Original Article

Mol Imaging Radionucl Ther 2026;35(2):105-113 **DOI:***10.4274/mirt.galenos.2026.48108*

Potential of Lean Body Mass ^{18}F-FDG PET/CT Parameters to Predict Pathologic Findings in Overweight Endometrial Cancer Cases

Aşırı Kilolu Endometriyal Kanser Olgularında Patolojik Bulguları Tahmin Etmede Yağsız Vücut Kütlesi ^{18}F-FDG PET/BT Parametrelerinin Potansiyeli

Furkan Avcı[1], Alpay Tunç[1], Burçin Karaşah Erkek[2], Ahmet Aydın Özsaran[3], Gürdeniz Serin[4], Osman Zekioğlu[4], Zeynep Burak[1]

[1]*Ege University Faculty of Medicine, Department of Nuclear Medicine, İzmir, Türkiye*
[2]*Ağrı Training and Research Hospital, Clinic of Nuclear Medicine, Ağrı, Türkiye*
[3]*Ege University Faculty of Medicine, Department of Obstetrics and Gynecology, İzmir, Türkiye*
[4]*Ege University Faculty of Medicine, Department of Pathology, İzmir, Türkiye*

Abstract

Objectives: Endometrial cancer is the second most common gynaecologic cancer in women worldwide. Due to the biology of endometrial cancer, most patients are overweight. Standard uptake value (SUV) measurements are known to vary depending on the patient's body weight. We aimed to evaluate whether lean body mass-adjusted ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) parameters [lean body mass-corrected standardized uptake value (SUL)-based metrics] are superior to conventional SUV-based parameters for predicting adverse histopathologic features in overweight patients with endometrial cancer, and to explore their association with progression-free survival (PFS).

Methods: In this retrospective single-center study, 73 overweight patients with endometrial cancer who underwent preoperative ^{18}F-FDG PET/CT followed by primary surgery were included. SUV- and SUL-based metabolic parameters were compared with histopathologic risk factors. ROC analyses were performed to determine discriminatory performance and optimal cut-off values. PFS was assessed using Kaplan-Meier analysis.

Results: SUV_{mean} (SUL_{mean}) demonstrated significant associations with deep myometrial invasion, lymphovascular space invasion, lymph node involvement, and higher tumor grade. In ROC analysis, SUL_{mean} showed moderate discriminatory ability for lymph node involvement (area under the curve: 0.78). However, PFS did not differ significantly between groups stratified by the ROC-derived SUL_{mean} cut-off (log-rank p=0.46).

Conclusion: Lean body mass-adjusted PET parameters, particularly SUL_{mean}, were more strongly associated with adverse histopathologic features than conventional SUV metrics in overweight patients with endometrial cancer. Although SUL-based parameters may contribute to preoperative risk assessment, their prognostic value for survival remains uncertain.

Keywords: Endometrial cancer, lean-body-mass, ^{18}F-FDG PET/CT, SUV, SUL

Address for Correspondence: Zeynep Burak, Ege University Faculty of Medicine, Department of Nuclear Medicine, İzmir, Türkiye
E-mail: profdrzeynep@gmail.com **ORCID ID:** orcid.org/0000-0002-3187-9447
Received: 27.07.2025 **Accepted:** 03.05.2026 **Publication Date:** 04.06.2026

Cite this article as: Avcı F, Tunç A, Karaşah Erkek B, Özsaran AA, Serin G, Zekioğlu O, Burak Z. Potential of lean body mass ^{18}F-FDG PET/CT parameters to predict pathologic findings in overweight endometrial cancer cases. Mol Imaging Radionucl Ther. 2026;35(2):105-113.

Öz

Amaç: Endometriyal kanser, dünyada kadınlar arasında en yaygın ikinci jinekolojik kanserdir. Endometriyal kanserin biyolojisi nedeniyle, çoğu hasta aşırı kiloludur. Standart alım değeri (SUV) ölçümlerinin, hastanın vücut ağırlığına bağlı olarak değişebileceği bilinmektedir. Bu çalışmanın amacı, aşırı kilolu endometriyal kanserli hastalarda vücut yağsız kütlesine göre ayarlanmış ^{18}F-fluorodeoksiglukoz pozitron emisyon tomografi/bilgisayarlı tomografi (^{18}F-FDG PET/CT) parametrelerinin [yağsız vücut kütlesine göre düzeltme yapılmış standartlaştırılmış alım değeri (SUL) tabanlı ölçütler] konvansiyonel SUV tabanlı parametrelerden daha üstün olup olmadığını araştırmak ve bu parametrelerin progresyon-free survival (PFS) ile ilişkisini incelemektir.

Yöntem: Bu retrospektif tek merkezli çalışmada, preoperatif ^{18}F-FDG PET/CT çekimi yapılan ve ardından primer cerrahi uygulanan 73 aşırı kilolu endometriyal kanser hastası dahil edilmiştir. SUV- ve SUL tabanlı metabolik parametreler, histopatolojik risk faktörleriyle karşılaştırılmıştır. ROC analizleri, ayırıcı performansı ve optimal kesme değerlerini belirlemek için yapılmıştır. PFS, Kaplan-Meier analizi ile değerlendirilmiştir.

Bulgular: SUL_{mean} (SUL_{mean}), derin miyometrial invazyon, lenfovasküler alan invazyonu, lenf nodu tutulumu ve yüksek tümör derecesi ile anlamlı ilişkiler göstermiştir. ROC analizinde, SUL_{mean}, lenf nodu tutulumu için orta derecede ayırt edici bir yetenek göstermiştir (eğri altında alan: 0.78). Ancak, ROC tabanlı SUL_{mean} kesme değeri ile gruplar arasındaki PFS, anlamlı şekilde farklılık göstermemiştir (log-rank p=0.46).

Sonuç: Yağsız vücut kütlesine göre ayarlanmış PET parametreleri, özellikle SUL_{mean}, aşırı kilolu endometriyal kanserli hastalarda konvansiyonel SUV ölçütlerinden daha güçlü bir şekilde olumsuz histopatolojik özelliklerle ilişkilidir. SUL tabanlı parametreler, preoperatif risk değerlendirmesine katkı sağlasa da, hayatta kalma üzerindeki prognostik değerleri belirsizdir.

Anahtar Kelimeler: Endometriyal kanser, yağsız vücut kütlesi, ^{18}F-FDG PET/BT, SUV, SUL

Introduction

Endometrial cancer is the second most common gynecological malignancy among women worldwide (1,2). However, in terms of mortality, it ranks lower, which can largely be attributed to the fact that endometrial cancer is typically diagnosed at an early stage (3). Obesity is a well-established risk factor for endometrial cancer (1,4). With increasing obesity rates worldwide, the incidence of endometrial cancer has been rising steadily, posing a growing public health challenge. Importantly, obesity not only increases the risk of developing endometrial cancer but may also influence tumor biology, imaging characteristics, and perioperative risk assessment, thereby complicating preoperative evaluation (5).

Histopathological features are essential for prognostication and clinical management in endometrial cancer. Histologic grade and myometrial invasion depth are key determinants of tumor aggressiveness and recurrence risk. Lymphovascular space invasion (LVSI), and lymph node involvement are strong predictors of extrauterine spread and poor survival. Cervical involvement contributes to FIGO staging and surgical planning. p53 mutations reflect tumor proliferation and molecular subtype, particularly in high-grade lesions. Additionally, estrogen receptor/progesterone receptor (ER/PR) receptor expression is often associated with hormone responsiveness and favorable prognosis. Evaluating these parameters provides critical insight into disease behavior and supports individualized treatment strategies. Accurate preoperative identification of these adverse pathological features remains clinically relevant, as it may influence the extent of surgical staging, lymph node assessment, and adjuvant treatment decisions (6).

In the diagnostic and staging process of endometrial cancer, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) imaging is widely used to assess tumor metabolism and disease burden. Traditional parameters such as the standardized uptake value (SUV) have long played a critical role in evaluating tumor metabolic activity. The metabolic data obtained from ^{18}F-FDG PET/CT can help guide more accurate and personalized treatment decisions, ultimately supporting cancer management and improving patient outcomes (7). Although SUV-based metrics provide a convenient and reproducible assessment of tumor metabolism, their accuracy can be compromised in populations with altered body composition, such as obese patients.

SUV measurements are known to vary depending on the patient's body weight. As body weight and body mass index (BMI) increase, SUV values in tumor tissues and normal tissues also tend to rise (8), potentially leading to inconsistent results across patients, and predicting therapy response within a patient (9). To overcome these limitations, lean body mass-corrected standardized uptake value (SUL) have emerged as a promising alternative, offering superior reproducibility across individuals with varying body compositions (10). Recent studies have shown that parameters like SUL maximum (SUL_{max}) provide more stable measurements than SUV, especially in patients with high BMI (11,12,13). However, data specifically addressing the clinical utility of lean body mass-adjusted (LBM) PET parameters in overweight or obese patients with endometrial cancer remain limited.

In this study, we aimed to evaluate whether metabolic and volumetric PET/CT parameters corrected for lean body mass are more effective in predicting pathological features in

overweight patients diagnosed with endometrial cancer. In addition, we explored the potential prognostic implications of LBM PET parameters by performing progression-free survival (PFS) analyses based on ROC derived cut-off values. Our goal was to determine whether SUL-based imaging metrics can enhance the accuracy of preoperative risk stratification and support more personalized treatment planning.

Materials and Methods

Study Population

This single-center retrospective study included consecutive patients diagnosed with endometrial cancer between January 2021 and December 2024. A total of 412 patients were initially screened. After applying predefined inclusion and exclusion criteria, 73 patients were included in the final analysis. The patient selection process is summarized in Figure 1. Surgical treatment, consisting of total abdominal hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection, was performed within two weeks following PET/CT imaging in all cases.

Demographic characteristics, clinicopathological variables, and postoperative histopathological findings were retrieved from the institutional electronic medical records system. Histopathological evaluation included tumor grade, depth of myometrial invasion, LVSI, cervical stromal involvement, and lymph node status, when available. The approval has been granted by the Ethics Committee of Ege University Medical Research with (decision no: 25-3.1T/87, date: 20.03.2025).

PET/CT Acquisition and Image Analysis

All PET/CT scans were performed using the same PET/CT scanner (Biograph True Point 16; Siemens Healthcare, Henkester, Germany) in accordance with the Uniform Protocols for Imaging in Clinical Trials (UPICT) guidelines (14). PET/CT imaging was performed from the vertex to the mid-thigh following at least 6 hours of fasting, and blood glucose levels were confirmed to be below 150 mg/dL prior to tracer injection. The PET/CT images were independently analyzed by two experienced nuclear medicine physicians who were blinded to the patients' clinical information. Any discrepancies were resolved by consensus. PET/CT data were evaluated both visually and semi-quantitatively. Semi-quantitative parameters, including maximum SUV (SUV_{max}), SUV mean (SUV_{mean}), and peak (SUV_{peak}), were calculated for each lesion. Additionally, [maximum SUL (SUL_{max}), SUL mean (SUL_{mean}) and peak (SUL_{peak}] were derived using the James formula, implemented within the PET/CT workstation software. Volumetric parameters such as metabolic tumor volume (MTV) and total lesion glycolysis (TLG) were also obtained, along with TLG-LBM to assess overall metabolic burden.

Follow-up and Outcome Assessment

Patients were followed through review of electronic medical records. Recurrence status was assessed based on radiologic and/or histopathologic confirmation during follow-up. Recurrent disease was defined morphologically as radiologic evidence of locoregional or distant tumor reappearance after primary surgical treatment. PFS was calculated from the date of surgery to the date of documented recurrence or last clinical follow-up.

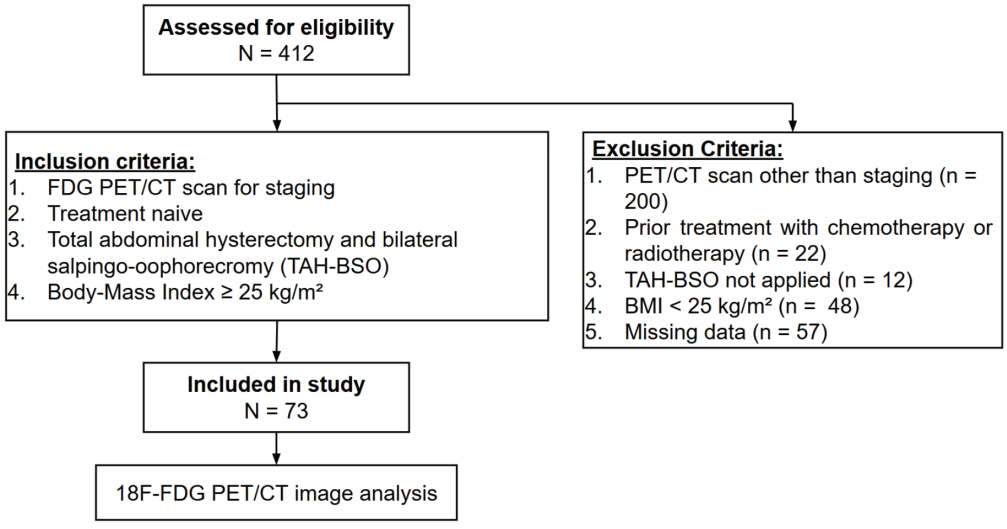

Figure 1. Flow diagram of patient selection
^{18}F-FDG PET/CT: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography, TAH-BSO: Total abdominal hysterectomy and bilateral salpingo-oophorectomy, BMI: Body mass index

Patients without recurrence were censored at the time of last follow-up.

Statistical Analysis

For statistical analysis, we compared PET/CT-derived metabolic and volumetric parameters—including SUV_{max}, SUV_{mean}, SUV_{peak}, SUL_{max}, SUL_{mean}, SUL_{peak}, MTV, TLG, and SUL-TLG—with key clinicopathological features. These included histological grade, depth of myometrial invasion, LVSI, lymph node involvement, cervical stromal invasion, hormone receptor status (ER/PR), p53 mutation status, age at diagnosis, and tumor size. Continuous variables were assessed for correlations using Spearman's rank correlation coefficient. Group comparisons were performed using non-parametric tests (Mann-Whitney U or Kruskal-Wallis) as appropriate. ROC curve analyses were conducted to evaluate the discriminative ability of PET/CT parameters for relevant binary outcomes, and optimal cut-off values were determined using the Youden J index. All tests were two-tailed, and a p-value of <0.05 was considered statistically significant. All statistical analyses were conducted using SPSS version 25 (IBM Corp., Armonk, NY, USA).

Results

A total of 73 patients with endometrial cancer who underwent preoperative ^{18}F-FDG PET/CT followed by primary surgical treatment were included. Baseline clinical characteristics, histopathologic features, and follow-up data are summarized in Table 1. The study population predominantly consisted of patients with early-stage disease, while individual histopathologic risk factors—including deep myometrial invasion, LVSI, cervical stromal involvement, and lymph node metastasis—were variably present.

The distribution of PET-derived metabolic and volumetric parameters, including SUV-based, SUL-based, and volumetric measurements, is presented in Table 2. All PET parameters demonstrated non-normal distributions and were therefore summarized using median and interquartile range values.

Comparisons of PET-derived metabolic parameters according to adverse histopathologic features are detailed in Table 3. Among evaluated parameters, SUL-based measurements demonstrated significant differences across several adverse pathologic characteristics, including LVSI and lymph node involvement. Representative PET/CT images illustrating differences in primary tumor FDG uptake according to LVSI status are shown in Figure 2. Both SUV_{mean} and SUL_{mean} differed significantly according to the depth of myometrial invasion.

Table 1. Baseline clinical and histopathologic characteristics of the study population

Total patient	**n**	**73**
Recurrent malignancy	n (%)	5 (6.8)
Continuous variables		
Age (years)	Median [IQR]	61 (53-66)
BMI (kg/m²)	Median [IQR]	32.4 (29.3-38.6)
Pre-operative CA-125 (U/mL)	Median [IQR]	14 (10-23.5)
Tumor size (cm)	Median [IQR]	3.5 (2.5-5)
Follow-up duration (months)	Median [IQR]	28 (15-41)
Categorical variables		
FIGO stage, n (%)	Stage 1	58 (79.5)
	Stage 2	6 (8.2)
	Stage 3	9 (12.3)
Histologic type, n (%)	Endometroid	63 (86.3)
	Non-endometroid	10 (13.7)
Histologic tumor grade, n (%)	Grade 1	10 (13.7)
	Grade 2	52 (71.2)
	Grade 3	11 (15.1)
Myometrial invasion status, n (%)	Inner half (<1/2)	47 (64.4)
	Outer half (≥1/2)	26 (35.6)
Lymphovascular space invasion, n (%)	Absent	53 (72.6)
	Present	20 (27.4)
Cervix involvement, n (%)	Absent	64 (87.7)
	Present	9 (12.3)
Lymph node involvement, n (%)	No dissection	16 (21.9)
	Negative	52 (71.2)
	Positive	5 (6.8)
Microsatellite instability mutation, n (%)	Unexamined	17 (23.3)
	Negative	38 (52.1)
	Positive	18 (24.7)
p53 mutation, n (%)	Wild-type	57 (78.1)
	Aberrant-type	16 (21.9)
Estrogen receptor expression, n (%)	Negative	4 (5.5)
	Positive	69 (94.5)
Progesterone receptor expression, n (%)	Negative	10 (13.7)
	Positive	63 (86.3)

Continuous variables are presented as mean ± standard deviation or median (interquartile range) according to distribution. Categorical variables are presented as number (percentage). BMI:Body mass index, LVSI: Lymphovascular space invasion, MSI: Microsatellite instability, FIGO: International Federation of Gynecology and Obstetrics, IQR: Interquartile range, CA-125: Cancer antigen 125

Table 2. Distribution of ^{18}F-FDG PET/CT derived metabolic and volumetric parameters	
Parameter	**Median [IQR]**
SUV_{max}	19.81 [14.88-29.05]
SUV_{mean}	9.1 [7.23-11.52]
SUV_{peak}	13.71 [9.15-20.76]
SUL_{max}	11.37 [8.07-15.54]
SUL_{mean}	4.91 [3.94-6.28]
SUL_{peak}	7.50 [5.05-10.50]
MTV	8.71 [4.30-20.37]
TLG	72.06 [32.23-197.87]
SUL-TLG	39.42 [17.01-117.41]

Data are presented as median (interquartile range) due to non-normal distribution. SUV: Standardized uptake value, SUL: Lean body mass-corrected standardized uptake value, MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, IQR: Interquartile range, ^{18}F-FDG PET/CT: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography

PET-derived metabolic parameters also differed significantly across histologic tumor grades, as shown in Table 4. Global differences were observed for multiple SUV- and SUL-based parameters, including SUL_{mean}. Pairwise post-hoc analyses revealed significant differences primarily between low-grade and higher-grade tumors, whereas no significant differences were observed between intermediate- and high-grade tumors.

Spearman correlation analyses demonstrated moderate to strong positive correlations between tumor size and volumetric PET parameters, particularly MTV and TLG (r values ranging from approximately 0.68 to 0.73, p<0.001). SUV_{mean} and SUL_{mean} also showed significant positive correlations with tumor size, although with lower correlation coefficients (r=0.38-0.50, p<0.001).

Table 3. Comparison of PET-derived metabolic parameters according to adverse pathologic features			
Myometrial invasion status	**Inner half (< 1/2), median [IQR]**	**Outer half (≥ 1/2), median [IQR]**	**p-value**
SUV_{mean}	8.16 [7.13-10.31]	10.81 [7.84-12.71]	0.024
SUL_{mean}	4.73 [3.76-5.43]	5.64 [4.22-7.57]	0.022
Lymphovascular space invasion	**Absent, median [IQR]**	**Present, median [IQR]**	**p-value**
SUL_{mean}	4.57 [3.73-5.76]	5.70 [4.65-7.01]	0.015
Lymph node involvement	**Negative, median [IQR]**	**Positive, median [IQR]**	**p-value**
SUL_{mean}	5.01 [4.05-6.44]	6.56 [5.54-12.70]	0.037

Data are presented as median (interquartile range). Comparisons between two groups were performed using the Mann-Whitney U test. A two-tailed p-value<0.05 was considered statistically significant
IQR: Interquartile range, SUV: Standardized uptake value, SUL: Lean body mass-corrected standardized uptake value, PET: Positron emission tomography

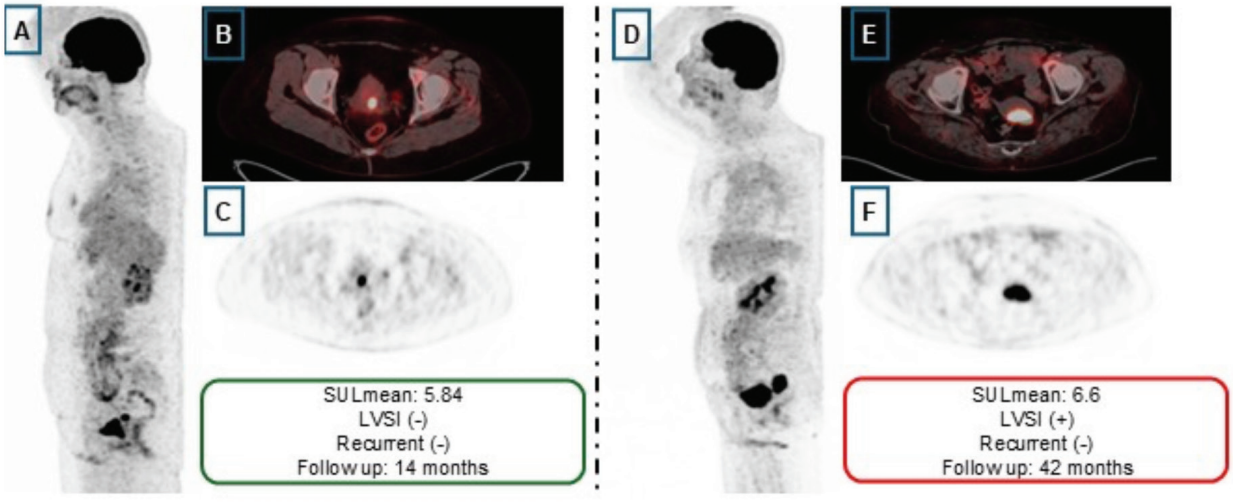

Figure 2. Representative ^{18}F-FDG PET/CT images of primary endometrial tumors according to LVSI status. (A-C) LVSI-negative case, (D-F) LVSI-positive case. (A, D) MIP images; (B, E) axial fused PET/CT; (C, F) axial PET images. Both patients were non-recurrent during follow-up
^{18}F-FDG PET/CT: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography, LVSI: Lymphovascular space invasion. MIP: Maximum intensity projection, SUL: Lean body mass-corrected standardized uptake value

Preoperative cancer antigen 125 levels demonstrated weak to moderate correlations with tumor size and volumetric PET-derived parameters (r=0.30-0.40, p<0.05).

The diagnostic performance of PET-derived parameters for predicting individual histopathologic risk factors was evaluated using receiver operating characteristic analysis, with results summarized in Table 5. SUL_{mean} demonstrated higher discriminative ability compared with SUV-based parameters for the prediction of LVSI and lymph node involvement.

ROC analysis was performed to evaluate the diagnostic performance of PET-derived parameters for predicting individual histopathologic risk factors (Table 5). Among the evaluated parameters, SUL_{mean} demonstrated the highest discriminative ability for lymph node involvement. An optimal SUL_{mean} cut-off value of 6.04 was identified based on the Youden index (Youden J =0.55), yielding a sensitivity of 80%, specificity of 75%, positive predictive value of 76%, and negative predictive value of 78% for the prediction of lymph node involvement.

Because lymph node involvement represents a clinically relevant adverse prognostic factor and SUL_{mean} demonstrated the strongest diagnostic performance for this endpoint, the ROC-derived cut-off value of 6.04 was selected for subsequent survival analyses. Patients were dichotomized into low (≤6.04) and high (>6.04) SUL_{mean} groups according to this threshold. Kaplan-Meier analysis was performed to assess PFS. During follow-up, recurrence events occurred in a limited number of patients. Survival distributions did not differ significantly between the two groups (log-rank p=0.46; Figure 3). Median PFS was not reached in either group due to the low event rate. Given the limited number of events, further survival modeling was not conducted.

Discussion

In this retrospective cohort of overweight patients with endometrial cancer, lean body mass-adjusted PET/CT parameters—particularly SUL_{mean}—demonstrated

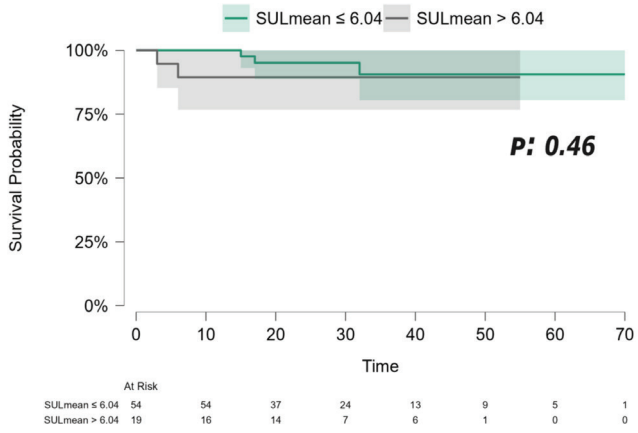

Figure 3. Kaplan-Meier curves for progression-free survival stratified by SUL_{mean} cut-off (6.04). Survival distributions were compared using the log-rank test
SUL: Lean body mass-corrected standardized uptake value

Table 4. Comparison of PET-derived metabolic parameters across histologic tumor

PET parameters	Grade 1, median [IQR]	Grade 2, median [IQR]	Grade 3, median [IQR]	p-value
SUV_{mean}	6.58 [5.38-9.42]	9.03 [7.29-11.62]	9.96 [7.79-13.56]	0.050
SUL_{max}	7.67 [6.45-11.29]	11.55 [9.07-15.02]	16.30 [8.89-19.76]	0.041
SUL_{peak}	4.79 [3.94-7.05]	7.65 [5.72-10.05]	10.5 [5.63-14.44]	0.037
SUL_{mean}	3.90 [2.88-5.20]	4.93 [4.12-5.82]	6.56 [4.57-8.68]	0.025

Data are presented as median (interquartile range). Differences among groups were assessed using the Kruskal-Wallis test. A two-tailed p-value<0.05 was considered statistically significant
IQR: Interquartile range, SUV: Standardized uptake value, SUL: Lean body mass-corrected standardized uptake value, PET: Positron emission tomography

Tablo 5. ROC analysis of PET-derived parameters for prediction of histopathologic risk factors

Outcome	Parameter	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Myometrial invasion status	SUV_{mean}	0.34 (0.20-0.47)	9.56	29	34	31	33
Myometrial invasion status	SUL_{mean}	0.33 (0.20-0.47)	5.83	17	50	25	37
Lymphovascular space invasion	SUL_{mean}	0.68 (0.55-0.81)	5.9	50	81	72	61
Lymph node involvement	SUL_{mean}	0.78 (0.58-0.98)	6.04	80	75	76	78

Optimal cut-off values were determined using the Youden index. Sensitivity and specificity are reported for the corresponding cut-off values
AUC: Area under the curve, CI: Confidence interval, SUV: Standardized uptake value, SUL: Lean body mass-corrected standardized uptake value, PPV: Positive predictive value, NPV: Negative predictive value

stronger and more consistent associations with adverse histopathologic features than conventional SUV-based metrics. Specifically, SUL_{mean} was significantly higher in tumors with deep myometrial invasion, LVSI, lymph node involvement, and higher histologic grade. In ROC analyses, SUL_{mean} showed moderate discriminative ability for LVSI and the highest performance for lymph node involvement, whereas SUV-based parameters were less consistent across these endpoints.

From a biological and methodological perspective, these findings suggest that lean body mass correction may reduce variability introduced by excess adipose tissue and provide a metabolically more stable estimate of tumor glycolytic activity in overweight individuals. SUV measurements are known to be influenced by total body weight and adiposity, potentially leading to overestimation of uptake in obese patients. In contrast, lean body SUL reduce this dependency and improve inter-patient comparability (12,13,15).

While both SUV_{mean} and SUL_{mean} were associated with depth of myometrial invasion, SUL_{mean} demonstrated additional discriminatory value for LVSI and nodal metastasis, two features closely linked to extrauterine spread and the need for comprehensive surgical staging in accordance with current guidelines (6,16). Notably, SUL_{mean} values increased stepwise across tumor grades, with the most pronounced differences observed between low-grade and higher-grade tumors, supporting its potential role as a marker of tumor aggressiveness.

Importantly, although a ROC-derived SUL_{mean} cut-off of 6.04 demonstrated reasonable sensitivity and specificity for lymph node involvement, Kaplan-Meier analysis did not reveal a statistically significant difference in PFS between low and high SUL_{mean} groups (log-rank p=0.46). This negative survival result must be explicitly acknowledged. Several factors likely contributed to the absence of a significant PFS difference: the predominance of early-stage disease, the very low number of recurrence events (n=5), and a follow-up duration that may be insufficient to capture late recurrences in this generally favorable-risk population (1,2,3). In addition, although SUL_{peak} is emphasized in PERCIST criteria for treatment response assessment (7), the prognostic role of baseline SUL-based parameters in endometrial cancer—particularly in relation to PFS—remains insufficiently studied. Therefore, our findings do not support the use of SUL_{mean} as an independent survival predictor and should be interpreted cautiously.

The present results are partially consistent with prior studies reporting associations between FDG uptake and adverse pathologic features in endometrial cancer. According to Yao et al. (17), no significant correlation was observed between estrogen receptor (ER) expression and FDG uptake on PET/CT. Takagi et al. (18) demonstrated a significant association between SUV_{max} and histological grade, while Vural Topuz et al. (19) reported correlations between SUV_{max}, MTV, TLG, and several adverse pathologic features, including nodal involvement. However, these analyses were based on weight-normalized SUV metrics and did not incorporate lean body mass correction. Studies focusing on SUL in gynecologic malignancies have suggested potential advantages in reflecting tumor differentiation (11), yet direct comparisons between SUV- and SUL-based parameters in overweight endometrial cancer populations remain limited. Sürer Budak et al. (20) reported that SUV_{max} and apparent diffusion coefficient minimum were independently associated only with deep myometrial invasion, with moderate predictive performance. In contrast, our findings suggest that lean body mass-adjusted PET parameters were associated with a broader spectrum of adverse histopathologic features, including LVSI and nodal involvement. Although magnetic resonance imaging was not evaluated in our study, the incorporation of SUL-based metrics may provide complementary metabolic information beyond myometrial invasion assessment.

The theoretical advantage of SUL is particularly relevant in endometrial cancer, a malignancy strongly associated with obesity (4,5). Because SUV is normalized to total body weight, excess adipose tissue—which exhibits relatively low FDG uptake—may artificially inflate calculated tumor uptake values (8). Lean body mass correction addresses this limitation and has been shown to reduce variability related to body composition (12,13,15). Our findings support this methodological rationale by demonstrating stronger associations between SUL_{mean} and adverse histopathologic characteristics in an overweight cohort.

Nevertheless, not all evaluated parameters performed equally. Volumetric metrics such as MTV and TLG correlated strongly with tumor size, which is expected given their volumetric nature, but they did not consistently outperform SUL-based indices for specific adverse features. Furthermore, metabolic parameters did not show significant associations with certain molecular markers, including p53 status, despite its recognized biological relevance in endometrial carcinoma (21). This lack of association may reflect limited statistical power, early-stage predominance, or the fact that FDG uptake captures glucose metabolism rather than the full spectrum of molecular alterations.

This study has several strengths. The exclusive inclusion of overweight patients addresses a clinically relevant population in which SUV variability is most problematic.

PET/CT imaging was performed within a short preoperative interval using a standardized protocol consistent with UPICT recommendations (14). Image interpretation was conducted by experienced nuclear medicine physicians blinded to clinical data, minimizing observer bias. Comprehensive histopathologic correlation and ROC-based cut-off analyses further enhance the interpretability of the findings, although these thresholds require external validation.

Study Limitations

However, important limitations must be acknowledged. The retrospective, single-center design introduces potential selection bias. The sample size was modest, and the number of lymph nodes–positive cases and recurrences was low, limiting statistical power. Multivariable survival analysis could not be performed due to the small number of PFS events. External validation in an independent cohort was not undertaken. Moreover, the predominance of early-stage disease restricts extrapolation to advanced-stage or high-risk populations.

Conclusion

Lean body mass–adjusted PET/CT parameters, particularly SUL_{mean}, demonstrated stronger associations with adverse histopathologic features than conventional SUV-based metrics in overweight patients with endometrial cancer. SUL_{mean} showed moderate discriminatory performance for LVSI and lymph node involvement, suggesting that lean body mass correction may enhance metabolic characterization in populations with elevated BMI. However, SUL_{mean} did not predict PFS in this predominantly early-stage cohort. These findings indicate that SUL-based parameters may contribute to preoperative risk assessment in overweight patients, but their prognostic significance remains uncertain. Prospective, multicenter studies with larger event numbers are required to validate these observations and to clarify the role of SUL metrics in clinical decision-making.

Ethics

Ethics Committee Approval: The approval has been granted by the Ethics Committee of Ege University Medical Research with (decision no: 25-3.1T/87, date: 20.03.2025).

Informed Consent: This single-center retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.A.Ö., G.S., O.Z., Concept: F.A., Z.B., Design: F.A., Z.B., Data Collection or Processing: F.A., A.T., Analysis or Interpretation: F.A., B.K.E., Literature Search: F.A., A.T., Writing: F.A., B.K.E., Z.B.

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

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

Refereneces

1. Crosbie EJ, Kitson SJ, McAlpine JN, Mukhopadhyay A, Powell ME, Singh N. Endometrial cancer. Lancet. 2022;399:1412-1428.
2. International Agency for Research on Cancer. Global Cancer Observatory. Cancer Today. https://gco.iarc.fr/today/en/dataviz/bars?mode=cancer&group_populations=1&sexes=2 (2024, accessed January 19, 2025).
3. Turkish Society of Gynecologic Oncology. Endometrial Cancer Management Guidelines. https://trsgo.org/files/yonetim-kilavuzlari/Endometrium-Kanseri.pdf (2023, accessed January 19, 2025).
4. McDonald ME, Bender DP. Endometrial cancer: obesity, genetics, and targeted agents. Obstet gynecol Clin North Am. 2019;46:89-105.
5. Fasmer KE, Sæterstøl J, Ljunggren MBS, Brun AMK, Pijnenborg JMA, Woie K, Krakstad C, Haldorsen I. S. Abdominal fat distribution in endometrial cancer: from diagnosis to follow-up. BMC Cancer 2025;25:879.
6. Concin N, Matias-Guiu X, Cibula D, Colombo N, Creutzberg CL, Ledermann J, Mirza M. R., Vergote I., Abu-Rustum NR, Bosse T, Chargari C, Espenel S, Fagotti A, Fotopoulou C, Gatius S, González-Martin A, Lax S, Levy B, Lorusso D, Macchia G, Nout R. A. ESGO-ESTRO-ESP guidelines for the management of patients with endometrial carcinoma: update 2025. Lancet Oncol. 2025;26:e423-e435.
7. Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: Evolving considerations for PET response criteria in solid tumors. J Nucl Med. 2009;50Suppl 1:122S-150S.
8. Thie JA. Understanding the standardized uptake value, its methods, and implications for usage. J Nucl Med. 2004;45:1431-1434.
9. Ziai P, Hayeri MR, Salei A, Salavati A, Houshmand S, Alavi A, Teytelboym OM. Role of optimal quantification of FDG PET imaging in the clinical practice of radiology. Radiographics 2016;36:481-496.
10. Aroldi F, Lord SR. Window of opportunity clinical trial designs to study cancer metabolism. Br J Cancer. 2020;122:45-51.
11. Mititelu R, Sîrbu C, Cuzino D, Jinga M, Radu F, Mazilu C, Spiridon PM. PET-CT with ^{18}F-FDG in gynecological malignancies. Prognostic significance of the standardized uptake value. Romanian J Mil Med. 2024;127:162-167.
12. Gafita A, Calais J, Franz C, Rauscher I, Wang H, Robertson A, Czernin J, Weber WA, Eiber M. Evaluation of SUV normalized by lean body mass (SUL) in ^{68}Ga-PSMA11 PET/CT: a bi-centric analysis. EJNMMI Res. 2019;9:103.
13. Sarikaya I, Albatineh AN, Sarikaya A. Revisiting weight-normalized SUV and lean-body-mass-normalized SUV in PET Studies. J Nucl Med Technol. 2020;48:163-167.
14. Graham MM, Wahl RL, Hoffman JM, Yap JT, Sunderland JJ, Boellaard R, Linden HM, Kinahan PE. Summary of the UPICT protocol for ^{18}F-FDG PET/CT imaging in oncology clinical trials. J Nucl Med. 2015;56:955-961.
15. Jochimsen TH, Zeisig V, Schulz J, Butz M, Barthel H, Sabri O, Sattler B. Lean body mass correction of standardized uptake value in simultaneous whole-body positron emission tomography and magnetic resonance imaging. Phys Med Biol. 2015;60:4651-4664.
16. Altindag SD, Yiğit S, Şen S. Is microcystic, elongated, and fragmented pattern of myometrial invasion in endometrioid endometrial carcinoma associated with survival? Turk J Med Sci. 2022;52:1569-1579.

17. Yao X, Tan X, Zhang H, Yuan H, Zeng B, He L, Jiang L. Relationship between ^{18}F-fluorodeoxyglucose PET/computed tomography metabolic parameters and clinicopathology in endometrial cancer. Nucl Med Commun. 2022;43:1233-1238.
18. Takagi H, Sasagawa T, Shibata T, Minato H, Takahashi T. Association between ^{18}F-fluorodeoxyglucose-PET/CT and histological grade of uterine endometrial carcinoma. Taiwan J Obstet Gynecol. 2018;57:283-288.
19. Vural Topuz Ö, Aksu A, Erinç SR, Tokgözoğlu N, Tamam MÖ. The evaluation of preoperative ^{18}F-FDG PET/CT in patients with endometrial cancer and the correlation between PET parameters and postoperative pathology results. Mol Imaging Radionucl Ther. 2022;31:16-22.
20. Sürer Budak E, Toptaş T, Aydın F, Öner AO, Çevikol C, Şimşek T. Correlation of minimum apparent diffusion coefficient and maximum standardized uptake value of the primary tumor with clinicopathologic characteristics in endometrial cancer. Mol Imaging Radionucl Ther. 2017;26:24-32.
21. Morice P, Leary A, Creutzberg C, Abu-Rustum N, Darai E. Endometrial cancer. Lancet. 2016;387:1094-1108.