



# The Evaluation of Preoperative <sup>18</sup>F-FDG PET/CT in Patients with Endometrial Cancer and the Correlation Between PET Parameters and Postoperative Pathology Results

Endometriyum Kanserli Hastalarda Preoperatif <sup>18</sup>F-FDG PET/BT'nin Değerlendirilmesi ve PET Parametreleri ile Postoperatif Patoloji Sonuçları Arasındaki Korelasyon

Özge Vural Topuz<sup>1</sup>, Ayşegül Aksu<sup>2</sup>, Sadife Rüya Erinç<sup>1</sup>, Nedim Tokgözoğlu<sup>3</sup>, Müge Öner Tamam<sup>1</sup>

<sup>1</sup>University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital, Clinic of Nuclear Medicine, İstanbul, Turkey

<sup>2</sup>University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of Nuclear Medicine, İstanbul, Turkey

<sup>3</sup>University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital, Clinic of Gynecology and Obstetrics, İstanbul, Turkey

## Abstract

**Objectives:** Endometrial cancer (EC) is the most common gynecological malignancy. The <sup>18</sup>fluorine-fluorodeoxyglucose (<sup>18</sup>F-FDG) positron emission tomography/computed tomography (PET/CT) is used for initial staging, evaluating treatment response, and detecting recurrence. This study aimed to investigate the diagnostic value of preoperative PET/CT in EC staging and determine the volumetric PET parameters that are accurate predictors of histopathological tumor characteristics.

**Methods:** Preoperative PET/CT data of 66 patients with EC were retrospectively analyzed. Patients were divided into low and high-risk groups according to the European Society for Medical Oncology criteria. The maximum standardized uptake value (SUV<sub>max</sub>), SUV<sub>mean</sub>, metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of the primary lesion and pathological lymph nodes were noted. The International Federation of Gynecology and Obstetrics (FIGO) classifications, histopathology, the depth of myometrial invasion (MI), lymph node metastasis (LNM), cervical stromal invasion (CSI), and tumor sizes were noted.

**Results:** The SUV<sub>max</sub>, TLG, and MTV values of high and low-risk groups were significantly different. TLG was the most useful parameter in differentiating risk groups. PET/CT had 90% sensitivity, 96.3% specificity, 81.8% positive predictive value, 98.1% negative predictive value, and 95.45% accuracy in assessing LNM. MTV and TLG values in patients with non-endometrioid pathology were higher than those with endometrioid. The SUV<sub>max</sub>, MTV, and TLG of patients with deep MI were higher than those with superficial MI. TLG values of patients with CSI were higher than those without CSI. Patients with LNM had higher MTV and TLG values than those without LNM. A significant difference was found in TLG, MTV, and SUV<sub>max</sub> values between patients with FIGO stage I-II and patients with FIGO stage III and above.

**Conclusion:** SUV and volumetric parameters obtained from PET/CT, especially TLG, are strong predictors of tumor characteristics, such as MI and CSI, FIGO stages, and LNM, and are useful in noninvasively defining the risk groups in the preoperative period.

**Keywords:** Endometrial cancer, <sup>18</sup>F-FDG PET/CT, SUV<sub>max</sub>, volumetric parameters

## Öz

**Amaç:** Endometriyum kanserleri (EK) en sık görülen kadın genital sistemi malignitesidir. <sup>18</sup>Flor-florodeoksiglukoz (<sup>18</sup>F-FDG) ile işaretli pozitron emisyon tomografisi/bilgisayarlı tomografi (PET/BT), EK'lerinde evreleme, tedavi yanıtının değerlendirilmesi ve nüks hastalığın belirlenmesi amacıyla sıkça kullanılmaktadır. Çalışmamızın amacı EK'lerinde preoperatif dönemde evreleme amaçlı yapılan PET/BT parametreleri ile postoperatif patoloji sonuçları arasındaki korelasyonun araştırılmasıdır.

**Address for Correspondence:** Özge Vural Topuz MD, University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital, Clinic of Nuclear Medicine, İstanbul, Turkey **Phone:** +90 212 314 55 55 **E-mail:** ozgevuraltopuz@gmail.com ORCID ID: orcid.org/0000-0001-7197-5866

**Received:** 16.05.2021 **Accepted:** 05.09.2021

©Copyright 2022 by Turkish Society of Nuclear Medicine  
Molecular Imaging and Radionuclide Therapy published by Galenos Yayınevi.

**Yöntem:** Preoperatif evreleme amaçlı PET/BT çekimi yapılan 66 EK tanılı hasta çalışmaya dahil edildi.  $^{18}\text{F}$ -FDG PET/BT çalışmalarında primer lezyonların ve patolojik lenf nodlarının maksimum standardize alım değeri ( $\text{SUV}_{\text{maks}}$ ),  $\text{SUV}_{\text{mean}}$ , metabolik tümör hacmi (MTV) ve toplam lezyon glikoliz (TLG) değerleri ölçüldü. Postoperatif patoloji sonuçlarından Uluslararası Jinekoloji ve Obstetrik Federasyonu (FIGO) sınıflandırmaları, tümörlerin histolojik tipleri, myometrial invazyon derinlikleri (Mİ), maksimum tümör çapları, servikal stromal invazyonları ve lenf nodu metastaz bulguları kaydedildi.

**Bulgular:** Yüksek ve düşük riskli hasta grupları arasında TLG, MTV ve  $\text{SUV}_{\text{maks}}$  değerlerinde istatistiksel olarak anlamlı farklılık izlenirken,  $\text{SUV}_{\text{mean}}$ 'de anlamlı fark mevcut değildi. Risk gruplarını ayırt etme gücü en yüksek olan parametre TLG olarak belirlendi.  $^{18}\text{F}$ -FDG PET/BT'nin lenf nodu saptamada duyarlılığı %90; özgüllüğü %96,43, pozitif prediktif değeri %81,81, negatif prediktif değeri %98,18 ve doğruluğu %95,45 olarak hesaplandı. Non-endometrioid tümör tanılı hastalarda MTV ve TLG değerleri endometrioid tipe göre anlamlı yüksek saptandı. Mİ >1/2 olan hastalarda primer tümör  $\text{SUV}_{\text{maks}}$ , MTV ve TLG değerleri Mİ <1/2 olan gruba göre anlamlı düzeyde yüksekti. Servikal stromal invazyon izlenen hastalarda TLG değerleri, invazyon izlenmeyen gruba göre anlamlı düzeyde yüksekti. Histopatolojik olarak lenf nodu metastazı olan hastalarda primer tümörden elde edilen MTV ve TLG değerleri, lenf nodu metastazı olmayan hastalara göre daha yüksek düzeydeydi. FIGO II olan hastalar ile FIGO III ve üstü olan hastalar arasında TLG, MTV ve  $\text{SUV}_{\text{maks}}$  değerlerinde anlamlı farklılık izlendi.

**Sonuç:**  $^{18}\text{F}$ -FDG PET/BT; TLG başta olmak üzere SUV ve volumetrik parametreleri sayesinde preoperatif dönemde tümöre ait myometrial invazyon, servikal stromal invazyon, FIGO evresi, lenf nodu metastazları gibi histopatolojik özellikleri ön görebilmeyi ve bu dönemde risk gruplarının da belirlenmesini sağlayabilecek önemli bir noninvaziv yöntemdir.

**Anahtar kelimeler:** Endometriyum kanseri, evreleme,  $^{18}\text{F}$ -FDG PET/BT,  $\text{SUV}_{\text{maks}}$ , volumetrik parametreler

## Introduction

Endometrial cancer (EC) is the fifth most common cancer among females worldwide and is the most common gynecological malignancy in developed countries. The most important prognostic factors used for EC are staging, grading, tumor histopathology, depth of myometrial invasion (MI), tumor size, cervical stromal invasion (CSI), and lymph node metastases (LNM) (1).

EC is surgicopathologically staged according to the International Federation of Gynecology and Obstetrics (FIGO) system. The current 2010 FIGO recommendation for the surgical staging of EC includes hysterectomy, bilateral salpingo-oophorectomy, pelvic and paraaortic lymphadenectomy, and biopsy of any suspicious lesions (2). Stage I reflects EC that is confined to the uterine corpus and is further divided into stage IA (none or <50% MI) and IB (equal to or >50% MI). Tumors that invade cervical stromal but do not extend beyond the uterus are defined as stage II. Stage III represents a tumor that has spread beyond the uterus but not outside the true pelvis and is further divided into stage IIIA (uterine serosa and/or adnexa invasion), stage IIIB (parametrium and/or vaginal involvement), stage IIIC1 (positive pelvic nodes), and IIIC2 (positive paraaortic lymph nodes). Stage IVA includes tumors with bladder or bowel metastases and stage IVB with distant metastases (3).

Several prognostic factors for EC were identified, including an advanced FIGO surgical stage, non-endometrioid histological subtype, poorly differentiated histology, more than half MI, a larger tumor size, lymphovascular space involvement (LVS), CSI, ovarian metastasis, and pelvic/paraaortic LNM (4,5).

The maximum standardized uptake value ( $\text{SUV}_{\text{maks}}$ ), a semiquantitative parameter determined by positron emission tomography (PET), is described as the highest  $^{18}\text{F}$ fluorine-fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) uptake of a single-pixel within a region of interest that is manually drawn over a hypermetabolic lesion.  $\text{SUV}_{\text{maks}}$  represents the measurement from only one voxel of the most hypermetabolic area of a tumor lesion and only shows the highest intensity of  $^{18}\text{F}$ -FDG uptake, thus it cannot reflect the whole tumor metabolic burden and can be affected by various patient characteristics and imaging parameters. The  $\text{SUV}_{\text{maks}}$  has some limitations and it cannot be used to assess the overall glucose metabolic activity of a tumor mass, thus other useful PET parameters are used, which can better reflect metabolic tumor burden than  $\text{SUV}_{\text{maks}}$ , such as metabolic tumor volume (MTV) to measure the overall glucose metabolic activity of a tumor lesion and total lesion glycolysis (TLG) that combines the information of metabolic activity and tumor volume (6,7).

This study aimed to investigate the diagnostic value of the preoperative  $^{18}\text{F}$ -FDG PET/computed tomography (CT) for EC staging and determine the volumetric  $^{18}\text{F}$ -FDG PET/CT parameters that are accurate predictors of histopathological tumor characteristics.

## Materials and Methods

### Patient Characteristics

From January 2016 to November 2017, data from patients with histologically confirmed EC who had undergone a preoperative PET/CT scan before total abdominal hysterectomy and bilateral salpingo-oophorectomy with and without pelvic and/or paraaortic lymphadenectomy

were retrospectively analyzed. All patients had PET/CT scans in 6 weeks leading up to their surgery.

Patients with any of the following criteria were excluded from the study: Another malignant disease, tumors with no  $^{18}\text{F}$ -FDG avidity, uncontrolled diabetes mellitus, neoadjuvant chemotherapy or preoperative radiotherapy, and inoperable tumor.

Diagnoses were confirmed by preoperative endometrial biopsy and are surgically staged following the FIGO criteria.

Histology, tumor grade, maximum tumor diameter, MI, CSI, and LNM were noted. All patients were divided into low-risk and high-risk groups according to the European Society for Medical Oncology criteria. Patients with endometrioid histology, histological grades 1 or 2, and MI of  $<1/2$  were classified as the low-risk group, whereas those with histological grade 2/3 (G2/3), positive LVSI, or MI of  $\geq 1/2$  were the high-risk group (8).

### Image Analysis

Whole-body PET/CT imaging was performed on a biograph (Siemens Biograph 6, Chicago, IL, USA) using a full-ring HI-REZ LSO PET and a six-slice CT scanner.

All patients fasted for at least 5 h before the PET/CT imaging. The serum glucose levels measured at the time of  $^{18}\text{F}$ -FDG injections were  $<150$  mg/dL in all patients. Approximately, 50 min later, an initial low-dose non-enhanced CT scan was performed with the following parameters: 40-60 mAs, 140 kV, and 5-mm section thickness. Positron emission scanning with 3 min per bed position was then acquired on the identical transverse field of view in the caudocranial direction. The total scanning time was approximately 25 min per patient. CT transmission images were used for attenuation correction, and all images were reconstructed and stored in axial, coronal, and sagittal slices.

Image analysis and interpretation were performed on a dedicated workstation (Esoft). A semi-automatic ellipsoid-shaped volume of interest (VOI) around the primary uterine tumors that included the entire lesion in the axial, sagittal, and coronal planes was drawn.  $\text{SUV}_{\text{max}}$ ,  $\text{SUV}_{\text{mean}}$ , and MTV of the primary uterine tumors that were automatically generated by the software on the workstation were recorded. Voxels greater than the set threshold of 41% of  $\text{SUV}_{\text{max}}$  in the VOI were used for MTV and  $\text{SUV}_{\text{mean}}$  measurement. After the MTV measurement, TLG was also calculated using the following equation:  $\text{TLG} = \text{SUV}_{\text{mean}} \times \text{MTV}$ .

### Ethical Approval

University of Health Sciences Turkey, Okmeydani Training and Research Hospital Ethics Committee approval was

obtained (number: 48670771-514.10) and all patients signed written informed consent.

### Statistical Analysis

Number Cruncher Statistical System (Kaysville, Utah, USA) was used for statistical analysis. P values of  $<0.05$  were considered statistically significant. Normally distributed data were presented as mean  $\pm$  standard deviation, whereas non-normal distributed data were given as median (range). Data with abnormal distribution were analyzed using the Mann-Whitney U test. The Mc Nemar test was used to compare dependent categorical data. Spearman's correlation analysis was used to evaluate the relationship between variables. The area under the receiver operating characteristic (ROC) curve (AUC) was presented as a measure of discrimination. Cut-off values were identified from the ROC curves using the Youden index. The percentages of sensitivity and specificity were determined at these cut-off values.

### Results

Patients and tumor characteristics are listed in Table 1.

This study included 66 patients with an age range of 41 to 84 years (mean age:  $63.56 \pm 10.11$ ), of whom 87.9% (58/66) were postmenopausal.

Table 1. Patients and tumor characteristics			
		n	%
Menopausal status	Premenopausal	8	12.1
	Postmenopausal	58	87.9
Pathology	Endometrioid	48	72.7
	Non-endometrioid	18	27.3
FIGO stage	IA	25	37.9
	IB	21	31.8
	II	2	3.0
	IIIA	1	1.5
	IIIC1	7	10.6
	IIIC2	8	12.1
Myometrial invasion	$<1/2$	27	40.9
	$>1/2$	39	59.1
Cervical stromal invasion	No	54	81.8
	Yes	12	18.2
Lymph node metastases (pathological)	No	56	84.8
	Yes	10	15.2
Lymph node metastases (PET/CT)	No	55	83.3
	Yes	11	16.7

FIGO: International Federation of Gynecology and Obstetrics, PET: Positron emission tomography, CT: Computed tomography

The median  $SUV_{max}$ , MTV, and TLG of 66 primary uterine tumors were 16.8 (range: 3.5-41.1), 27.81 mL (range: 0.1-251), and 225.19 g (range: 0.2-2347.3), respectively.

Of the 66 patients, 54 (81.8%) were postoperatively diagnosed with high-risk carcinoma and 12 (18.2%) with low-risk carcinoma. Patients with high-risk carcinoma showed significantly higher  $SUV_{max}$ , TLG, and MTV than those with low-risk carcinoma. The mean  $SUV_{max}$  value of patients in the low-risk and high-risk groups was  $11.6 \pm 5.5$  and  $17.9 \pm 8.4$ , respectively ( $p=0.018$ ). The mean TLG value of patients in the low-risk and high-risk groups was  $28.3 \pm 25.7$  g and  $268.9 \pm 439.8$  g, respectively ( $p<0.001$ ). The mean MTV value of patients in the low-risk and high-risk groups was  $5.9 \pm 6.5$  mL and  $32.6 \pm 50$  mL, respectively ( $p=0.002$ ). The  $SUV_{mean}$  did not show a significant difference between the two groups ( $p=0.14$ ).

The TLG had the highest AUCs for predicting the high-risk group ( $p<0.001$ , AUC: 0.852, 95% confidence interval: 0.753-0.951). ROC curve analysis was performed to determine the cut-off value of TLG for distinguishing high-risk and low-risk disease groups. The optimal TLG cut-off value of 52.7 g that was determined by ROC analysis showed 74.1% sensitivity and 91.7% specificity for risk stratification.

TLG, MTV, and  $SUV_{max}$  values of patients with FIGO IB ( $n=20$ ) were significantly higher than those with FIGO IA ( $n=26$ ) ( $p<0.001$ ,  $p=0.004$ , and  $p=0.025$ , respectively). Tumor sizes obtained from postoperative pathology results of these two groups were also considerably different ( $p<0.001$ ).

A statistically significant difference was found in the TLG, MTV, and  $SUV_{max}$  values in patients with tumors that are limited to the uterus (FIGO I and II) ( $n=48$ ) compared to those with FIGO 3 criteria and above ( $p<0.001$ ,  $p<0.001$ , and  $p=0.045$ , respectively). According to ROC curve analysis results for the differentiation of FIGO stage I or II from stage III and above, the cut-off value of  $SUV_{max}$  was 16 with 72.2% sensitivity and 64.6% specificity, whereas the MTV was 23.35 mL with 66.7% sensitivity and 81.2% specificity and 173.45 g for TLG with 66.7% sensitivity and 83.3% specificity. A substantial difference was also detected in tumor sizes obtained from postoperative pathology results between these two groups. The mean tumor size of patients with FIGO stages I and II was  $3.52 \pm 1.95$  cm, whereas the mean tumor size was  $6.06 \pm 2.68$  cm in patients with higher FIGO stages ( $p<0.001$ ).

Patients with non-endometrioid pathology ( $n=18$ ) had significantly higher MTV and TLG parameters compared to patients with endometrioid adenocarcinoma ( $p=0.008$  vs. 0.019, respectively). When ROC curve analysis was

performed to determine the cut-off value of MTV and TLG to differentiate non-endometrioid adenocarcinoma from endometrioid, the optimal cut-off value of MTV was 28.7 mL with 55.6% sensitivity and 81.2% specificity. The optimal cut-off value of TLG was 255 g with 50% sensitivity and 87.5% specificity. ROC curve analysis did not show a significant  $SUV_{max}$  cut-off value for histopathologic types. Tumor sizes showed a significant difference in the non-endometrioid subtype of EC compared with the endometrioid subtype ( $p=0.001$ ). Additionally, the rate of LNM was higher (38.9%) in patients with non-endometrioid pathology than in patients with endometrioid adenocarcinoma (6.3%) ( $p=0.001$ ).

The mean maximum primary tumor diameter on final pathology was  $4.2 \pm 2.4$  cm (range: 0.5-12.5 cm).

A moderate correlation between the TLG and MTV values that are obtained in the preoperative period and the postoperative tumor diameter ( $p<0.001$ ,  $\rho: 0.661$ ;  $p<0.001$ ,  $\rho: 0.557$ , respectively). The correlation of tumor sizes with  $SUV_{max}$  values was weaker ( $p=0.001$ ,  $\rho: 0.388$ ).

The  $SUV_{max}$ , MTV, and TLG values of patients with a maximum tumor size of  $\geq 4$  cm were higher than those with  $<4$  cm ( $p=0.028$ ,  $p<0.001$ ,  $p<0.001$ , respectively).

Of the patients, 16.7% had LNM in the preoperative PET scan and 15.2% had LNM in the postoperative pathological results. No significant difference was found between the preoperative PET scan and postoperative pathological results ( $p>0.05$ ). PET/CT identified LNM in 9 out of 10 patients with LNM at final pathology, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 90%, 96.43%, 81.81%, 98.18%, and 95.45%, respectively (Table 2).

The MTV and TLG values were significantly higher in tumors with LNM compared to those without LNM ( $p=0.024$  and  $p=0.035$ , respectively). However, no difference was observed in  $SUV_{max}$  values. Pathologically proven LNM showed a weak correlation with tumor diameter ( $p=0.011$ ,  $\rho: 0.311$ ), MTV ( $p=0.022$ ,  $\rho: 0.281$ ), TLG ( $p=0.034$ ,  $\rho: 0.262$ ), MI ( $p=0.004$ ,  $\rho: 0.352$ ), and CSI ( $p=0.004$ ,  $\rho: 0.349$ ).

The  $SUV_{max}$ , MTV, and TLG values of the primary lesion in patients with deep MI (MI  $\geq 1/2$ ) ( $n=39$ ) (59.1%) were significantly higher than those with superficial MI (MI  $<1/2$ ) ( $p<0.05$ ).  $SUV_{mean}$  value did not differ between these two groups ( $p>0.05$ ) (Table 3).

Patients with CSI had higher TLG values than those without ( $p<0.05$ ). No statistically significant difference was found in MTV,  $SUV_{max}$ , and  $SUV_{mean}$  values between these two groups (Table 3).

**Table 2. Metastatic lymph node status according to preoperative PET/CT data and postoperative pathology results**

	Pathology						p	
	Positive		Negative		Total			
	n	%	n	%	n	%		
PET/CT	Positive	9	13.6	2	3.0	11	16.7	1.000
	Negative	1	1.5	54	81.8	55	83.3	
	Total	10	15.2	56	84.8	66	100	
Sensitivity			90.00					
Specificity			96.43					
Positive predictive value			81.81					
Negative predictive value			98.18					

\*p<0.05 Mc Nemar test, PET: Positron emission tomography, CT: Computed tomography

**Table 3. Association between metabolic parameters and surgicopathological findings in endometrial cancer patients**

	Myometrial invasion		p	Cervical stromal invasion		p value
	<1/2	>1/2		Yes	No	
Tumor SUV <sub>max</sub> Median (range)	13 (3.5-29)	16.2 (5.3-41.1)	0.019*	15.4 (5.3-41.1)	15.4 (3.5-31.9)	0.954
Tumor SUV <sub>mean</sub> Median (range)	5.7 (3.1-18.8)	7.6 (3.4-24.8)	0.098	7.3 (3.1-20.7)	7.6 (3.7-24.8)	0.746
Tumor MTV Median (range)	3.3 (0.1-34.5)	22 (1.1-251)	<b>0.001*</b>	10.5 (0.1-251)	20.6 (4.7-106.6)	0.090
Tumor TLG Median (range)	41.6 (0.2-588.9)	168.1 (15.6-2347.3)	0.001*	67.8 (0.2-2347.3)	145.3 (17.2-900.7)	0.049*

\*p<0.05 Mann-Whitney U test, SUV<sub>max</sub>: Maximum standardized uptake value, SUV<sub>mean</sub>: Mean standardized uptake value

The SUV<sub>max</sub>, SUV<sub>mean</sub>, MTV, and TLG values of the primary tumor did not differ with the pre or postmenopausal conditions (p>0.05).

## Discussion

Preoperative identification of some prognostic factors, such as patients with deep MI, LNM, histology, and differentiating high-risk from those with low-risk may be critical in planning the surgical procedure or treatment approach in patients with EC. SUV<sub>max</sub>, MTV, and TLG are PET/CT parameters commonly used in the preoperative assessment of EC. SUV<sub>max</sub> and volumetric parameters that are obtained from <sup>18</sup>F-FDG PET/CT differ in high- and low-risk patient groups and FIGO stages. Therefore, <sup>18</sup>F-FDG PET/CT allows us to access this information in the preoperative period.

Our results showed that MTV and TLG are superior to SUV<sub>max</sub> as preoperative predictors of clinicopathologic characteristics. SUV<sub>max</sub> focuses on a single-pixel with the highest <sup>18</sup>F-FDG uptake within the tumor, thus it cannot be used to evaluate the overall metabolic state of the tumor. Mean tumor volume measures the volume of a tumor

bulk that is metabolically active. Thus, it reflects the overall metabolic state of the tumor.

Liu et al. (9) determined the cut-off value for TLG as 51.7 g and revealed a sensitivity of 84.2% and a specificity of 77.3% for TLG in distinguishing high-risk and low-risk diseases (AUC: 0.778). Similarly, our study revealed significantly higher TLG and MTV values in the high-risk group, whereas no difference in SUV<sub>max</sub> values. The ROC curve analysis was performed to determine the most useful metabolic primary tumor parameter in differentiating high-risk and low-risk EC, and our series revealed that TLG had the highest AUCs for predicting the high-risk group. A TLG cut-off of 52.7 g determined by ROC analysis showed 74.1% sensitivity and 91.7% specificity for risk stratification. Similar to our study, Kitajima et al. (5) revealed AUCs for distinguishing high-risk from low-risk carcinoma as 0.797 for TLG. The optimal determined TLG cut-off value of 70.2 g by ROC analysis was found to have 72.0% sensitivity and 74.2% specificity for risk stratification (5).

Our study revealed higher MTV and TLG values in patients with non-endometrioid subtype compared to those with endometrioid subtype, but without significant difference in

SUV<sub>max</sub> values. Moreover, tumor diameter from pathology samples in the non-endometrioid subtype was also significantly higher ( $p=0.001$ ). The obtained volumetric data from <sup>18</sup>F-FDG PET/CT was also supported by postoperative pathology results. Few studies have analyzed SUV and volumetric PET parameters between these two pathological subtypes. Mapelli et al. (10) included 57 patients in their study and found that SUV<sub>max</sub> and SUV<sub>mean</sub> were the only parameters that distinguish endometrioid from non-endometrioid subtype. They did not observe any difference between the MTV and TLG values of these two groups. Other studies revealed no significant difference in <sup>18</sup>F-FDG PET/CT parameters regarding these two pathological subtypes. Husby et al. (11) included 129 patients and Kitajima et al. (5) with 56 patients noted no difference between the endometrioid and non-endometrioid histological types in the SUV<sub>max</sub>, MTV, and TLG values. The reason for the discrepancy between the studies may have been due to the differences in patient datasets. Our study group revealed endometrioid pathology in 72.7% of patients and non-endometrioid pathology in 27.3%, whereas Kitajima et al. (5) revealed only 5 (9%) patients with non-endometrioid pathology. The number of patients with non-endometrioid adenocarcinoma is very low, thus a significant difference could not be determined between the SUV<sub>max</sub>, MTV, and TLG values of the two groups.

The difference in SUV<sub>max</sub> values of the primary tumor according to nodal metastasis was not statistically significant; however, the MTV and TLG values of the primary tumors were significantly higher in patients with nodal metastasis. This was compatible with previous studies (5,9). These findings also show the superiority of MTV and TLG to SUV<sub>max</sub>. In the literature, the relationship between the SUV<sub>max</sub> values of the primary tumor and presence of LNM is unclear. Husby et al. (11) detected a considerable difference between the SUV<sub>max</sub> values of these two groups, whereas Stewart et al. (12) found no differences in primary tumor characteristics on PET/CT imaging between patients with positive and negative lymph nodes.

Our study revealed significantly higher TLG values of patients with CSI. The study of Kitajima et al. (5) revealed a significantly higher MTV and TLG in patients with CSI, whereas other studies revealed a significant difference only in MTV values (11,13). The discrepancy among these studies may have been due to patient numbers. However, these results suggest that volumetric <sup>18</sup>F-FDG PET/CT parameters are more successful than SUV<sub>max</sub> in predicting CSI.

Similar to other studies in the literature [Kitajima et al. (5), Husby et al. (11), and Fasmer et al. (13)], SUV<sub>max</sub>, MTV,

and TLG were found to be reliable predictors of deep MI in our study. Data that are obtained from PET/CT in the preoperative period may be helpful in non-invasively predicting the depth of MI.

### Study Limitations

Our study had several limitations. First, it was retrospectively designed. Moreover, non-parametric tests, which are usually less powerful than corresponding parametric tests, were used due to insufficient normal distribution.

### Conclusion

Obtained volumetric parameters from <sup>18</sup>F-FDG PET/CT, especially TLG, can predict tumor characteristics, such as FIGO stages, LNM, MI, and cervical CSI, in the preoperative period. Furthermore, these parameters may alter the type of operation and the approach of treatment by providing more accurate risk classification.

### Ethics

**Ethics Committee Approval** University of Health Sciences Turkey, Okmeydani Training and Research Hospital Ethics Committee approval was obtained (number: 48670771-514.10).

**Informed Consent:** All patients signed written informed consent.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: N.T., Concept: Ö.V.T., A.A., S.R.E., M.Ö.T., Design: Ö.V.T., A.A., Data Collection or Processing: Ö.V.T., A.A., Analysis or Interpretation: A.A., Literature Search: Ö.V.T., A.A., Writing: Ö.V.T., A.A., S.R.E.

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

**Financial Disclosure:** The author declared that this study has received no financial support.

### References

- Berretta R, Patrelli TS, Migliavacca C, Rolla M, Franchi L, Monica M, Modena AB, Gizzo S. Assessment of tumor size as a useful marker for the surgical staging of endometrial cancer. *Oncol Rep* 2014;31:2407-2412.
- Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol* 2010;17:1471-1474.
- Creasman W. Revised FIGO staging for carcinoma of the endometrium. *Int J Gynaecol Obstet* 2009;105:109.
- Wright JD, Barrena Medel NI, Sehouli J, Fujiwara K, Herzog TJ. Contemporary management of endometrial cancer. *Lancet* 2012;379:1352-1360.
- Kitajima K, Suenaga Y, Ueno Y, Maeda T, Ebina Y, Yamada H, Okunaga T, Kubo K, Sofue K, Kanda T, Tamaki Y, Sugimura K. Preoperative risk

- stratification using metabolic parameters of (18)F-FDG PET/CT in patients with endometrial cancer. *Eur J Nucl Med Mol Imaging* 2015;42:1268-1275.
6. Shim SH, Kim DY, Lee DY, Lee SW, Park JY, Lee JJ, Kim JH, Kim YM, Kim YT, Nam JH. Metabolic tumour volume and total lesion glycolysis, measured using preoperative 18F-FDG PET/CT, predict the recurrence of endometrial cancer. *BJOG* 2014;121:1097-1106; discussion 1106.
  7. Liu DD, Li J, Li X, Xie L, Qin L, Peng F, Cheng MH. Prognostic value of metabolic tumor volume and total lesion glycolysis from <sup>18</sup>F-FDG PET/CT in lymph node metastases and risk stratification of endometrial carcinoma. *J Gynecol Oncol* 2019;30:e89.
  8. Bendifallah S, Canlorbe G, Raimond E, Hudry D, Coutant C, Graesslin O, Touboul C, Huguet F, Cortez A, Daraï E, Ballester M. A clue towards improving the European Society of Medical Oncology risk group classification in apparent early stage endometrial cancer? Impact of lymphovascular space invasion. *Br J Cancer* 2014;110:2640-2646.
  9. Liu DD, Li J, Li X, Xie L, Qin L, Peng F, Cheng MH. Prognostic value of metabolic tumor volume and total lesion glycolysis from <sup>18</sup>F-FDG PET/CT in lymph node metastases and risk stratification of endometrial carcinoma. *J Gynecol Oncol* 2019;30:e89.
  10. Mapelli P, Bergamini A, Fallanca F, Rancoita PMV, Cioffi R, Incerti E, Rabaiotti E, Petrone M, Mangili G, Candiani M, Gianolli L, Picchio M. Prognostic role of FDG PET-derived parameters in preoperative staging of endometrial cancer. *Rev Esp Med Nucl Imagen Mol (Engl Ed)* 2019;38:3-9.
  11. Husby JA, Reitan BC, Biermann M, Trovik J, Bjørge L, Magnussen IJ, Salvesen ØO, Salvesen HB, Haldorsen IS. Metabolic tumor volume on 18F-FDG PET/CT improves preoperative identification of high-risk endometrial carcinoma patients. *J Nucl Med* 2015;56:1191-1198.
  12. Stewart KI, Chasen B, Erwin W, Fleming N, Westin SN, Dioun S, Frumovitz M, Ramirez PT, Lu KH, Wong F, Aloia TA, Soliman PT. Preoperative PET/CT does not accurately detect extrauterine disease in patients with newly diagnosed high-risk endometrial cancer: A prospective study. *Cancer* 2019;125:3347-3353.
  13. Fasmer KE, Gulati A, Dybvik JA, Ytre-Hauge S, Salvesen Ø, Trovik J, Krakstad C, Haldorsen IS. Preoperative 18F-FDG PET/CT tumor markers outperform MRI-based markers for the prediction of lymph node metastases in primary endometrial cancer. *Eur Radiol* 2020;30:2443-2453.