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Risk stratification of endometrial cancer and lymph node metastases prediction using ^{18}F-FDG PET/CT: role of metabolic tumor volume and total lesion glycolysis

Mostafa M. Abdelkawi[1], Mohamed S. Sweed[2], Mohamed A. Ali[2] and Eman A. NasrElDin[1*]

Abstract

Background: Endometrial cancer is the commonest gynecologic malignancy. Pelvic lymph node metastasis is considered one of its most important prognostic factors. Surgery is considered the most important and effective treatment, still there is controversy about indication and necessity of pelvic lymph node dissection. ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography is investigated in his study to evaluate its value in preoperative detection of lymph node metastases and risk stratification of endometrial cancer.

Results: Reviewing the records of 33 women with endometrial cancer, all ^{18}F-FDG PET/CT studied indices, SUV_{max}, SUV_{mean}, MTV and TLG, mean difference was statistically significant in all the studied risk categories (tumor grade, Myometrial invasion, lymphovascular space invasion, tumor stage, and risk stratification). SUV_{max} and TLG showed highest area under the curve for detection of Myometrial invasion > 50% (AUC = 0.911) with cut-off value of SUVmax > 14.55 showing 88.89% sensitivity and 86.67% specificity, and TLG > 192.653 having 88.89% sensitivity and 80% specificity. TLG showed highest AUC (0.889 and 0.921) for detection of LVSI and LNMs with 100% sensitivity and 66.67% specificity for cut-off value > 179.374 and 88.89% sensitivity and 83.33% specificity for cut-off value > 249.366, respectively. Concerning risk stratification of EC, SUV_{max} and TLG showed highest AUC (0.839) with cut-off value > 14.55 showing 77.27% sensitivity and 90.91% specificity, and > 192.653 having 77.27% sensitivity and 81.82% specificity, respectively.

Conclusion: The results of this study suggest that ^{18}F-FDG PET/CT is a very valuable tool for prediction of lymph node metastases and risk stratification in endometrial cancer patients. Applying TLG cutoff values increases the accuracy and preoperative diagnosis of lymph node metastases which aids in sparing women with low-risk early stage EC unnecessary surgical risk and morbidity of lymphadenectomy.

Keywords: Endometrial neoplasms, Positron emission tomography computed tomography, Lymphatic metastasis, Risk assessment, Tumor burden

Background

Endometrial cancer (EC) is the commonest gynecologic malignancy that is prevalent among women in developed countries and the second most common among those in developing countries [1]. Natural course of EC is slow and is characterized by rather good prognosis [2]. However, women with recurrent or advanced disease, or

*Correspondence: dremansalam77@gmail.com
[1] Department of Radiology, Helwan University, Cairo 16646, Egypt
Full list of author information is available at the end of the article

when fertility preservation is required, limited treatment options are available [3]. Important risk factors for disease recurrence and survival are advanced International Federation of Gynecology and Obstetrics (FIGO) surgical stage, non-endometrioid histological sub-type, poorly differentiated tumor, more than half myometrial invasion, large tumor size, lymph-node metastasis, and lymphovascular space invasion (LVSI) [4, 5].

Pelvic lymph node metastasis (LNMs) is considered one of the most important prognostic factors in EC [6, 7]. The survival rate would be lower if the EC patients had pelvic or para-aortic LNMs [8–10].

Surgery is considered the most important and effective treatment of primary EC, but there is still a great deal of controversy about indication and necessity of pelvic lymph node dissection [11]. Clinicians do not support lymphadenectomy in low-risk group EC women based on low probability of LNMs [12], because only 5% are present or suspected [13]. Also, iliac lymphadenectomy is not considered an easy procedure and is often associated with complication due to the anatomical complexity in this region [12]. It seems to be of great importance to find the subgroup of patients with the good prognosis, who would not need comprehensive surgical staging and further treatment. It is especially important for older patients who suffer from severe concomitant diseases with high risk of complications during and after surgery. It is also very important for young patients, where fertility preservation is desired [14]. For preoperative risk stratification, a noninvasive diagnostic method that is able to predict tumor aggressiveness and pathological features would be useful [15].

^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) is an advanced imaging modality that has combined morphological and functional imaging capabilities and is widely used for diagnosis and re-staging of cancer [8]. In the current practice, maximum standardized uptake value (SUV_{max}), a semi-quantitative parameter determined by positron emission tomography (PET), is known to be a useful indicator of tumor aggressiveness and prognosis in a variety of malignant tumors. Several groups have addressed the relationship between SUV_{max} and histological prognostic factors in EC [16]. However, SUV_{max} has the limitation of measuring from a single spot of the most hyper-metabolic area of the tumor mass [17]. It cannot be used for assessment of the tumor mass overall glucose metabolic activity [18]. On the other hand, total lesion glycolysis (TLG) and metabolic tumor volume (MTV) are indicators of metabolic activity throughout the tumor volume. Therefore, these parameters potentially reflect tumor biology, treatment response, and prognosis more accurately than SUV_{max} [19]. Only few studies addressed the prognostic value of TLG and MTV in EC preoperative risk stratification [16].

The aim of this study is to evaluate the value of ^{18}F-FDG PET/CT in preoperative risk stratification of women with EC.

Methods

This retrospective study was conducted during the period from January 2017 to June 2021. Retrospective collection of data was done for women with EC who underwent hysterectomy and bilateral salpingo-oophorectomy (TAH + BSO) with pelvic lymphadenectomy and had preoperative ^{18}F-FDG PET/CT done for them. Women who had ^{18}F-FDG PET/CT done more than one month before surgery, incomplete surgical staging, or unavailable postoperative pathology report were excluded from the study.

18F-FDG PET/CT imaging protocol

Special pre-procedure precautions were done [fasting for 4–6 h, blood glucose level less than 200 mg/dl, avoidance of vigorous activity 24 h before the procedure and avoidance of talking following injection of the radioisotope to avoid physiologic background muscle uptake of the tracer]. PET/CT examination was performed using machine [Philips® Ingenuity TF 128 multi slice PET/CT] and GE® multislice Discovery IQ 5 Rings machine with Dual Acquisition Channels, 50-slice equivalent CT speed. For all cases, 5–10 mCi (approximate dose to patient, 1 mCi /10 kg) of 18F-FDG was the usual dose administered to each patient about one hour before the examination. The examination started with a low-dose non-enhanced routine CT scan from the skull base to the mid-thigh performed for attenuation correction. The images were acquired with 6 to 8 bed positions on a 3D mode for 3 min per bed position; then, PET study was performed. Following this, a diagnostic enhanced CT scan was obtained using 60–100 ml of non-ionic iodinated contrast material according to patient's weight. The parameters of the CT scan were 150 kV, 150–250 mAs, slice thickness of 3.5 mm pitch = 0.9, covering the same transverse field of view. Delayed images after 2 h following micturition were taken when necessary, e.g.: LNs near UB.

All PET/CT images were reviewed by two independent experienced nuclear medicine physicians who had no knowledge of the patient's clinical information, and a standard PET/ CT imaging report was generated. The artifactual and physiological soft tissue accumulation of 18F-FDG was taken into consideration for accurate interpretation. Primary tumor lesions were diagnosed when abnormal FDG uptake increase in irregular, nodular, or lumpy appearance on PET images was encountered,

with SUV_{max} over 2.5. Using GE® advanced workstation (AW05) and Philips® intellispace Portal workstation. Volume of interests (VOIs) was delineated on PET images, and manual adjustment was performed on axial, sagittal, and coronal images obtaining the optimal boundary of primary focus. The SUV_{max}, $SUV_{mean,}$ and MTV were generated automatically by the workstation (Figs. 1, 2, 3). TLG was calculated as MTV × SUV_{mean}.

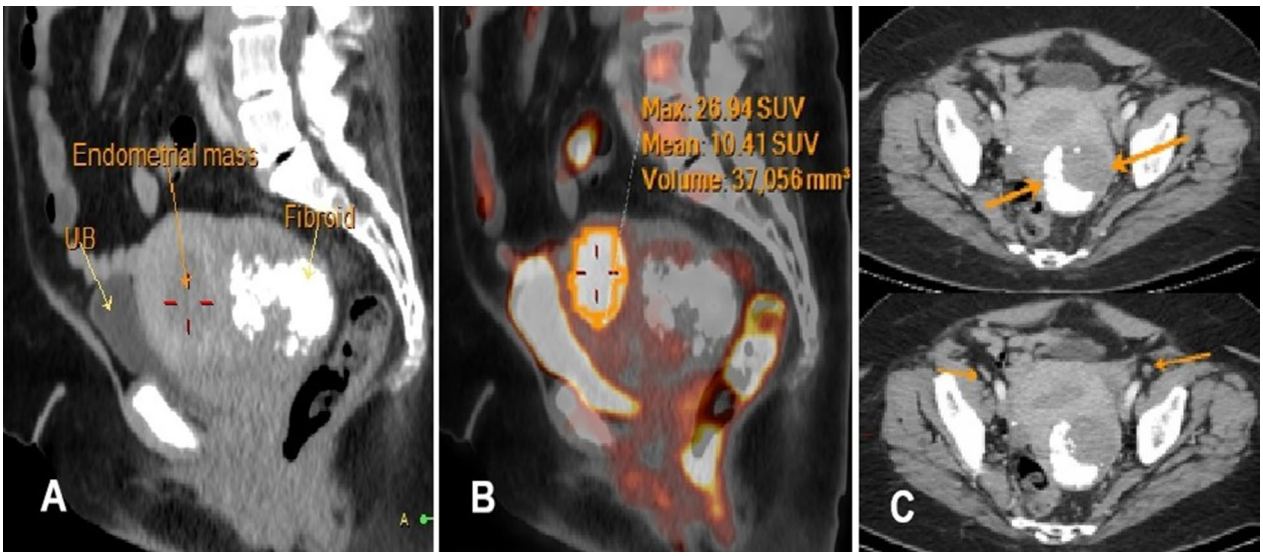

Fig. 1 The uterus is enlarged, showing endometrial intensely avid heterogeneous soft tissue lesion, measuring ± 40 × 34 × 19 mm [Image **A**]. The myometrium shows few fibroids, and the largest one [measuring ± 7 × 6 cm] is seen at the posterior wall, accommodating internal confluent dystrophic calcifications. The endometrial lesion achieves 26.9 SUV_{max}, 10.4 SUV_{mean} and MTV = 37,056 mm^3 at the corresponding PET images [image **B**]. Bilateral few small non-avid external iliac lymph nodes [arrows, image **C**, superior image], measuring 11 × 4mm and 10 × 9mm on the right and left side, respectively. No hypermetabolic pelviabdominal lymphadenopathy detected

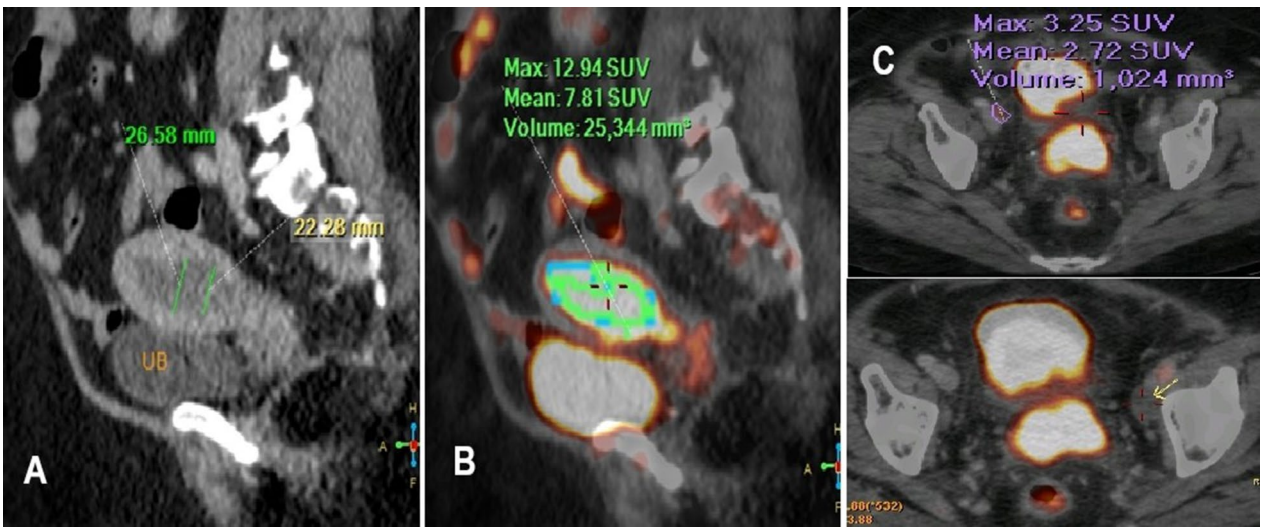

Fig. 2 The uterus is mildly enlarged in size, showing irregular hypermetabolic hypodense remarkable endometrial soft tissue thickening reaching up to 26.5 mm in maximal thickness with zones of active myometrial invasion at the fundus and posterior wall [image **A**], achieving up to 12.9 SUV_{max}, 7.81 SUV_{mean} and MTV = 1024 mm^3 on corresponding PET images [image **B**]. A small right external iliac LN is noted [image **C** superior image], measuring about 10 mm achieving 3.25 SUV max, 2.7 SUVmean and Volume = 1024 mm3. Another nonavid larger LN seen in the opposite left external iliac group [image **C**, inferior image] measuring about 22 × 17 mm devoid of any appreciable metabolic activity with loss of its fatty hilum

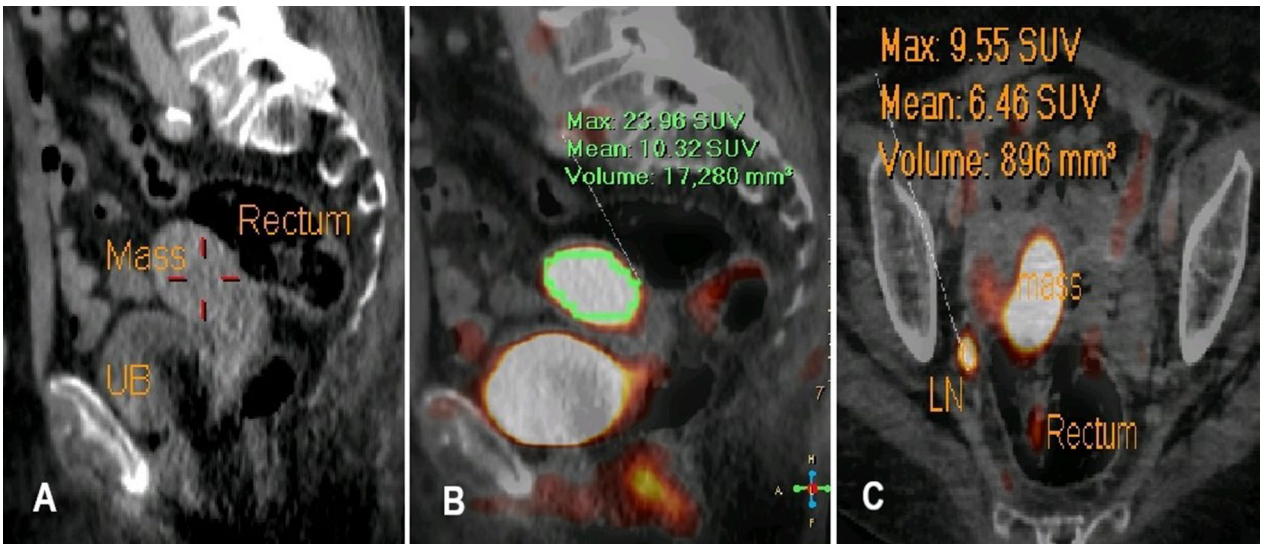

Fig. 3 A large hypermetabolic endometrial soft tissue thickening [image **A**], mainly involving the left lateral aspect of the endometrium, measuring ± 36 × 30 × 41mm at its maximal AP, TR & CC dimensions having intense avidity for FDG uptake [23.9 SUV_{max}, SUV_{mean} 10.32 and MTV = 17,280 mm^3], on corresponding PET image [image **B**]. Associated infiltration of more than 50% of the myometrial coat yet no associated extra uterine or parametrial extensions. Regional solitary right internal iliac LN is noted about 13 × 12 mm having intense metabolic activity [image **C**], 9.5 SUV max, 6.46 SUVmean and vol. = 896 mm^3

Postoperative pathological reports were reviewed. Women with EC were classified either to low-risk or high-risk groups according to risk stratification standards proposed by European Society for Medical Oncology; Low-risk: histological grade 1 (G1), Myometrial invasion (MI) less than half of the myometrium, and FIGO stage IA, and high-risk: histological grade 2/3 (G2/3), positive lymphovascular space involvement (LVSI), MI more than half of the myometrium, or non-endometrioid EC [20]. Also, lymph nodes status and LNMs were reported. Results of ^{18}F-FDG PET/CT were compared to pathological outcome.

Statistical analysis performed using IBM© SPSS© Statistics version 20 (IBM© Corp., Armonk, NY, USA). Data were collected, tabulated and then, analyzed using appropriate statistical tests. The D'Agostino–Pearson test was used to test the normality of numerical data distribution. Numerical data are presented as mean and standard deviation (if normally distributed) or as median and interquartile range (if skewed). Categorical data are presented as number and percentage or as ratio. The following diagnostic indices were calculated for each diagnostic tool: sensitivity, specificity, positive predictive value, and negative predictive value. Receiver-operating characteristic (ROC) curve analysis was used to examine the value of the diagnostic indices for the diagnosis of abnormal PI. The best cut-off value was identified as that associated with the highest Youden (J) index. *P*-value < 0.05 is considered statistically significant.

Results

During the period from January 2017 to June 2021, 44 ^{18}F-FDG PET/CT done for women with endometrial cancer were reviewed. Five cases were excluded as the pathology report showed that they underwent hysterectomy without formal staging, and six cases were excluded due to unavailability of pathology reports. Thus, 33 women were included in the study with mean age 56.67 ± 6.66 years (42–71 years) and BMI 30.4 ± 2.49 kg/m^2 (23.6–35.7 kg/m^2). The histological characteristics of EC in the studied women are shown in Table 1 (Table 1), where only 5 cases showed non-endometrioid carcinoma (three cases were papillary serous carcinoma (9.1%), and two were clear cell carcinoma (6.1%)).

All ^{18}F-FDG PET/CT studied indices, SUV_{max}, SUV_{mean}, MTV and TLG, showed significant difference between; histological grade 1 tumor and grade 2&3, Myometrial invasion < 50% and > 50%, the presence of LVSI, LNMs, and between low- and high-risk tumors (Table 2). Sensitivity and specificity of different PET-CT parameters for LNMs detection and risk stratification of EC are shown in Table 3, SUV_{max}, and TLG showed highest area under the curve for detection of Myometrial invasion > 50% (AUC = 0.911) with cut-off value of SUV_{max} > 14.55 showing 88.89% sensitivity and 86.67% specificity, and TLG > 192.653 having 88.89% sensitivity and 80% specificity. TLG showed highest AUC (0.889 and 0.921) for detection of LVSI and LNMs with 100% sensitivity and 66.67% specificity for cut-off

Table 1 Histopathological characteristics of EC

Histological characteristic	Number of cases (%)
Histopathological type	
Non-endometrioid	5/33 (15.2%)
Endometrioid	28/33 (84.8%)
Histopathological grade	
G 1	15/33 (45.5%)
G 2	11/33 (33.3%)
G 3	7/33 (21.2%)
FIGO stage	
IA	15/33 (45.5%)
IB	6/33 (18.2%)
II	2/33 (6.1%)
IIIB	1/33 (3%)
IIIC	7/33 (21.2%)
IVB	2/33 (6%)
Myometrial invasion	
< 50%	15/33 (45.5%)
> 50%	18/33 (54.5%)
LVSI	
Yes	15/33 (45.5%)
No	18/33 (54.5%)
LNMs	
Yes	9/33 (27.3%)
No	24/33 (72.7%)
Risk stratification	
Low risk	11/33 (33.3%)
High risk	22/33 (66.7%)

LVSI, Lymphovascular space invasion, LNMs, Lymph nodes metastases

value > 179.374 and 88.89% sensitivity and 83.33% specificity for cut-off value > 249.366, respectively. Concerning risk stratification of EC, SUV_{max} and TLG showed highest AUC (0.839) with cut-off value > 14.55 showing 77.27% sensitivity and 90.91% specificity, and > 192.653 having 77.27% sensitivity and 81.82% specificity, respectively (Table 3).

When predicting higher stage of EC than stage IA, all parameters showed significantly lower values in EC with stage IA compared to higher stages (Table 4). SUV_{max} and TLG showed highest AUC (cut-off value > 14.55, sensitivity 88.89%, specificity 86.67%; AUC = 0.911, *p*-value = < 0.0001, 95% CI 0.759 to 0.982) and (cut-off value > 192.653, sensitivity 88.89%, specificity 80%; AUC = 0.911, *p*-value = < 0.0001, 95% CI 0.759 to 0.982), respectively. SUV_{mean} showed sensitivity 88.89%, specificity 73.33% for cut-off value > 7.15 (AUC = 0.852, *p*-value = < 0.0001, 95% CI 0.685 to 0.951), while MTV showed sensitivity 77.78%, specificity 80% for cut-off value > 25.596 (AUC = 0.837, *p*-value = < 0.0001, 95% CI 0.667 to 0.942).

When comparing ROC curves of the four studied PET-CT parameters for prediction of LNMs and EC risk stratification testing for equal areas under the curve across tumor quantifications AUCs, *p*-value was > 0.05 showing no significant difference in any of them (Fig. 4).

Discussion

Endometrial cancer continues to be a serious problem facing women worldwide, with pelvic lymphadenectomy remaining as one of the important procedures performed in the management of EC. Diagnosing LNMs in EC and subsequent proper removal of these nodes allows proper staging of EC thus offering the appropriate adjuvant chemo- or radiotherapy, improves the survival rate for these women [21], also several studies reported that EC patients with LNMs had much worse prognosis than those without [9, 10]. Still, surgical lymphadenectomy is considered invasive and not without risks or potential morbidities taking in consideration the complexity of structures surrounding the lymph nodes. Several clinicians suggest omitting lymphadenectomy in low-risk EC owing to low incidence of LNMs in this group of patients and the high risk of morbidities related to the procedure [12, 22].

Accordingly, several studies have searched for the ideal pre-operative tool that can replace surgical lymphadenectomy. Reviewing literature, PET/CT was found to be superior to CT in detection of LNMs and other metastases [23]. MRI is useful in assessment of MI, tumor size, cervical involvement, and LNMs; it has better resolution for outlining anatomical lesions compared to PET/CT. Still, its diagnosis of LNMs depends on LN size (≥ 10 mm) and morphology (shape, signal intensity, and contour) which seems to be unreliable especially with the significant overlap with reactive lymph nodes [24]. Diffusion-Weighted MRI (DW-MRI) use to assess tissue diffusion and cellularity is now used with pelvic MRI to improve preoperative nodal staging but still with variable results [25].

Several authors found FDG PET/CT to have better diagnostic performance in LNMs detection compared to MRI [26, 27]. FDG PET/CT was also found superior to diffusion MRI in LNMs prediction in EC [28]. Still some overlap was found between precancerous and early EC concerning SUV-related parameters, which are sometimes difficult to discriminate between, making these early lesions non-avid to FDG PET/CT [29]. Other tracers as Fluoro-ethyl-choline (FEC)-PET/CT are studied, as cell line studies found several-fold increase of ^{3}H choline by EC cells compared to endometrial stromal cells [30]. The MAPPING trial found better diagnostic performance for FEC PET/CT over FDG PET/CT in LNMs detection (87.5% vs. 80%) but not statistically significant. Still, all

Table 2 PET-CT indices and EC risk stratification

Parameter	Cases (%)	SUV_{max}	SUV_{mean}	MTV	TLG
Histopathological grade					
G 1	15 (45.5%)	14.64 ± 4.26	7.39 ± 1.97	21.09 ± 9.57	166.97 ± 105.75
G 2&3	18 (54.5%)	19.19 ± 7.3	9.06 ± 3.34	37.53 ± 16.51	348.05 ± 222.83
P-value		0.0414	0.0986	0.0019	0.0071
95% CI		0.188 to 8.912	− 0.33 to 3.67	6.59 to 26.29	52.975 to 309.185
Myometrial invasion					
< 50%	15 (45.5%)	12.75 ± 2.23	6.52 ± 1.71	19.95 ± 9.86	132.86 ± 84.91
> 50%	18 (54.5%)	20.77 ± 6.67	9.79 ± 2.89	38.49 ± 15.32	376.48 ± 202.22
P-value		0.0001	0.0006	0.0003	0.0001
95% CI		4.34 to 11.7	1.538 to 5.002	9.172 to 27.908	129.356 to 357.884
LVSI					
Negative	15 (45.5%)	14.06 ± 4.28	6.65 ± 1.88	20.64 ± 8.94	139.63 ± 82.05
Positive	18 (54.5%)	19.68 ± 6.95	9.68 ± 2.92	37.91 ± 16.42	370.83 ± 209.69
P-value		0.0104	0.0016	0.0010	0.0004
95% CI		1.416 to 9.824	1.244 to 4.816	7.599 to 26.941	113.708 to 348.692
LNMs					
Negative	24 (72.7%)	14.8 ± 4.33	7.22 ± 2.09	24.47 ± 12.37	176.26 ± 97.99
Positive	9 (27.3%)	23.32 ± 7.27	11.19 ± 2.87	44.98 ± 15.15	504.36 ± 209.42
P-value		0.0002	0.0001	0.0004	< 0.0001
95% CI		4.336 to 12.704	2.123 to 5.817	10.032 to 30.988	219.842 to 436.358
Risk stratification					
LR	11 (33.3%)	12.76 ± 2.07	6.61 ± 1.54	18.72 ± 9.46	132.06 ± 91.49
HR	22 (66.7%)	19.3 ± 6.88	9.15 ± 3.08	35.73 ± 15.65	332.58 ± 207.02
P-value		0.0045	0.0154	0.0024	0.0047
95% CI		2.184 to 10.896	0.52 to 4.56	6.499 to 27.521	66.358 to 334.682

LVSI, Lymphovascular space invasion, LNMs, Lymph nodes metastases, LR, Low Risk, HR, High Risk

studied imaging techniques did not have enough sensitivity to replace nodal surgical staging, yet, FDG PET/CT showed high sensitivity and low false positive results that might be helpful in the arbitration of surgical planning decisions [31]. FESPET Study: Female EStrogen recePtor in Endometrial Cancer Treatment (FES-PET) is an ongoing study investigating the feasibility of FES-PET scan in EC. It combines PET-CT scan with an estrogen tracer, allowing noninvasive visualization of estrogen receptor, even in metastasis difficult to reach by biopsy [32].

In the current retrospective study, ^{18}F-FDG PET/CT has been found to be a very valuable tool for prediction of LNMs in EC patients, all metabolic parameters of the primary tumor were found to be significantly higher in patients with LNMs compared to those without. SUVmean showed 100% sensitivity for prediction of LNMS but with relatively fair specificity, 62.50%. TLG had the highest AUC with a considerably accepted sensitivity 88.89% and specificity 83.33%. Also, the pooled mean difference of all ^{18}F-FDG PET/CT parameters was found to be statistically significant in all the studied risk categories (tumor grade, MI, LVSI, and risk stratification). Several studies suggested the value of ^{18}F-FDG PET/CT in EC, with different sensitivity and specificity, three previous meta-analyses supported the results of this study specially indicating high specificity of this technique for detection of LNMs in EC [16, 33, 34]. They suggest that the relatively high pooled specificity of ^{18}F-FDG PET/CT for detection of LNMS in EC could safely argue the replacement of surgical lymphadenectomy in low-risk patients. Still, these meta-analyses found the pooled sensitivity of ^{18}F-FDG PET/CT to be much lower than the suggested by this study reaching maximum 73%. They suggested an explanation for this that the avidity of ^{18}F-FDG PET/CT depends on the presence of sufficient malignant cells to produce an increase in glucose metabolism, and the spatial resolution might be not reliable enough to detect small tumors or micro-metastasis with no established threshold for LN size in EC for ^{18}F-FDG PET/CT to detect LNMs [33, 34].

Still, ^{18}F-FDG PET/CT might be a preoperative solution for patients with high surgical risk and early stage EC where omitting lymphadenectomy might be an excellent alternative and even vaginal hysterectomy using

Table 3 Sensitivity and Specificity of different PET-CT parameters for LNMs detection and risk stratification of EC

	AUC	*P* value	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)
Histopathological grade						
SUV_{max}	0.711	0.0246	0.528 to 0.855	> 14.65	72.22	73.33
SUV_{mean}	0.663	0.0963	0.478 to 0.817	> 7.12	77.78	53.33
MTV	0.796	0.0003	0.620 to 0.916	> 25.596	77.78	80
TLG	0.759	0.0025	0.579 to 0.890	> 192.653	77.78	66.67
Myometrial invasion						
SUV_{max}	0.911	< 0.0001	0.759 to 0.982	> 14.55	88.89	86.67
SUV_{mean}	0.852	< 0.0001	0.685 to 0.951	> 7.15	88.89	73.33
MTV	0.837	< 0.0001	0.667 to 0.942	> 25.596	77.78	80
TLG	0.911	< 0.0001	0.759 to 0.982	> 192.653	88.89	80
LVSI						
SUV_{max}	0.848	< 0.0001	0.681 to 0.949	> 14.65	86.67	77.78
SUV_{mean}	0.804	0.0002	0.629 to 0.921	> 9.15	66.67	88.89
MTV	0.848	< 0.0001	0.681 to 0.949	> 25.596	86.67	77.78
TLG	0.889	< 0.0001	0.731 to 0.971	> 179.374	100	66.67
LNMs						
SUV_{max}	0.856	< 0.0001	0.691 to 0.954	> 18.34	77.78	87.50
SUV_{mean}	0.861	< 0.0001	0.696 to 0.956	> 7.54	100	62.50
MTV	0.852	< 0.0001	0.685 to 0.951	> 30.125	88.89	79.17
TLG	0.921	< 0.0001	0.773 to 0.986	> 249.366	88.89	83.33
Risk stratification						
SUV_{max}	0.839	< 0.0001	0.670 to 0.943	> 14.55	77.27	90.91
SUV_{mean}	0.785	0.0007	0.608 to 0.908	> 7.12	81.82	72.73
MTV	0.826	< 0.0001	0.655 to 0.935	> 25.596	72.73	90.91
TLG	0.839	< 0.0001	0.670 to 0.943	> 192.653	77.27	81.82

AUC, Area Under the Curve, LVSI, Lymph-vascular space invasion, LNMs, Lymph nodes metastases

Table 4 PET-CT parameters and EC stage

Parameter	Cases (%)	SUV_{max}	SUV_{mean}	MTV	TLG
FIGO stage					
IA	15 (45.5%)	12.75 ± 2.23	6.52 ± 1.79	19.95 ± 9.86	132.86 ± 84.91
> IA	18 (54.5%)	20.77 ± 6.67	9.79 ± 2.89	38.49 ± 15.32	376.48 ± 202.22
P-value		0.0001	0.0006	0.0003	0.0001
95% CI		4.34 to 11.7	1.52 to 5.02	9.172 to 27.908	129.356 to 357.884

regional anesthesia might be the ideal management for these patients thus alleviating both the surgical and anesthetic risk. This was supported by the statistically significant difference between the mean values of all ^{18}F-FDG PET/CT metabolic parameters in patients with stage IA EC and those with higher stage.

Still, this study has different limitations, the retrospective design of the study and the relatively small number of cases, this was attributed to the fact that ^{18}F-FDG PET/CT is still an evolving diagnostic tool in EC where not all clinicians are still aware of its importance which made it difficult to construct a prospective study and to attain larger number of cases which are still needed to validate the results of this study. Also, this study did not compare this technique with the value of other techniques as dynamic post-contrast magnetic resonance imaging (MRI) using diffusion/ADC map and perfusion data which even seems to superior in detection of LNMs according to few reports [35, 36]. Third, none of the included cases had para-aortic lymphadenectomy which is especially important in high-grade EC and is reported to be present in 2.7% of EC

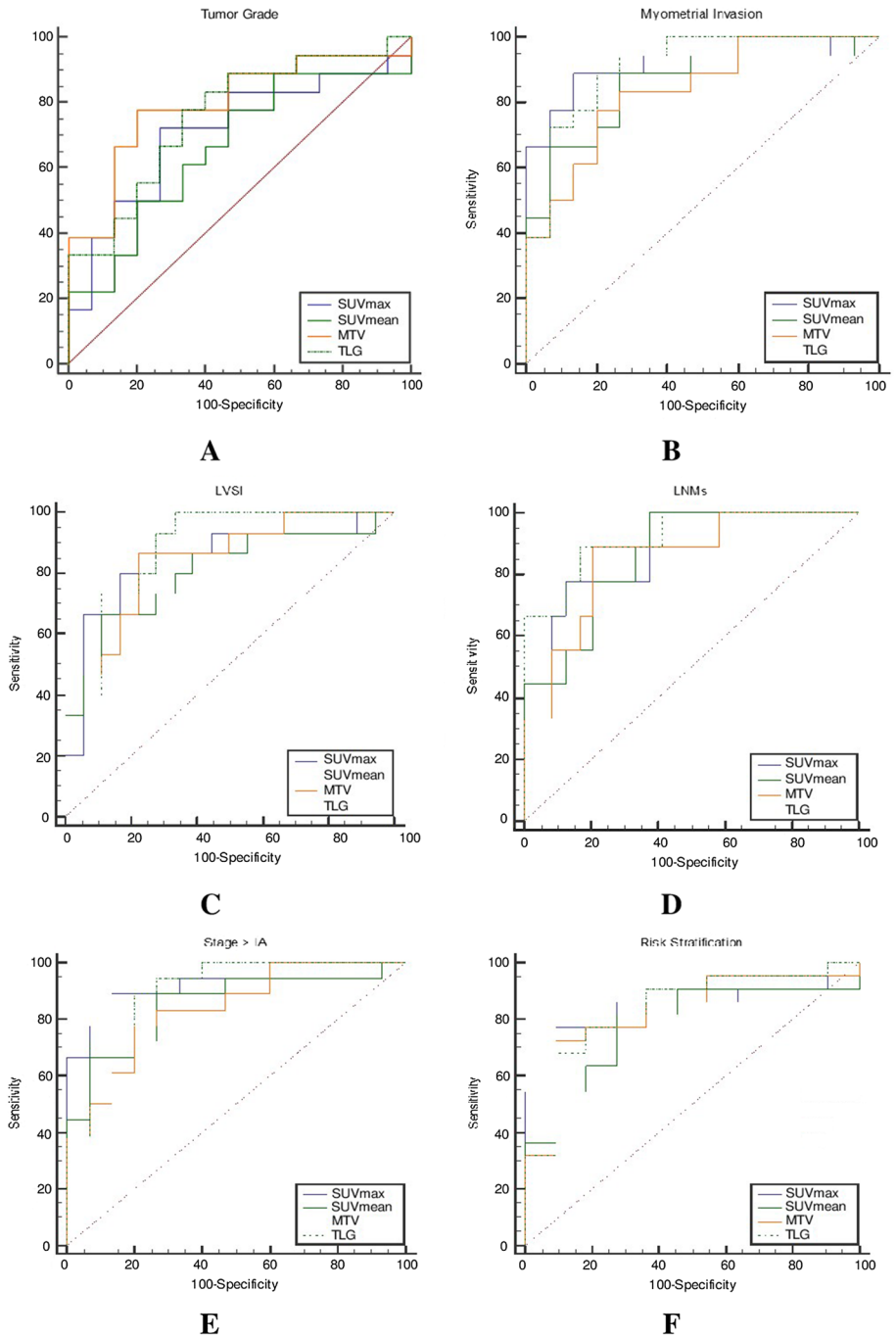

Fig. 4 ROC curves for various tumor quantifications for prediction of Tumor grade (**A**), MI (**B**), LVSI (**C**), LNMs (**D**), stage > IA (**E**), and risk stratification (**F**) in patients with endometrial carcinoma

with absent pelvic LNMs [37]. Also, the retrospective nature of the study hindered the possibility of node-by-node or region-by-region evaluation, which would have provided valuable information, and the study of the prognostic value of ^{18}F-FDG PET/CT in EC and the

study of disease survival and recurrence due to unavailability of data.

Conclusion

^{18}F-FDG PET/CT has high accuracy in risk stratification of EC patients, TLG and SUV_{max} showed highest AUC for detection of MI > 50% and risk stratification with highest sensitivity and specificity, while TLG showed the highest AUC for detection of LVSI and LNMs with highest sensitivity and specificity. Thus, preoperative ^{18}F-FDG PET/CT can aid in omitting surgical lymphadenectomy in low-risk early stage EC, sparing these women the surgical risk and morbidity. Still, larger prospective studies are needed to validate these results.

Abbreviations

EC: Endometrial cancer; FIGO: International Federation of Gynecology and Obstetrics; LVSI: Lymphovascular space invasion; LNMs: Lymph node metastasis; ^{18}F-FDG PET/CT: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography; FEC PET/CT: Fluoro-ethyl-choline positron emission tomography/computed tomography; SUV_{max}: Maximum standardized uptake value; PET: Positron emission tomography; TLG: Total lesion glycolysis; MTV: Metabolic tumor volume; TAH + BSO: Hysterectomy and bilateral salpingo-oophorectomy; VOIs: Volume of interests; SUV_{mean}: Mean standardized uptake value; MI: Myometrial invasion; AUC: Area under the curve; CT: Computed tomography; MRI: Magnetic resonance imaging; DW-MRI: Diffusion-Weighted magnetic resonance imaging; FES-PET: Female EStrogen- positron emission tomography/computed tomography.

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Authors' contributions

MA helped design the study, supervised the undertaking of the trial, undertook the analysis, edited the final manuscript and shared in funding the study. MS helped design the study, supervised the undertaking of the trial, undertook the analysis, wrote the first draft of the manuscript and shared in funding the study. MA helped design the study, shared in undertaking of the trial, assisted with data analysis, gave editorial feedback to versions of the manuscript and shared in funding the study. EN shared in undertaking of the trial, provided advice during the running of the trial, collected data for analysis, gave editorial feedback to versions of the manuscript, and shared in funding the study. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee for Human and Animal Research at the Faculty of Medicine, Helwan University (REC-FMHU) with approval number 35-2021.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Radiology, Helwan University, Cairo 16646, Egypt. [2]Department of Obstetrics and Gynecology, Ain Shams University, Cairo, Egypt.

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