. SUVmax was higher in patients with a PSA level of more than ten than those with a <10. The correlation of SUVmax with PSA and GS showed a significant correlation. **Conclusion:** The SUVmax of organ-confined prostate cancer correlates well with PSA level and GS Median SUVmax and PSA directly relate to GS.

Key words: Ga-68 prostate-specific membrane antigen positron emission tomography-computed tomography, Gleason score, Prostate cancer, Prostate specific antigen, SUVmax

Introduction

Carcinoma prostate is one of the most prevalent global cancers and is the fifth leading cause of men's cancer-related deaths.[1,2] Its incidence is increasing in many countries, likely due to advancements in diagnostic techniques or environmental factors.[3]

Multiparametric magnetic resonance imaging (mp-MRI) is recommended in men with increased serum prostate-specific antigen (PSA) levels on screening before biopsies.[4] An MRI has a 68% detection rate in diagnosing prostate cancer and classifies the detected prostate lesions into five categories.[5,6] A biopsy is recommended in PIRADS (Prostate Imaging Reporting and Data System) 3 or above lesions.[7] A TRUS (transrectal ultrasound scan) guided biopsy is the most common technique to diagnose carcinoma prostate. However, in 1/3rd patients, it is not an effective tool for diagnosis.[8-10] Results improve when TRUS-guided biopsy (TRUS-GB) is fused with mp-MRI. However, up to 35% of lesions remain undetected.[11-14]

Molecular imaging is an integral part of oncological imaging and numerous studies demonstrate the superiority of PET-CT over other modalities in terms of diagnostic accuracy.[15] Flourine-18 is the most frequently used positron emitter in PET-CT imaging. When these positron emitters are combined with tissue-specific markers, results are improved.

In recent years, Gallium-68 prostate-specific membrane antigen (PSMA) has shown promise as a PET tracer for detecting prostate cancer during staging workups. This is particularly useful since other imaging methods, such as CT and MRI scans and bone scintigraphy, have limitations.[16-18] PSMA is a transmembrane protein that is over-expressed in cancerous prostatic cells, resulting in increased maximum Standardised Uptake Value (SUVmax) on Gallium-68 PSMA PET-CT scan.[19] The intensity of PSMA expression also directly relates to tumour grade, as high-grade prostatic carcinoma shows increased uptake. Gallium-68 PSMA PET-CT helps in the accurate localisation of primary malignant prostatic carcinoma to improve biopsy results; apart from this, it also has the potential to differentiate benign from malignant lesions.[20]

Gallium-68 PSMA PET-CT had a sensitivity of 97% and a specificity of 66% for the initial detection of prostate carcinoma, so it has the potential to omit biopsy in patients with clinical or biochemical findings of suspected prostate cancer.[21] There are a limited number of studies with small sample sizes and variations in the results available to evaluate the role of Gallium-68 PSMA PET-CT for the initial diagnosis of suspected prostatic carcinoma and its correlation with PSA levels. The objective of our study is to find out the Standardised Uptake Value (SUVmax) in organ-confined adenocarcinoma of the prostate in Gallium-68 PSMA PET-CT and its correlation with PSA level and Gleason score (GS).

Materials and Methods

This retrospective cross-sectional study was conducted at the Department of Nuclear Medicine, Sindh Institute of Urology and Transplantation (SIUT) Karachi, Pakistan, between September 2017 and January 2022. The study was approved by the ethical review committee (approval no: SIUT-ERC-2022/A-209) of the SIUT, Karachi. Patients with histopathologically proven adenocarcinoma prostate gland with organ-confined disease, PSA level obtained within 6 weeks before the Galium-68 PSMA PET-CT, had not received any treatment and presented between September 2017 and January 2022 were investigated. On the contrary, patients with lymphatic spread or distant metastasis were excluded from the study.

Experienced nuclear physicians and radiologists reviewed PET-CT images of patients using the Philips Fusion Viewer. The SUVmax of the primary tumour, serum PSA level and GS were recorded in the datasheet. After preparing the PSMA labelled Gallium-68 in the semi-automated module, it was injected into all patients through the intravenous route and whole-body PET-CT imaging was acquired (2 min/bed), 50 min after injection using Phillips Gemini PET-CT 64-slice (CT parameters: Slice thickness 2 mm, 120 keV and 50 mAs).

Table 1: Values of SUVmax and in different

Tumour grading	GS	Number of patients	PSA level		SUVmax			
			Mean	Median	Minimum	Maximum	Mean	Standard deviation
Low grade	6	32	12.12	7.590	2.03	55	9.47	9.688
Medium grade	7	41	29.71	14	3.21	22.29	5.71	4.23
High grade	8	38	28.04	19	2.6	49.20	17.16	11.979
	9	34	53.65	35.82	3.9	11.2	21.17	19.834
	10	9	53.63	22	6.10	44.24	29.20	11.028

GS: Gleason score, PSA: Prostate specific antigen, SUVmax: Standardised Uptake Value

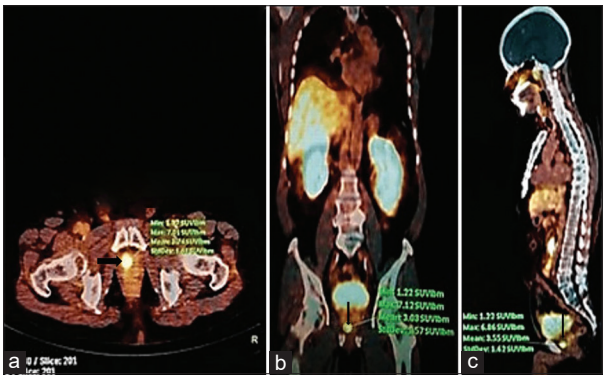

Figure 1: (a-c) 68-Gallium prostate-specific membrane antigen positron emission tomography (PET) scan and a computed tomography (CT) scan of 72-year-old male with Gleason score 6 and PSS level 7.32 ng/mL showing increased uptake in the peripheral zone in the right lobe of the prostate gland with SUVmax of 7.01 (A=Axial section, B=Coronal C=Sagittal PET-CT fused images)

Statistical analysis was done on SPSS software version 22.0. Results of SUVmax and PSA levels are expressed in means and medians. The Spearman correlation test was used to correlate SUVmax, PSA level and GS, visualised in a scatter plot graph. A two-tailed significance was applied and a probability value (I-value) of <0.05 was considered significant.

Results

A total of 495 patient files were reviewed. However, 154 patients met the inclusion criteria of the study. The rest of the subjects were excluded because there was lymphatic spread or distant metastasis, a PSA level obtained more than 6 weeks before the scan or they had received treatment for prostate cancer.

The average age of the study cohort was 66.57 ± 8.86 years. The age range of the sample varied from 40 to 91 years old. On analysis, the mean PSA level was found to be 32.33 ng/mL, with a median of 14.20 ng/mL and a range of 0.004–306.0 ng/mL. The GS value for all patients fell between 6 and 10 and the mean SUVmax for all patients was 14.67 ± 12.58, with a median of 10.76.

Further analysis was conducted to determine the mean SUVmax values based on the GS and PSA levels (Table 1). We observed that patients with PSA levels greater than 10 had significantly higher SUVmax values than those with PSA levels of <10 (Table 2). For example, in Figure 1, it is evident that low-grade prostate carcinoma exhibits a low SUVmax value.

There was a significant correlation between PSA and SUVmax and between GS and SUVmax (R Spearman 0.336, $P < 0.001$) and (R Spearman 0.312, $P < 0.001$), respectively, for patients with organ-confined prostate cancer. See Figures 2 and 3 for more information.

Discussion

The study aimed to determine the SUVmax in organ-confined adenocarcinoma of the prostate in Gallium-68 PSMA PET-CT and its correlation with PSA level and GS.

PSMA receptor is overexpressed in prostate cancer tissue than normal or benign prostate diseased cells, which increases SUVmax on Galium-68 PSMA

Table 2: Comparison of PSA values SUVmax and patients with PSA level<10 ng/mL and>10 ng/ml

Categories of PSA level	Number of patients	Mean SUV-max	Median SUV-max	Minimum SUVmax	Maximum SUVmax	Standard deviation
<10	63	11.82	8.4	2.03	55.11	10.21
>10	91	16.64	14	3.20	94.57	13.71

PSA: Prostate specific antigen, SUVmax: Standardised Uptake Value

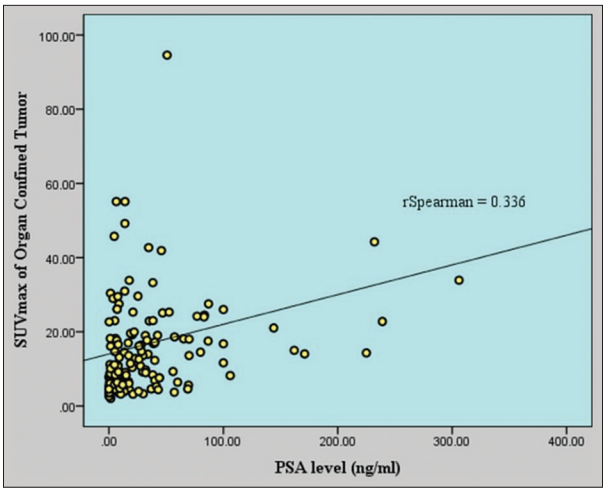

Figure 2: Scatter plot shows a correlation between prostate specific antigen level and Standardised Uptake Value in prostate cancer

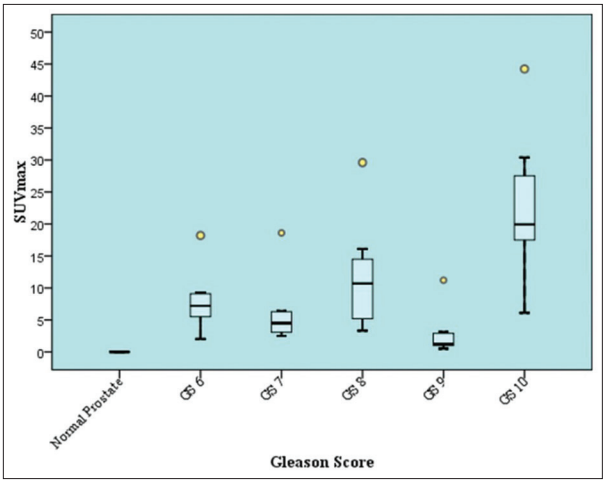

Figure 3: Box plot demonstrates that overall median Standardised Uptake Value is significantly higher with Gleason score of more than 6

PET-CT scan and can potentially discriminate between benign and malignant prostate tissue. Furthermore, PSMA receptor overexpression positively correlates with tumour grade; high-grade prostate cancers have more SUV max than low-grade cancers. Woythal *et al.* calculated the mean SUVmax (14.10 ± 15.60) in prostatic cancer tissue, comparable to our result of 14.67 ± 12.58.[22]

According to a study by Jianhua Jiao and colleagues, a SUVmax cutoff of 5.30 can effectively differentiate between benign prostatic hyperplasia (BPH) and carcinoma. This cutoff demonstrated a sensitivity of 85.85%, specificity of 86.21%, positive predictive value of 95.79%, negative predictive value of 62.50% and an overall accuracy of 85.93%. Out of all the participants in the study, 63.3% of those with a SUVmax up to 5.3 had BPH, while only 36.7% of those with a SUVmax below 5.3 had benign prostate carcinoma.[23] In addition, a significant correlation was reported between SUVmax and GS and SUVmax and PSA levels. Out of the prostate carcinoma patients examined in this study, 19.5% exhibited a SUVmax below 5.3, primarily those with low-grade tumours. It is worth mentioning that there was a significant correlation observed among SUVmax, GS and PSA levels.

A study by Demirci *et al.* explored the SUVmax of prostate cancer tissue in Galium-68 PSMA PET-CT scans. The study found that 21% of patients had their GS upgraded from low grade to high grade in biopsy samples. In comparison, 10% had their grade downgraded from high to low in the histopathology report of radical prostatectomy.[24] The study found that the average SUVmax was 13.2 ± 11.7, with a median value of 8.8. Our results were comparable, with an average SUVmax of 14.67 ± 12.58 and a median value of 10.76. Demirci *et al.* also observed a significant correlation between SUVmax and grade groups, with a Pearson's ρ of 0.50 and

P < 0.001. Similarly, our study found a significant correlation between SUVmax and Gleason grade, with a Spearman's r of 0.31 and *P* < 0.001. Rahbar *et al*. also had similar results, showing a significant correlation between SUVmax and GS.[25]

A 2017 retrospective study by Uprimny *et al*. found that 91.1% of patients had an increased SUVmax of 12.5 compared to surrounding normal prostatic tissue with a SUVmax of 3.9.[26] The study also discovered that high-grade tumours (GS>7) had significantly higher Mean SUVmax than low and intermediate-grade tumours (<7) (median SUVmax: 21.2 versus 8.3 p < 0.001). Patients with increased PSA levels (≥10.0 ng/mL) also had significantly higher SUV max (17.6) compared to those with low PSA levels (<10.0 ng/mL) SUV max, 7.7. The study concluded that GS and PSA levels correlated with SUV max prostate carcinoma lesion on Galium-68 PSMA PET-CT scan. Our study had similar results, where high-grade prostatic carcinoma patients had higher SUV max than low-grade/intermediate tumours (mean SUVmax 22.51 versus 7.59]. In addition, our research found that patients with increased PSA levels (>10 ng/mL) had higher SUVmax (SUV max 16.64) compared to those with low PSA levels (<10 ng/mL) SUVmax 11.82.

It is essential to approach the study results cautiously due to certain limitations. First, the investigation was conducted at a single centre and it had a retrospective study design. This can lead to reporting and recall biases and influence the correlations observed. In addition, the study only examined the correlation between SUVmax and pre-prostatectomy histopathology findings. The GS grade can change based on biopsy results for a significant proportion of patients. Future studies should be prospective and include pre- and post-prostatectomy samples. Likewise, the investigation should be conducted at multiple centres.

The study findings emphasise the advantages of SUVmax. In cases of organ-confined prostate cancer, there is a strong correlation between PSA level and SUVmax. Furthermore, median SUVmax and PSA have a direct relationship with GS. Hence, we suggest performing PSMA PET-CT in organ-confined tumours with a GS of 6 and a PSA level of >10, as they exhibit significant radiotracer uptake in the tumour. Focal radiotracer activity intensity can differentiate the disease site from a healthy portion of the prostate gland, making it a dependable guide for a needle biopsy.

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Author contributions

Conceived and designed the analysis: SRA and AH; Collected the data: HA; Contributed data or analysis tools: HA and SRA; Performed the analysis: HA; Wrote the paper: HA, SRA and AH