Original Article
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Is SUV Corrected for Lean Body Mass Superior to SUV of Body Weight in ^{68}Ga-PSMA PET/CT?

^{68}Ga PSMA PET/BT'de Yağsız Vücut Kütlesine Göre Düzeltilmiş SUV Vücut Ağırlığına Göre Hesaplanan SUV'den Daha mı Üstün?

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Abstract

Objectives: This study aimed to investigate the relationship between the standard uptake value (SUV) of body weight and SUV corrected for lean body mass (SUL) parameters obtained from the prostate gland in gallium-68 (^{68}Ga)-prostate-specific membrane antigen (PSMA) positron emission tomography-computed tomography (PET/CT) with Gleason grade (GG) groups, D'Amico risk groups, and presence of metastases.

Methods: Patients with prostate adenocarcinoma who underwent ^{68}Ga-PSMA PET/CT for staging at our center between February 2017 and October 2018 were evaluated retrospectively. Maximum SUV (SUV_{max}), SUV_{peak}, SUL_{max}, SUL_{peak}, SUV_{mean}, and SUL_{mean} values of the prostate tumor were obtained. The difference in these values between GG groups (≥3, <3) and D'Amico risk (low-moderate/high) groups was evaluated with the Mann-Whitney U test. The area under the curve values of SUV and SUL parameters were compared. In addition, SUV_{mean} and SUL_{mean} values were obtained from the right liver lobe, and their correlation with body weight was evaluated.

Results: A total of 79 patients were included in the study. Significant differences were found in the prostate SUV_{max}, SUL_{max}, SUV_{peak}, SUL_{peak}, SUV_{mean}, and SUL_{mean} values between the GG (≥3 and <3) groups and between D'Amico risk (low-moderate and high) groups. However, no significant difference was found in the discriminative power of any SUV or SUL parameter when compared with each other. A significant difference in any SUV and SUL parameters was found in patients with and without metastasis. Neither liver SUV_{mean} value nor SUL_{mean} value correlated with the body weight.

Conclusion: The superiority of SUL values obtained from ^{68}Ga-PSMA PET to SUV was not determined in our study. SUV parameters can also be used for quantitative analysis in ^{68}Ga-PSMA PET.

Keywords: SUV, SUL, lean body mass, prostate specific membrane antigen

Öz

Amaç: Amacımız, galyum-68 (^{68}Ga)-prostat spesifik membran antijeni (PSMA) pozitron emisyon tomografisi-bilgisayarlı tomografide (PET/BT) prostat bezinden elde edilen standart uptake değeri (SUV) ve yağsız vücut kütlesine göre düzeltilmiş SUV (SUL) parametrelerinin Gleason grade (GG) grupları, D'Amico risk grupları, metastaz varlığı değerlendirmedeki ilişkilerinin araştırılmasıdır.

Yöntem: Merkezimizde Şubat 2017-Ekim 2018 tarihleri arasında prostat adenokarsinomu tanısı ile evreleme amaçlı ^{68}Ga-PSMA PET/BT görüntülemesi yapılan hastalar retrospektif olarak değerlendirildi. Prostat bezinde görülen tümörden SUV_{maks}, SUV_{peak}, SUL_{maks}, SUL_{peak}, SUV_{mean} ve SUL_{mean} değerleri elde edildi. GG grupları (≥3, <3), D'Amico risk grupları (düşük-orta/yüksek) arasında bu değerler arasındaki fark Mann-Whitney

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U testi ile değerlendirildi. SUV ve SUL parametrelerinin eğri altındaki alan değerleri karşılaştırıldı. Ayrıca karaciğer sağ lobundan SUV_{mean} ve SUL_{mean} değerleri alınarak vücut ağırlığı ile korelasyonları değerlendirildi.

Bulgular: GG grupları (≥3 ve <3) arasında ve D'Amico risk grupları (düşük-orta ve yüksek) arasında prostat SUV_{maks}, SUL_{maks}, SUV_{peak}, SUL_{peak}, SUV_{mean} ve SUL_{mean} değerlerinde istatistiksel olarak anlamlı farklılıklar izlendi. Bununla birlikte, herhangi bir SUV veya SUL parametresinin bu grupları ayırt etme gücünde diğerine kıyasla önemli bir fark elde edilemedi. Metastaz olan ve olmayan hasta gruplarında hiçbir SUV ve SUL parametresinde istatistiksel olarak anlamlı bir fark saptanamadı. Ne karaciğer SUV_{mean} değeri ne de SUL_{mean} değeri vücut ağırlığı ile ilişkili değildi.

Sonuç: ^{68}Ga-PSMA PET'den elde edilen SUL değerlerinin SUV'ye üstünlüğü çalışmamızda belirlenememiştir. ^{68}Ga-PSMA PET'de SUV parametrelerinin kantitatif analiz için de kullanılabileceği düşünülmektedir.

Anahtar kelimeler: SUV, SUL, yağsız vücut kütlesi, prostat spesifik membran antijeni

Introduction

Positron emission tomography/computed tomography (PET/CT) is becoming a standard component of the diagnosis and staging in the field of oncology. Especially, ^{18}flourine-fluorodeoxyglucose (^{18}F-FDG) PET/CT is used to quantify radiopharmaceutical uptake and quantitatively determine treatment response in the evaluation of the metabolic response in various tumors (1,2,3). PET images are analyzed in clinical practice either qualitatively using visual comparison of metabolism in lesions with normal tissue or semi-quantitatively using standard uptake values (SUV). SUV is obtained as the tissue concentration (MBq/mL) divided by the injected activity (MBq/g) per body weight (BW). Factors affecting SUV have been discussed in many studies (4,5,6). Since fat contributes to BW but accumulates very little ^{18}F-FDG in a starvation state, SUV is relatively increased in patients who are obese than in thinner ones. A study found that lean body mass (LBM) SUV (SUL) correction is a more suitable quantitative method than BW or body surface area for patients who are obese (7).

Prostate-specific membrane antigen (PSMA) is a highly expressed human transmembrane protein that is low or moderate in normal or hyperplastic prostate tissues and high in primary adenocarcinomas and distinguishes malignant lesions from benign lesions with high accuracy and positively correlates with the degree of expression, tumor aggression, metastatic disease, and recurrence (8,9,10,11). In the literature, studies have shown that the SUV values obtained from a prostate tumor are higher as the Gleason score (GS) and prostate-specific antigen (PSA) value increase. Gafita et al. (12) investigated whether SUL is a more appropriate quantitative method than SUV, which is normalized by BW in gallium-68 (^{68}Ga)-PSMA 11 PET/CT. They found that correction with lean BW disrupts positive correlations between absolute SUV and BW and that SUL may be preferred over SUV for quantitative analysis in ^{68}Ga-PSMA 11 PET (12).

This study aimed to investigate the relationship between the SUV and SUL parameters obtained from the prostate tumor according to Gleason grade (GG) groups, D'Amico risk groups, and presence of metastasis in ^{68}Ga-PSMA PET/CT and to determine whether SUL is superior to SUV.

Materials and Methods

Patients

Patients with prostate adenocarcinoma who underwent ^{68}Ga-PSMA PET/CT for staging at our center between February 2017 and October 2018 were evaluated retrospectively. GG groups of patients were obtained from prostatectomy material in patients undergoing prostatectomy and fine-needle biopsy results in other patients. D'Amico criteria was considered for risk stratification [low risk group (PSA <10 ng/mL and GS <7 and T1-T2a), intermediate-risk group (PSA 10-20 ng/mL or GS 7 or T2b-T2c), and high-risk group (PSA >20 ng/mL or GS 8-10 or T3-T4)] (13). Patients were divided into two groups according to their GG (≥3 vs <3).

PET Image Analysis

Patients signed the informed consent form, and radiation safety and imaging protocol were described. An average of 3.2 millicurie (mCi) ^{68}Ga-PSMA Imaging and Therapy was injected intravenously. Low-dose CT was used for attenuation correction an hour after injection. PET images were obtained for 1.5 min in each bed position in the supine position from the vertex to the toe tip in Philips Gemini TF PET/CT (Eindhoven, Netherlands). Row action maximum likelihood algorithm was used for reconstruction.

Patients who had PSMA expression on ^{68}Ga-PSMA PET/CT images, which could be differentiated from background activity and thought to be related to prostate adenocarcinoma metastasis (PSMA-RADs 4 and 5) were considered to have metastatic disease (14).

Weights and heights of the patients were measured before imaging. LBM was calculated with the formula developed by Janmahasatian (15,16).

$LBM = (9.27\times10^3\times BW)/(6.68\times10^3+216\times BMI)$

In the prostate gland, a region of interest was drawn on the area where PSMA expression was observed above background activity. Maximum SUV (SUV_{max}), SUV_{mean}, and SUV_{peak} values were obtained from this area. SUL_{max}, SUL_{mean}, and SUL_{peak} values were calculated from SUV_{max}, SUV_{mean}, and SUV_{peak} values using the LBM value obtained from the Janmahasatian formula.

SUL = SUV × LBM/BW

In addition, a 3-cm volume of interest (VOI) was drawn to the right liver lobe to determine liver background activity. Liver SUV_{mean} and liver SUL_{mean} values were obtained from this VOI (17).

Statistical Analysis

The free version of the Statistical Package for the Social Sciences v. 26.0 was used for statistical analysis. The correlations among liver SUV_{mean}, liver SUL_{mean}, and BW were evaluated by Spearman correlation analysis. A $p<0.05$ value was considered significant.

The difference in SUV_{max}, SUL_{max}, SUV_{mean}, SUL_{mean}, SUV_{peak}, and SUL_{peak} values from the prostate tumor between low-moderate and high-risk groups was analyzed with the Mann-Whitney U test. In addition, the difference in the SUV and SUL values between GG groups, between PSA groups (≥10 and <10 ng/mL), and between D'Amico risk groups (low-moderate and high) was evaluated with the Mann-Whitney U test.

The potential of SUV and SUL parameters in distinguishing GG groups and risk groups was evaluated by the receiver operating characteristics analysis. The area under the curve (AUC) values were compared, and significant difference between them was evaluated.

Ethics Approval

Dokuz Eylül University Ethics Committee approval was obtained (decision no: 2020/18-37, date: 10.08.2020). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients gave their informed consent before their inclusion in the study.

Results

The study included 79 patients with a mean age of 65±7 (range, 44-78) years and mean BW of 81.5±14.5 (range, 53-125) kg. The median PSA value was 16 (range, 0.02-527.00) ng/mL. A total of 13 patients had a history of radical prostatectomy.

In this study, 7 (9%) patients had GG 1, 21 (27%) had GG 2, 12 (15%) had GG 3, 15 (19%) had GG 4, and 24 (30%) had GG 5. In ^{68}Ga-PSMA PET/CT, 41 (52%) patients did not have metastasis, while 38 patients had PSMA expression suggesting metastasis. Moreover, 33 (41.8%) patients had lymph node metastasis. Five of these patients had PSMA expression in cervical/mediastinal lymph nodes, 16 in abdominal lymph nodes, and 33 in pelvic lymph nodes. In addition, 19 (24.1%) patients had PSMA expression suggesting bone metastasis, whereas 2 (2.5%) patients had PSMA expression suggesting pulmonary metastasis. In the study group, no patient had liver metastasis. According to the D'Amico risk groups, two patients had low risk, 18 (22.8%) patients had moderate risk, and 59 (74.7%) patients had high-risk.

The mean ± standard deviation and median (range) values from the prostate tumor were calculated as follows: SUV_{max}, 11.5±9.3 and 8.0 (3.0-49.8); SUL_{max} value, 8.4±6.1 and 6.1 (2.2-34.4); SUV_{peak} value, 8.6±7.2 and 5.8 (2.4-37.6); SUL_{peak} value, 6.3±4.5 and 4.5 (1.7-25.9); SUV_{mean} value, 5.0±2.6 and 4.2 (1.9-13.8); and SUL_{mean} value, 3.7±3.3 and 3.2 (1.3-9.4).

A significant difference was found in the prostate SUV_{max}, SUL_{max}, SUV_{peak}, SUL_{peak}, SUV_{mean}, and SUL_{mean} values between patients with GG ≥3 and <3 (Table 1). However, when comparing AUC values of SUV and SUL parameters in distinguishing GG groups, no SUV/SUL parameters were superior to the other (Table 2).

No significant difference was observed in any SUV and SUL parameters between patients with GS 3+4 and 4+3.

Prostate SUV_{max}, SUL_{max}, SUV_{peak}, SUL_{peak}, SUV_{mean}, and SUL_{mean} values were significantly higher in the high-risk group than in the other D'Amico risk groups (Table 1). However, no SUV/SUL parameter was superior to others in distinguishing risk groups (Table 2).

While all SUV and SUL parameters were higher in patients with a PSA value ≥10 ng/mL than in those with <10 ng/mL (Table 1), no significant difference was found in the discrimination power of any SUV and SUL parameters (Table 2).

No significant difference was found in any SUV and SUL parameters in patient groups with and without metastasis.

The mean liver SUV_{mean} value was calculated as 4.0±1.1 (1.8-7.6), and the liver SUL_{mean} value was 3.0±1.4 (1.4-5.5). The liver SUV_{mean} and SUL_{mean} values did not correlate with BW ($p=0.387$ and 0.132, respectively).

Discussion

In this study, a significant correlation was found with the BW of neither SUV_{mean} nor SUL_{mean} obtained from the liver. Gafita et al. (12) reported that SUL can be preferred over SUV in ^{68}Ga-PSMA 11 PET/CT. In this study, while the liver SUV_{mean} value showed a significant correlation with BW, no significant correlation was found in the SUL_{mean} value. Despite the few studies on this subject, similar to our study, Li et al. (2) evaluated the ^{18}F-DCFPyL uptake but could not detect a significant correlation between liver SUV_{mean} and SUL_{mean} values and BW; as a result, they suggested using the SUV.

Several studies have also shown that PSMA SUV data are successful in differentiating GG groups and risk groups (18,19,20,21). Likewise, we were able to obtain significant differences in SUV parameters between these groups. However, our study is the first to evaluate the relationship between the success of SUL and SUV parameters obtained from ^{68}Ga-PSMA PET in differentiating GG groups and risk groups. In our study, SUL parameters obtained from ^{68}Ga-PSMA PET were not superior to SUV parameters in distinguishing GG groups and in distinguishing risk groups. Moreover, the studies that quantified uptake with body-weight-corrected SUV and LBM-corrected SUV have shown that the repeatability coefficient of SUL_{max} and SUV_{max} within the same patient in a test-retest setting is comparable (22,23,24). These results show that SUL and SUV parameters are not superior to each other in ^{68}Ga-PSMA PET in clinical practice.

Prostate SUV and SUL parameters were significantly higher in patients with GG ≥3 than in GG ≤2, and this is similar to the findings in the literature. Onal et al. (25) reported that SUV_{max} values obtained from primary tumors in 191 patients were significantly higher in patients with GS >7.

Table 1. Evaluation of SUV and SUL parameters in Gleason grade, D'Amico risk, and PSA groups

		GG		D'Amico risk groups		PSA	
		GG <3	**GG ≥3**	**Low-moderate**	**High**	**<10 ng/mL**	**≥10 ng/mL**
SUV_{max}	Mean ± standard	7.6±4.5	13.7±10.5	6.6±3.9	13.2±10.0	8.1±5.6	13.8±10.5
	Median (range)	5.4 (3.1-17.5)	10.5 (3.0-49.8)	5.2 (3.0-15.4)	10.2 (3.4-49.8)	3.6 (3.0-26.7)	11.0 (3.5-49.8)
	p value	0.003		0.001		0.001	
	AUC (95% CI)	0.706 (0.588-0.823)		0.755 (0.637-0.872)		0.705 (0.587-0.823)	
SUL_{max}	Mean ± standard	5.6±3.4	9.9±7.4	4.9±2.9	9.6±7.3	5.9±4.1	10±7.4
	Median (range)	4.0 (2.4-12.7)	7.5 (2.2-34.4)	3.8 (2.2-11.1)	7.3 (2.4-34.4)	4.4 (2.2-19.9)	8.4 (2.5-34.4)
	p value	0.002		0.001		0.001	
	AUC (95% CI)	0.709 (0.592-0.826)		0.760 (0.644-0.875)		0.707 (0.589-0.825)	
SUV_{mean}	Mean ± standard	3.8±1.6	5.6±2.9	3.4±1.1	5.5±2.8	3.8±1.6	5.7±2.9
	Median (range)	3.2 (2.1-7.6)	4.9 (1.9-13.8)	3.2 (1.9-5.5)	4.9 (2.1-13.8)	3.3 (2.0-8.0)	4.9 (1.9-13.8)
	p value	0.002		0.001		0.001	
	AUC (95% CI)	0.707 (0.591-0.823)		0.750 (0.636-0.863)		0.703 (0.588-0.819)	
SUL_{mean}	Mean ± standard	2.8±1.2	4.1±2.0	2.5±0.9	4.1±3.5	2.8±2.4	4.2±3.7
	Median (range)	2.4 (1.3-5.8)	3.5 (1.4-9.4)	2.4 (1.9-4.4)	3.5 (1.3-9.4)	2.4 (1.5-6.0)	3.0 (1.3-9.4)
	p value	0.002		0.001		0.001	
	AUC (95% CI)	0.714 (0.597-0.830)		0.756 (0.643-0.870)		0.703 (0.587-0.819)	
SUV_{peak}	Mean ± standard	5.6±3.5	10.2±8.1	3.5±2.8	9.9±7.7	5.9±4.2	10.3±8.2
	Median (range)	3.9 (2.5-13.3)	7.7 (2.4-37.6)	3.5 (2.4-11.3)	7.7 (2.6-37.6)	4.3 (2.5-19.0)	8.2 (2.4-37.6)
	p value	0.003		<0.001		0.001	
	AUC (95% CI)	0.701 (0.582-0.820)		0.767 (0.649-0.884)		0.706 (0.588-0.824)	
SUL_{peak}	Mean ± standard	4.1±2.6	7.4±5.5	3.5±2.2	7.2±5.5	4.4±3.0	7.5±5.8
	Median (range)	2.8 (1.9-2.5)	5.5 (1.7-25.9)	2.7 (1.7-9.0)	5.5 (1.9-25.9)	3.1 (1.8-14.2)	6.0 (1.7-25.9)
	p value	0.003		<0.001		0.001	
	AUC (95% CI)	0.705 (0.586-0.825)		0.769 (0.651-0.887)		0.700 (0.582-0.819)	

SUV: Standard uptake value, SUL: Lean body mass SUV, PSA: Prostate-specific antigen, GG: Gleason grade, AUC: Area under the curve, CI: Confidence interval, max: Maximum

Table 2. P values obtained in the comparison of the AUC of SUV and SUL parameters

	GG (≥3 and <3)	D'Amico risk groups (low-moderate and high)	PSA (≥10 and <10 ng/mL)
SUV_{max}-SUL_{max}	0.732	0.668	0.838
SUV_{max}-SUV_{peak}	0.721	0.324	0.935
SUV_{max}-SUL_{peak}	0.983	0.420	0.744
SUV_{max}-SUV_{mean}	0.945	0.808	0.933
SUV_{max}-SUL_{mean}	0.750	0.953	0.943
SUL_{max}-SUV_{peak}	0.578	0.666	0.945
SUL_{max}-SUL_{peak}	0.761	0.560	0.595
SUL_{max}-SUV_{mean}	0.916	0.617	0.850
SUL_{max}-SUL_{mean}	0.830	0.883	0.848
SUV_{peak}-SUL_{peak}	0.664	0.829	0.484
SUV_{peak}-SUV_{mean}	0.746	0.383	0.891
SUV_{peak}-SUL_{mean}	0.574	0.696	0.905
SUL_{peak}-SUV_{mean}	0.924	0.333	0.869
SUL_{peak}-SUL_{mean}	0.660	0.573	0.868
SUV_{mean}-SUL_{mean}	0.577	0.654	1.000

SUV: Standard uptake value, SUL: Lean body mass SUV, PSA: Prostate-specific antigen, GG: Gleason grade, AUC: Area under the curve, max: Maximum

In their study, Uprimny et al. (18) did not find a significant difference in SUV_{max} values between GG 2 and 3 tumors. Similarly, Ergül et al. (19) did not found a significant difference in SUV_{max} values between grade 2 and 3 tumors. In addition, in our study, neither SUV_{max} values nor other SUV and SUL values were detected differently in tumors with GG 2 and 3.

In a previous study, Ergül et al. (19) analyzed 78 patients and found a significant difference in SUV_{max} values of prostate tumors with and without metastasis. However, Liu et al. (20) did not observe a significant difference in SUV_{max} in patients with and without metastasis. In the present study, similar to the study of Liu et al. (20), no significant difference was found in any SUV and SUL parameters between these groups.

Study Limitations

First, the retrospective design limits the generalizability of the results. Second, histopathological correlation is not technically and ethically possible from all foci considered metastasis. Finally, prostatectomy could not be applied to all patients, and the GS of some patients could only be obtained from the biopsy sample.

Conclusion

In this study, the superiority of SUL values obtained from ^{68}Ga-PSMA PET to SUV was not determined. We think that both SUV and SUL parameters can be used for quantitative analysis in ^{68}Ga-PSMA PET.

Ethics

Ethics Committee Approval: Dokuz Eylül University Ethics Committee approval was obtained (decision no: 2020/18-37, date: 10.08.2020).

Informed Consent: Retrospective cross sectional study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.A., Concept: A.A., G.Ç.K., Design: A.A., G.Ç.K., Data Collection or Processing: A.A., Analysis or Interpretation: A.A., Literature Search: A.A., G.Ç.K., Writing: A.A., G.Ç.K.

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