Original Article

The Value of SUVmax of Gallium-68-PSMA PET/CT in Newly Diagnosed Prostate Cancer

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Abstract

OBJECTIVES: To evaluate the correlation between the intensity of prostate specific membrane antigen (PSMA) expression by Gallium-68-PSMA positron emission tomography/computer tomography (Ga-68-PSMA PET/CT) and the D'Amico risk classification of newly diagnosed prostate cancer patients.

MATERIALS AND METHODS: Retrospective reviews of 61 newly diagnosed prostate cancer patients, who underwent Ga-68-PSMA PET/CT between September 2017 and November 2021. Data of maximum standard uptake value (SUV max) of prostate tissue was collected. The correlation between SUV maximum value and D'Amico risk classification, as well as Gleason score (GS) grade group and prostate specific antigen (PSA) level, was evaluated. For the data analysis, the Kruskal-Wallis test, Pearson correlation, and receiver operating characteristic curve (ROC curve) analysis were carried out.

RESULTS: Most of the patients (50 patients, 82%) were in the high risk D'Amico risk classification. The mean SUVmax values of the primary tumor for all patients were 15.7 ± 10.5. The SUVmax values for low and intermediate-risk patients (9.5 ± 4.76) were significantly lower than those of high-risk patients (17.06 ± 10.93) (*p*-value 0.013). A positive correlation was found between SUVmax values and the GS grade group (*p*-value 0.025), while there was a low correlation between PSA level and SUVmax values. The cutoff SUVmax value of 8.3 showed a sensitivity (84%) and specificity (63.6%) for the detection of high-risk prostate cancer.

CONCLUSION: PSMA expression in primary tumors is significantly higher in patients with higher GS grade groups and high-risk D'Amico staging, but it is not correlated with PSA level. Ga-68-PSMA PET/CT can be used to screen high-risk prostate cancer patients and potentially help in an individualized treatment decision.

Keywords: prostate cancer, PET/CT, PSMA, SUV max, D'Amico risk classification, PSA, Gleason score grade group

Prostate cancer is the second most common malignancy among men worldwide, following lung cancer.[1] According to current guidelines, prostate cancer can be treated with various treatment options such as active surveillance, radical prostatectomy, radiation therapy, and systemic treatment. The selection of each treatment option is based on staging, so complete and accurate staging of newly diagnosed prostate cancer is necessary for clinical management. The usual diagnostic tools and staging for prostate cancer include digital rectal examination, PSA level, transrectal ultrasonography-guided prostate biopsy (TRUSBx), and conventional imaging.

The European Association of Urology Guidelines recommends 10-12 cores of TRUSBx for the primary diagnosis and risk stratification of prostate cancer.[2] However, TRUSBx sometimes has false negative, underestimating the actual GS. According to Demirci et al.,[3] prostatectomy had 41.1% upgrades and 7.8% downgrades in the GS grade group when compared to TRUSbx. Furthermore, TRUSBx is an invasive procedure that can result in minor complications such as hematuria (17.9-66.3%), hematospermia (13.9-38.8%), and rectal bleeding (2.8-28.4%).[4,5]

The randomized proPSMA study[6] demonstrated that Gallium-68 PSMA PET/CT has superior diagnostic accuracy for prostate cancer when compared to conventional imaging (namely, computer tomography of the abdomen/pelvis and bone scintigraphy with SPECT/CT). A meta-analysis found that CT and MRI have low sensitivity in detecting lymph node metastases from prostate cancer[7], whereas numerous retrospective studies reported that PSMA PET/CT has a high specificity and sensitivity for lymph node detection. The sensitivity of PET/CT for the detection of lymph node disease ranges from 85-99%, compared with a sensitivity of 38-42% for CT scan. Additionally, many studies confirmed that patients who underwent PSMA PET/CT imaging also resulted in a higher percentage of management changes.[6,8,9]

PSMA is a type II transmembrane glycoprotein that has higher expression in prostate cancer cells than in benign prostate tissue,[10-11] which may guide identifying target lesions before prostate biopsy and decrease false-negative biopsy results.[12-14] Moreover, it has been shown that SUVmax values in Ga-68-PSMA PET/CT reflected proliferative cellular activity, so the intensity of PSMA expression increased in high-grade tumors.[15]

Although Ga-68-PSMA PET/CT outperforms conventional imaging modalities for detecting cancer after biochemical recurrence[6,16] and is increasingly used in high risk prostate cancer, there is insufficient evidence to change initial staging guidelines.

The aim of this study is to access the Ga-68-PSMA PET/CT ability to identify D'Amico risk of prostate cancer in a single center and examine the relationship between the intensity of PSMA expression in prostate cancer (SUV max) and the GS grade group, as well as the PSA level in newly diagnosed prostate cancer.

Materials and Methods

We retrospectively evaluated the medical records and found 329 Ga-68-PSMA PET/CT scans performed at Wattanosoth Cancer Hospital, Bangkok, Thailand, between September 2017 and November 2021. From the records, patients were selected whose biopsies proved newly diagnosed prostate cancer and underwent Ga-68-PSMA PET/CT for primary staging. If the patients had received local or systemic treatment or if this was not their first Ga-68-PSMA PET/CT, they were excluded. A total of 61 patients met all the criteria and were included in the analysis (Figure 1).

According to D'Amico risk classification criteria, the patients were divided into low, intermediate, and high risk groups. The PSA level, biopsy results (Gleason scoring), and radiologic staging are all taken into account (low risk: those with a PSA less than or equal to 10, a Gleason score less than 7, or are in a clinical stage less than T2b; intermediate risk: those with a PSA between 10 and 20, a Gleason score of 7, or are in a clinical stage more than T2b; and high risk: those with a PSA more than or equal to 20).

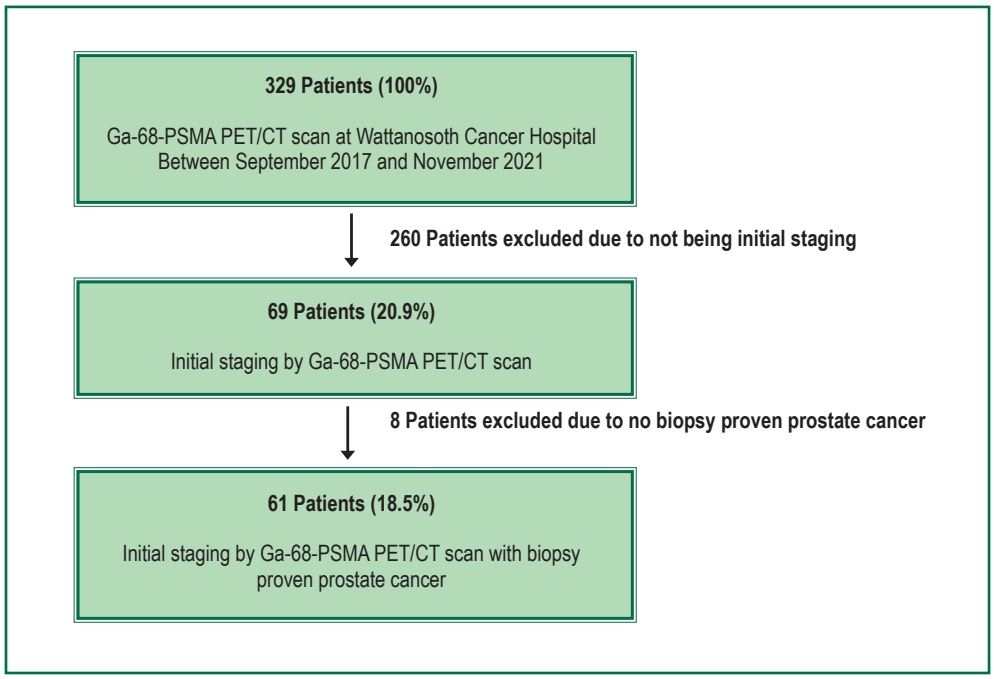

Figure1: Flowchart of patients. Ga-68-PSMA PET/CT: Gallium-68- prostate specific membrane antigen positron emission tomography/computer tomography

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In addition to the Gleason scoring system, the 2014 International Society of Urological Pathology revised the prostate cancer grading system, called the grade groups: grade group 1 (GS ≤ 6), grade group 2 (GS 3+4=7), grade group 3 (GS 4+3=7), grade group 4 (GS 4+4=8), and grade group 5 (GS 9-10). GS Grade group 1 is the least aggressive, and GS grade group 5 is the most aggressive.[17]

PSA levels were measured in all patients. Because this is a tertiary cancer center and many patients have been referred from other institutions for only the Ga-68-PSMA PET/CT PSMA scan, the time interval between PSA measurements and the Ga-68-PSMA PET/CT cannot be controlled.

Ethical consideration

This retrospective study was approved by the Bangkok committees on health research ethics, and the requirement to obtain informed consent was waived.

Image acquisition

Ga-68-PSMA at a dose of 5.4 ± 1.1 mci and 20 mg furosemide were injected intravenously 45-60 min before image acquisition. The patients were instructed to urinate immediately before the study began. A PET/CT scan of the kidney, ureter, and bladder (KUB) was obtained in a digital Biograph Vision PET/CT scanner (Siemens Healthcare), followed by a whole body PET/CT. First, low-dose CT KUB scan was performed without intravenous contrast enhancement using the following parameters: 120 Kvp tube voltage, 66 mAs with CARE dose, collimator width of 16x1.2 mm, pitch of 0.8, 0.5S gantry rotation, section thickness of 5 mm, and reconstruction thickness of 5 mm. Then, in the caudocranial direction, PET emission scanning of KUB was performed using flow motion at 1 mm per second with the same transverse field of view. Following that, a CT whole body with intravenous contrast enhancement (120 Kvp, 135 mAs; CARE dose) was obtained, followed by a whole body PET/CT. The CT data were used for attenuation correction, and axial image reconstruction was done via a standard algorithm.

Image analysis

All Ga-68-PSMA PET/CT scans were reviewed using a workstation (Syngo.via VB30A, Siemens Healthcare). PSMA PET/CT images were evaluated by board-certified nuclear medicine physicians and board-certified radiologists who were not blinded to any clinically relevant data. Any disagreement was resolved by consensus. ROI of the prostate was selected and the SUVmax was obtained.

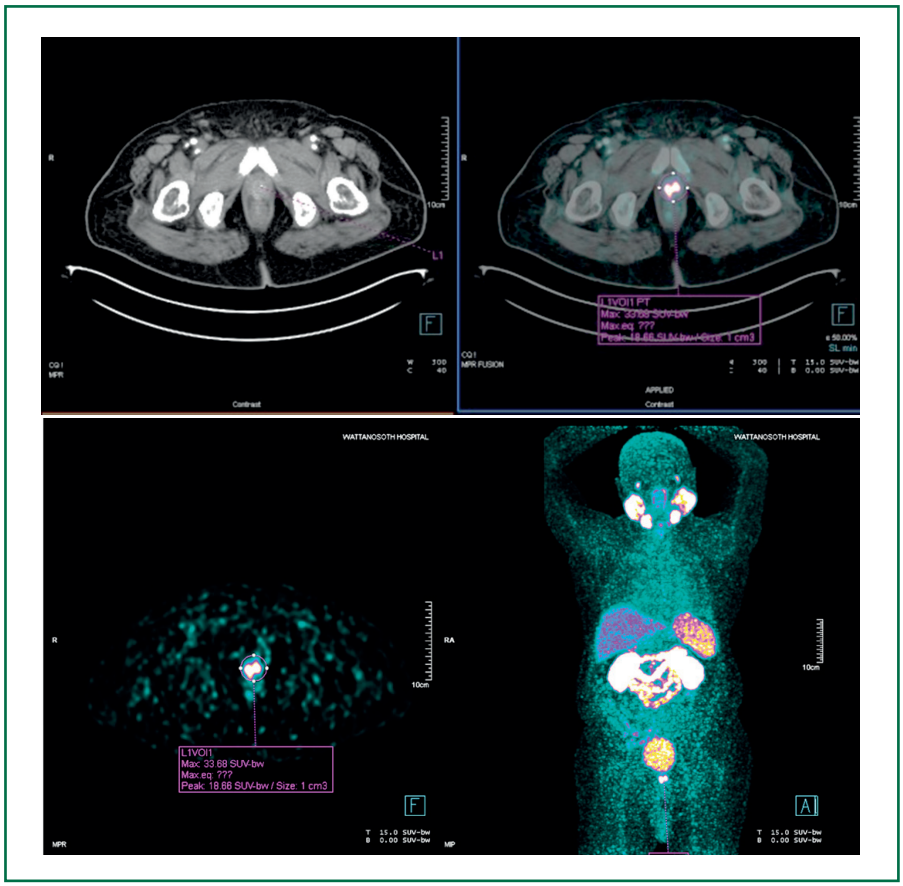

Figure2: The images of Ga-68-PSMA PET/CT of a 79-year-old patient with newly diagnosed high risk prostate cancer (Gleason score 8/Gleason score grade group4, and PSA level 10.8ng/mL). He has high PSMA expression in the prostate gland, SUVmax was 33.68.

Statistical analysis

Data analysis was performed with STATA version 15. All variables were summarized using descriptive statistics. The correlations between the SUVmax value of the prostate and the D'Amico risk, GS grade group were described by nonparametric techniques with the Kruskal-Wallis test. The correlation between the SUVmax value and PSA level was determined using the Pearson correlation test. ROC curve analysis was used to determine the optimal cutoff value of the SUVmax for identifying high-risk prostate cancer. For all statistical parameters, *P* values of less than 0.05 were considered statistically significant.

Results

The clinical characteristics of 61 newly diagnosed prostate cancer patients are summarized in Table 1. Mean age was 70.7 years with mean SUVmax 15.7. Most of the patients were in the high-risk group, accounting for 82%, while patients in the low-intermediate risk group were only 11 patients (18%). 18 patients (29.5%) have distant metastasis (M1 disease). There were 10 patients (16.4%) in GS grade group 1, 13 patients (21.3%) in GS grade group 2, 8 patients (13.1%) in GS grade group 3, 25 patients (41.0%) in GS grade group 4, and 5 patients (8.2%) in GS grade group 5. The patients have a wide range of PSA; the lowest value was 3.9 ng/mL, and the highest value was 11000.3 ng/mL. The mean PSA value across all patients was 222.7 ng/mL.

Correlation analysis

According to the Kruskal-Wallis test, the SUVmax values for low/intermediate-risk patients were significantly lower than those of high-risk patients, which were 9.5 ± 4.76 and 17.06 ± 10.93, respectively ($p = 0.013$). A positive correlation was shown between the SUVmax value of the primary tumor and the GS grade group. A lower SUVmax value was found in the low GS grade group ($p = 0.025$). The difference in SUVmax value between GS grade group 1,2,3 and those with GS grade group 4,5 was statistically significant ($p = 0.028$).

In terms of PSA level, Pearson correlation showed that there was a very low correlation between PSA level and SUVmax value (Table 3). The ROC curve analysis of the SUVmax value showed 8.3 as the cut-off value for high-risk prostate cancer (95%CI: 0.586 to 0.894). The sensitivity and specificity were 84% and 63.6%, respectively (Figure 3).

Discussion

In our study, the SUVmax values correlated significantly with the D'Amico risk classification and GS grade group. A higher D'Amico risk classification was associated with a higher SUVmax value. The optimal cutoff value of the SUVmax is 8.3, which can identify high-risk primary prostate cancer, and the sensitivity and specificity were 84% and 63.6%, respectively. This finding suggests that the uptake of Ga-68-PSMA has value in predicting clinically significant primary prostate cancer.

Table 1: Baseline Clinical and demographic characteristics of the subjects (n = 88)

Characteristics	n (%)
Age (years) ; Mean ± sd	70.7 ± 8.4
PSA(ng/ml) ; Mean ± sd	222.7 ± 10,405.8
SUV max of primary tumor (Mean ± sd)	15.7 ± 10.5
Gleason score grade group	
1 (GS ≤ 6)	10 (16.4)
2 (GS 3+4=7)	13 (21.3)
3 (GS 4+3=7)	8 (13.1)
4 (GS 4+4=8)	25 (41.0)
5 (GS 9-10)	5 (8.2)
D'Amico staging	
Low risk	4 (6.6)
Intermediate risk	7 (11.5)
High risk	50 (82.0)
TNM staging*	
T	
T2a	11 (18.0)
T2b	7 (11.5)
T2c	14 (23.0)
T3a	10 (16.4)
T3b	16 (26.2)
T4	3 (4.9)
N	
N0	43 (70.5)
N1	18 (29.5)
M	
M0	43 (70.5)
M1a	4 (6.6)
M1b	8 (13.1%)
M1c	6 (9.8%)

PSA: prostate specific antigen, SUV max: standard uptake value maximum value, GS: Gleason score
*American Joint Committee on Cancer (AJCC) TNM Staging System for Prostate Cancer (8th ed., 2017)

Our results are consistent with other retrospective studies. Uprimney et al.[18] and Fajardo-Ordóñez et al.[19] have reported that the intensity of tracer accumulation in the primary tumor of prostate cancer patients on Ga-68-PSMA PET/CT correlated with the GS and PSA levels. Koerver et al.[20] conducted a study with 100 patients who recently were diagnosed with prostate cancer, and they found that the patients with a higher PSA level, a higher GS, and a higher D'Amico risk classification had a higher PSMA uptake on PET/CT.

In contrast to other studies, our study found a low correlation between the PSA level and the SUVmax value of a primary tumor. This could be because the time interval between PSA measurements and Ga-68-PSMA PET/CT cannot be controlled. Furthermore, some patients underwent PSA after TRUSBx, which can result in a higher PSA level.[21] For the last reason, our study had a wide range of PSA values; the highest value was 11000.3 ng/mL, but the mean PSA value for all patients was only 222.7 ng/mL, which may lead to misinterpretation.

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Table 2: SUVmax value of primary tumor (n = 61)

SUVmax value of primary tumor	n	SUVmax, mean ± SD	*p*
D'Amico staging			0.013*
Low/Intermediate	11	9.5 ± 4.76	
High	50	17.06 ±10.93	
Total	61	15.7 ± 10.49	
Gleason score grade group			
1	10	7.99 ± 3.9	0.025*
2	13	14.61 ± 7.93	
3	8	15.91 ± 11.32	
4	25	18.78 ± 11.37	
5	5	18.2 ± 14.4	
Total	61	15.7 ± 10.49	
GS grade group 1+2+3 and GS grade group 4+5			
1+2+3	31	12.81 ± 8.45	0.028*
4+5	30	18.68 ± 11.65	
Total	61	15.7 ± 10.49	

Table 3: Correlation between SUVmax value of primary tumor and PSA level

PSA	SUVmax of primary tumor
Pearson Correlation	-0.0489
Sig. (2-tailed)	0.7084
Level of correlation	very low
n	61

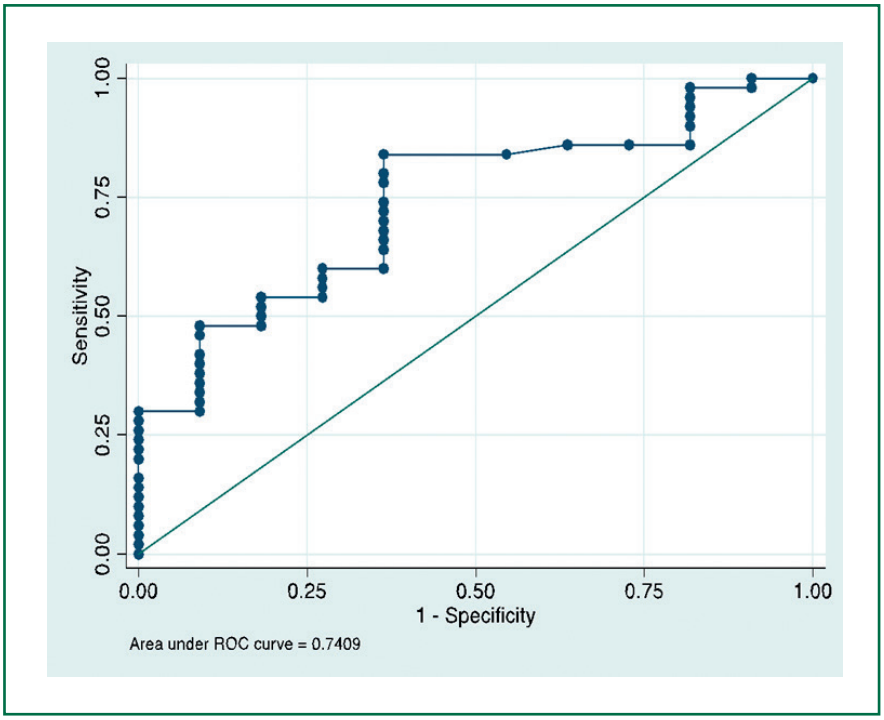

Figure3: ROC curve of the SUVmax for high risk prostate cancer.
The optimal cutoff value of SUVmax was set as 8.3.
95% confidence interval [CI], 0.586 to 0.894; sensitivity: 84%; specificity: 63.6%

Limitation

This study has limitations due to its retrospective nature, and in addition to that, we analyzed GS grade groups obtained from biopsy specimens rather than final pathology from radical prostatectomy, which may not reflect the actual grade group. More prospective studies are needed to determine the value of SUVmax in prostatectomy patients and value of Ga-68-PSMA PET/CT in clinical staging prostate cancer.

Conclusion

SUVmax values from Ga-68-PSMA PET/CT have a strong correlation with the D'Amico risk classification and GS grade group, but it is not correlated with PSA level. The Ga-68-PSMA PET/CT was useful for identifying high-risk prostate cancer and potentially improving treatment decision-making. However, prospective studies are required to determine the correlation between SUVmax value and clinical data.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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