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Title page

Evaluation of Dual Time Point Imaging ^{18}F-FDG PET/CT for Lymph Node Staging in Vulvar Cancer

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Abstract

This study aimed to assess the value of dual time point (DTP) ^{18}F-FDG-PET/CT in the prediction of lymph node (LN) status in patients with invasive vulvar cancer (VC) scheduled for inguinofemoral lymph node dissection (IFLD).

Methods: From April 2013 to July 2015, all consecutive patients with VC scheduled for IFLD were prospectively enrolled. All patients underwent a preoperative whole-body ^{18}F-FDG-PET/CT scan at 1-hour (standard exam) and an additional scan from T11 to the groins at 3-hour (delayed exam) after ^{18}F-FDG injection. On both scans each groin was visually scored 0 or 1 concerning ^{18}F-FDG LN uptake relative to background. Semi-quantitative analysis included maximum standardized uptake value (SUV_{max}), and the corresponding retention index of SUV_{max} (RI_{max}), measured on both scans. The optimal cut-off value of these parameters was defined using a receiver operating characteristic (ROC) analysis. Histopathology was the standard of reference.

Results: Thirty three patients were included with a total of 57 groins dissected and histologically evaluated.

At histopathology 21 of 57 (37%) groins contained metastatic LNs. Concerning visual score, sensitivity, specificity, negative predictive value, positive predictive value and accuracy were 95.2%, 75%, 96.4%, 69%, 82.5% on standard scan and 95.2%, 77.8%, 96.6%, 71.4%, 84.2% on delayed scan, respectively. At ROC analysis, sensitivity and specificity were 95.2% and 77.8% on standard and delayed ^{18}F-FDG-PET/CT for a SUV_{max} cut-off >1.32 and >1.88, respectively and 95.2% and 80% for a RI_{max} cut-off > 0.

Conclusion: Standard ^{18}F-FDG-PET/CT is an effective preoperative imaging for the prediction of LN status in VC, allowing to predict pathologically negative groins and thus to select the patients suitable for minimally invasive surgery. Delayed ^{18}F-FDG PET/CT did not improve the specificity and the positive predictive value in our series. Larger studies are needed for a further validation.

Keywords

Vulvar cancer; ^{18}F-FDG; Dual time point PET/CT; Groin lymph node metastasis; FDG-retention index.

Introduction

Invasive vulvar carcinoma (VC) is an uncommon gynecological tumor, with an incidence of 2.4 new cases/100000 women per year *(1)*. The pattern of dissemination of VC is mainly lymphatic, with prevalent involvement of the groins, while hematogenous spread is rare *(2)*. Thus, the most important prognostic factor is the presence of metastatic lymph nodes (LNs) in the groins *(3)*. In fact, the 5-year survival rate decreases from 94.7%, when locoregional LNs are negative, to 62% when they contain metastases *(4)*. Therefore, an accurate preoperative LN staging is critical in order to customize the extent of groin surgery and to select patients suitable for minimally invasive procedure, thus avoiding unnecessary inguinofemoral lymph node dissection (IFLD), which is associated with a high morbidity and worse quality of life. In recent years, positron emission tomography/computed tomography (PET/CT) using the glucose analogue ^{18}F-fluorodeoxyglucose (FDG) has been used more and more for the evaluation of LNs status in gynecologic malignancies *(5)*, but only recently it has been recommended in VC *(6)*. However, because of low incidence of VC there are very few studies in small series on the diagnostic accuracy of ^{18}F-FDG PET/CT in detection of metastatic LNs in VC; the reported sensitivity ranges from 67% to 92% and the specificity from 91% to 95% per groin *(7-8)*. Recently, dual time-point (DTP) or dual-phase ^{18}F-FDG-PET/CT has been suggested as a means for detecting metastatic LN in several gynecological cancers *(9)*, but its usefulness in VC has not yet been evaluated. In particular, DTP ^{18}F-FDG-PET/CT requires two acquisitions after a single injection of the radiotracer, i.e. standard images (1 hour after injection) followed by delayed images (3 hours after injection) of the body region under assessment. The rationale is that malignant cells, compared to benign cells, usually show increased ^{18}F-FDG-uptake retention on delayed time point imaging due to the high glycolysis activity *(10)*.

The aim of this prospective study was to investigate the value of dual time point ^{18}F-FDG-PET/CT for the assessment of LN status in patients with VC scheduled for IFLD.

Materials and methods

Patients and study design

The Institutional Review Board approved this longitudinal prospective monocenter study and all patients signed a written informed consent. Between April 2013 to July 2015, all consecutive patients with primary histologically proven invasive VC (i.e. depth of stromal invasion >1 mm) referred to the Division of

Gynecologic Oncology at A. Gemelli Hospital were evaluated with clinical exam and conventional imaging *(6)*. The surgical plan was traced on the base of the disease site and extent, according to international recommendations *(6, 11)*. All patients scheduled for IFLD were considered eligible for the study and underwent preoperative ^{18}F-FDG PET/CT scan with DTP acquisition.

Patients with the following characteristics were excluded: *(a)* prior inguinal surgery dissection; *(b)* previous chemotherapy and/or loco-regional radiotherapy within the last 5 years; *(c)* contraindication to the surgery due to age or comorbidities; *(d)* pregnancy or breast-feeding; *(e)* blood glucose > 200 mg/dl; *(f)* surgery performed more than 20 days after ^{18}F-FDG PET/CT. Pathological results were used as the standard of reference to assess the presence of LN metastases.

^{18}F-FDG PET/CT acquisition

^{18}F-FDG PET/CT scans were performed according to the standard procedure of our center *(12)*. All patients fasted for at least 6 hours, and the glucose blood levels were less than 190 mg/dl before the ^{18}F-FDG injection. According to body weight, 118-303 MBq of ^{18}F-FDG were intravenously administrated. Before ^{18}F-FDG PET/CT acquisition, patients were hydrated with 500 ml of saline solution by intravenous administration. No oral or intravenous contrast agents were used. All ^{18}F-FDG PET/CT scans were acquired, using the same PET scanner (Gemini GXL Philips, Cleveland OH, or Biograph mCT Siemens Medical Solutions USA, Inc.) for each patient at two time points: 60±10 min (standard ^{18}F-FDG-PET/CT scan) and 180±10min (delayed ^{18}F-FDG-PET/CT scan) after ^{18}F-FDG injection. Standard ^{18}F-FDG PET/CT scans were performed from the skull base to mid-thigh. Delayed ^{18}F-FDG-PET/CT scans were obtained from the 11th vertebra (T11) to the inguinal region. Before the ^{18}F-FDG PET/CT acquisition, low-dose CT images (using a voltage of 110-120 kVp and tube current of 20-40mAs, with the patient breathing normally) were acquired for anatomical reference and attenuation correction. PET images were then acquired in a 3-dimensional mode, with 7-8 acquisition beds (of approximately 2.5 minutes each) on standard scans and 1-2 acquisition beds (of approximately 4 minutes each) on delayed scans. Matched CT and PET images were reconstructed with a field of view (FOV) of 50 cm. The line-of-response row-action maximum likelihood algorithm (LOR-RAMLA) was used for reconstruction with 144x144 or 256x256 matrix. Attenuation-corrected PET images were reviewed in transverse, sagittal and coronal planes. PET data were also displayed in a rotating maximum-intensity projection (MIP images). To

evaluate the images, PET and CT datasets were transferred to an independent computer workstation by DICOM (Digital Imaging and Communications in Medicine) transfer.

^{18}F-FDG PET/CT image analysis

All ^{18}F-FDG PET/CT images were interpreted and visually scored by two nuclear medicine physicians (A.C. and V.R) in consensus.

Qualitative analysis:

Qualitative analysis was performed both on standard and delayed PET/CT, and the degree of ^{18}F-FDG uptake in the LNs was classified as follows: 1) normal: uptake lower than or equal to background (score 0); 2) abnormal: uptake higher than background (score 1). The gluteus muscle tissue was used to estimate background activity. The size of the largest LN per groin (short axis) was detected on transaxial CT images of PET/CT.

Semi-quantitative analysis:

A spherical volume of interest (VOI) was placed over the inguinal LN with the highest glucose uptake on the transaxial PET images, for each groin, using an isocontour threshold of 40% method (Syngo.via, MM oncology VA30, Siemens Medical Solution) based on the standardized uptake value (SUV) *(13-14)*. SUV normalization to body weight and to injected dose was automatically assessed using the following equation:

$$SUV = \frac{\text{Tissue radioactivity concentration (MBq/ml)}}{\text{Injected dose (MBq)/Body weight (g)}}$$

The maximum standardized uptake value (SUV_{max}) within the VOI was measured on standard (SUV_{max} standard) and delayed (SUV_{max} delayed) PET images. VOI were carefully placed in exactly the same anatomical site, both on standard and delayed PET/CT scans. When several hypermetabolic lymph nodes per groin were seen on PET/CT images, the highest SUV_{max} was considered the representative value of that groin. When inguinal LNs did not show a significant FDG uptake, an arbitrary value of 1 for SUV_{max} was adopted.

Furthermore, we calculated the retention index of SUV_{max} (RI_{max}) using the following formula:

$$RImax = (SUV_{max}\,\text{delayed} - SUV_{max}\,\text{standard}) \times 100 / SUV_{max}\,\text{standard}$$

The ^{18}F-FDG PET/CT findings and histopathological results for the inguinal LNs were compared on a groin-by groin analysis.

Statistical analysis

Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy of standard and delayed PET/CT were calculated considering qualitative analysis. The receiver operating characteristic (ROC) analysis was used to determine the optimal cut-off values of SUV_{max} standard, SUV_{max} delayed and RI_{max}, for differentiating benign and malignant inguinal LNs. Differences in sensitivity, specificity and accuracy between standard and delayed PET/CT were determined using the chi-square or Fisher test. A p value of <0.05 was considered statistically significant. Statistical analysis was performed using MedCalc Statistical Software version 15.11.4.

Results

A total of 60 patients with primary VC were referred to the Division of Gynaecologic Oncology during the study period. Among these, 33 patients fulfilled the inclusion criteria (Fig. 1). Patients' characteristics are reported in Table 1. All patients had a squamous cell carcinoma (SCC) of the vulva. The time interval between the ^{18}F-FDG injection and PET/CT acquisition was 60±11minutes for standard PET/CT and 162±24 minutes for delayed PET/CT. Most PET/CT studies (22/33 patients, 67%) were acquired using GXL scan. The time interval between ^{18}F-FDG PET/CT study and surgery was 18±11 days. A total of 57 groins (24 bilateral, 9 unilateral) in 33 patients were dissected. At pathologic examination, 21 groins contained metastatic LNs and 36 groins were negative for metastases.

The mean size of all measured LNs was 9.4 ± 3.6 mm (median 8 mm; range 5-21 mm). The mean size of metastatic LNs was 11.8 ± 4.6 mm (median 10 mm; range 6-21 mm), while the mean size of non-metastatic LNs was 8.1 ± 1.7 mm (median 8 mm; range 5-12 mm). Significant difference was found between the size of metastatic and non-metastatic LNs measured on low-dose CT ($p< 0.002$).

Qualitative analysis

Standard ^{18}F-FDG PET/CT was positive in 29/57 groins and negative in 28/57 groins. Visual score results are reported in Table 2. Out of the 21 groins with metastatic LNs at pathological exam, standard ^{18}F-FDG PET/CT showed FDG uptake above the background (score 1) in 20 groins and under background (score 0) in one groin. Of the 36 groins with no metastatic LNs at pathological exam, standard ^{18}F-FDG PET/CT was negative in 27 groins and positive in 9 groins. On a groin-by-groin basis, standard ^{18}F-FDG PET/CT yielded a sensitivity of

95.2% (95% CI: 85.2-99.8), specificity of 75% (95% CI: 61.5-85.1), NPV of 96.4% (95% CI: 86.7-99.4), PPV of 69% (95% CI: 55.2-80.2), and accuracy of 82.5% (95% CI: 72.7-92.3) (Table 3).

Delayed ^{18}F-FDG PET/CT was positive in 28/57 groins and negative in 29/57 groins (Table 2). Out of the 21 groins with metastatic LNs at pathological exam, delayed ^{18}F-FDG PET/CT showed abnormal FDG uptake in 20 groins, with a false negative (FN) result occurring in one groin (same groin that was FN at standard imaging). Out of the 36 groins with no metastatic LNs at pathological exam, delayed ^{18}F-FDG PET/CT was true negative (TN) in 28 groins and false positive (FP) (Fig. 2) in 8 groins. On a groin-by-groin basis, delayed ^{18}F-FDG PET/CT yielded a sensitivity of 95.2% (95% CI: 85.2-98.8), specificity of 77.8% (95% CI: 64.5-87.3), NPV of 96.6%, (95% CI: 86.9-99.4), PPV of 71.4% (95% CI:57.7-82.2), and accuracy of 84.2% (95% CI: 74.8-93.6) (Table 3). No significant differences in sensitivity, specificity and accuracy between standard and delayed PET/CT were found.

Semi-quantitative analysis

Mean and median values of SUV_{max} standard, SUV_{max} delayed and RI_{max} for metastatic groins (group 1) and non-metastatic groins (group 0) are shown in Table 4. SUV_{max} standard, SUV_{max} delayed and RI_{max} were significantly higher for group 1 than for group 0 ($p < 0.0001$) (Fig. 3). The area under the curve (AUC) was larger in SUV_{max} standard, which was 0.919 (p<0,0001; 95% CI=81.5-97.5%) compared with 0.899 in SUV_{max} delayed (p<0.0001; 95% CI= 79-96.3%) and 0.833 in RI_{max} (p<0,0001; 95% CI= 71-92%). There was no significant difference between the AUCs in SUV_{max} standard and SUV_{max} delayed (p=0.10) not between SUV_{max} delayed and RI_{max} (p=0.055), whereas a significant difference was found between SUV_{max} standard and RI_{max} (p=0.04). At ROC analysis, the optimal cut-off values of SUV_{max} standard, SUV_{max} delayed and RI_{max} were >1.32, >1.88 and >0, respectively. Using these cut-off values, the sensitivity and specificity were 95.2% and 77.8%, for both SUV_{max} standard and SUV_{max} delayed and 95.2% and 80% for RI_{max}, respectively (Fig. 4).

Discussion

In this prospective study we evaluated the value of dual time point ^{18}F-FDG-PET/CT for LN staging. We chose to include only patients candidates for lymphadenectomy, excluding those addressed to the sentinel node biopsy (SNB), to ensure that the reference standard (histopathological results), could include all the inguinal LNs examined preoperatively by ^{18}F FDG PET/CT. Moreover, given the rapid progression of VC, we decided to

include only those patients for whom a maximum 3-week interval between the pre-operative study and surgery was compiled. Based on criteria that considered metastatic LNs if they have ^{18}F-FDG uptake higher than background, standard ^{18}F-FDG-PET/CT showed high sensitivity (95.2%) and relatively low specificity (75%) in detecting metastatic groins. In particular, we found nine FP groins and one FN groin, the latter due to a metastatic LN of 8 mm in diameter. In nine FP groins, pathological examination revealed no LN metastases in seven groins and inflammatory LNs in two groins. Concerning the FP results, it is widely known in the literature that inflammatory cells and activated macrophages represent a common cause of increased FDG uptake, as occurring in inguinal reactive LNs following vulvar biopsy or shaving *(15)*. Conversely, FN results are most likely be associated to PET undetected micro-metastatic foci in not enlarged nodes as well as to extensive necrosis within metastatic LNs with subsequent loss of ^{18}F-FDG uptake *(7)*. Previous PET or PET/CT studies in the literature showed a range of sensitivity (from 50 to 100%) and specificity (from 91 to 100%) for detecting metastatic involvement of inguinofemoral LNs in VC patients *(7-8, 16-17)*. In those studies, no cut-off values of SUV_{max} were determined for metastatic LNs. In our study, a SUV_{max} value >1.32 was found to be the optimal cut-off point on standard PET/CT to provide a similar sensitivity as the one obtained from visual analysis (95.2%) but accompanied with a slightly better (77.8% vs 75%) although not statistically significant (p=0.81) specificity, in detecting metastatic groins. As already mentioned, increased ^{18}F-FDG uptake is not specific for neoplastic involvement, since it may also be reactive to inflammation or infection *(18)*. Based on our data, standard ^{18}F-FDG-PET/CT showed a high NPV (96.4%) together with a low PPV (69%) in detecting metastatic groins. Therefore, a negative ^{18}F-FDG-PET/CT scan is highly predictive in excluding groin metastases and could potentially be used to select patients candidate for a minimal groin surgery. On the contrary, a positive ^{18}F-FDG-PET/CT scan is not highly predictive for groin metastases and needs to be interpreted with caution. Based on our data, significant difference was found between the size of metastatic and non-metastatic LNs measured on low-dose CT. However, further studies are needed to investigate whether the combination of PET and CT criteria can better differentiate between metastatic and non-metastatic LNs.

The rationale of DTP ^{18}F-FDG-PET/CT is that ^{18}F-FDG uptake usually increases in malignant lesions for several hours after intravenous injection, whereas benign lesions and inflammatory cells show stable or decreasing ^{18}F-FDG uptake over time *(19-20)*. Such different behavior on delayed PET/CT is believed to be due

to increased cell proliferation rate, enhanced expression of hexokinase type-II and glucose transporter-1 in malignant lesions as well as to continued clearance of background activity, thus resulting in images with improved contrast to noise ratio *(10)*. Up till now, no studies have yet been performed using qualitative and semi-quantitative parameters on both standard and delayed ^{18}F-FDG-PET/CT to assess LN status in VC. To our knowledge, only Lin et al. performed delayed PET scan in VC staging, showing that it did not modify the qualitative analysis of a standard scan. However, they did not apply semi-quantitative evaluation and the sample size in their study was limited (11 patients) (8). According to our qualitative analysis, delayed ^{18}F-FDG-PET/CT showed similar sensitivity and NPV (95.2% and 96.5%) as standard scan with relatively higher specificity (77.8% vs 71.4%) and PPV (75% vs 69%) not reaching statistical significance (p=0.7) in detecting metastatic groins. In particular, in the patient with FN groin no ^{18}F-FDG uptake, even on the delayed scan was seen, most likely due to the limited extent of the metastatic involvement (with micro-metastases on histopathology). Moreover, on delayed PET/CT we found 8 FP groins compared to 9 FP groins on standard PET/CT. This finding suggests that the behavior of inflammatory lesions as concerning FDG uptake is not always predictable, and that delayed PET/CT appears to not reduce the rate of FP results. According to other studies, inflammatory lesions as well as infection may induce higher FDG uptake on delayed scan mimicking malignant lesions *(21-24)*. In the literature, the use of DTP ^{18}F-FDG-PET/CT in gynecological malignancies is still a subject of discussion and in our study, the delayed ^{8}F-FDG-PET/CT also was not superior to standard images in detecting LN disease. This is in accordance with the results reported in a recent meta-analysis by Shen et al. *(21)*, which concluded that DTP ^{8}F-FDG-PET/CT had higher sensitivity, but lower specificity in detecting LNs metastases on a per-patient analysis, and performed only slightly better than standard PET/CT on a per-lesion basis. On the contrary, in a retrospective study on cervical, endometrial, and ovarian cancer patients, Nogami et al. reported that DTP ^{8}F-FDG-PET/CT only significantly improved the specificity for detection of LN metastases, but also concluded that DTP scan had an unsatisfactory impact on the overall diagnostic efficacy for LN metastasis *(9)*. Regarding the semi-quantitative analysis, a SUV_{max} value >1.88 was considered the optimal cut-off point on delayed PET/CT providing a same sensitivity and specificity of standard ^{8}F-FDG-PET/CT images. Concerning the retention index (RI), prior studies reported that the RI might improve the accuracy of DTP ^{8}F-FDG-PET/CT in gynecological cancer for detecting LN metastases (*9, 25*). In the present study, we found that a RI>0% was the optimal cut-off

point for nodal evaluation since it improved the specificity (80% for RI on delayed exam compared to 77.8% for SUV_{max} on standard PET/CT p=0.8) but did not improve the sensitivity (95.2% in both cases).

Our study suffered some limitations: first, the population was relatively small, but in accordance with the incidence of VC (2.4 /100000 inhabitants per year) *(1)*; second, the patients were scanned on two different scanners in our department and this could have minimally affected the SUV homogeneity *(26-27)*; however, only 11 patients were scanned on a different scanner; third, the cut-off value of SUV_{max} and RI in this study was based on the data collected at our institute alone, and the absolute value of SUV_{max} might vary somewhat according to different imaging systems used at other institutions. However, this study has yet several strengths: first, it is the first prospective study to evaluate the comparison between standard and delayed scan using qualitative and semi-quantitative analysis; second, it evaluates only patients who underwent surgery shortly after PET/CT, in order to compare PET/CT results with histopathological findings.

Conclusion

In the light of our results, standard ^{18}F-FDG-PET/CT has high sensitivity and negative predictive value in detecting groin lymph node metastases in VC patients. This confirms that standard ^{18}F-FDG-PET/CT represents an effective preoperative imaging for LN staging in VC, allowing to better plan groin surgical procedures and selecting patients potentially suitable for minimally invasive surgery. However, delayed PET/CT has not significantly been able to improve the specificity and the positive predict value in our study. Larger studies are needed to further validate our results.

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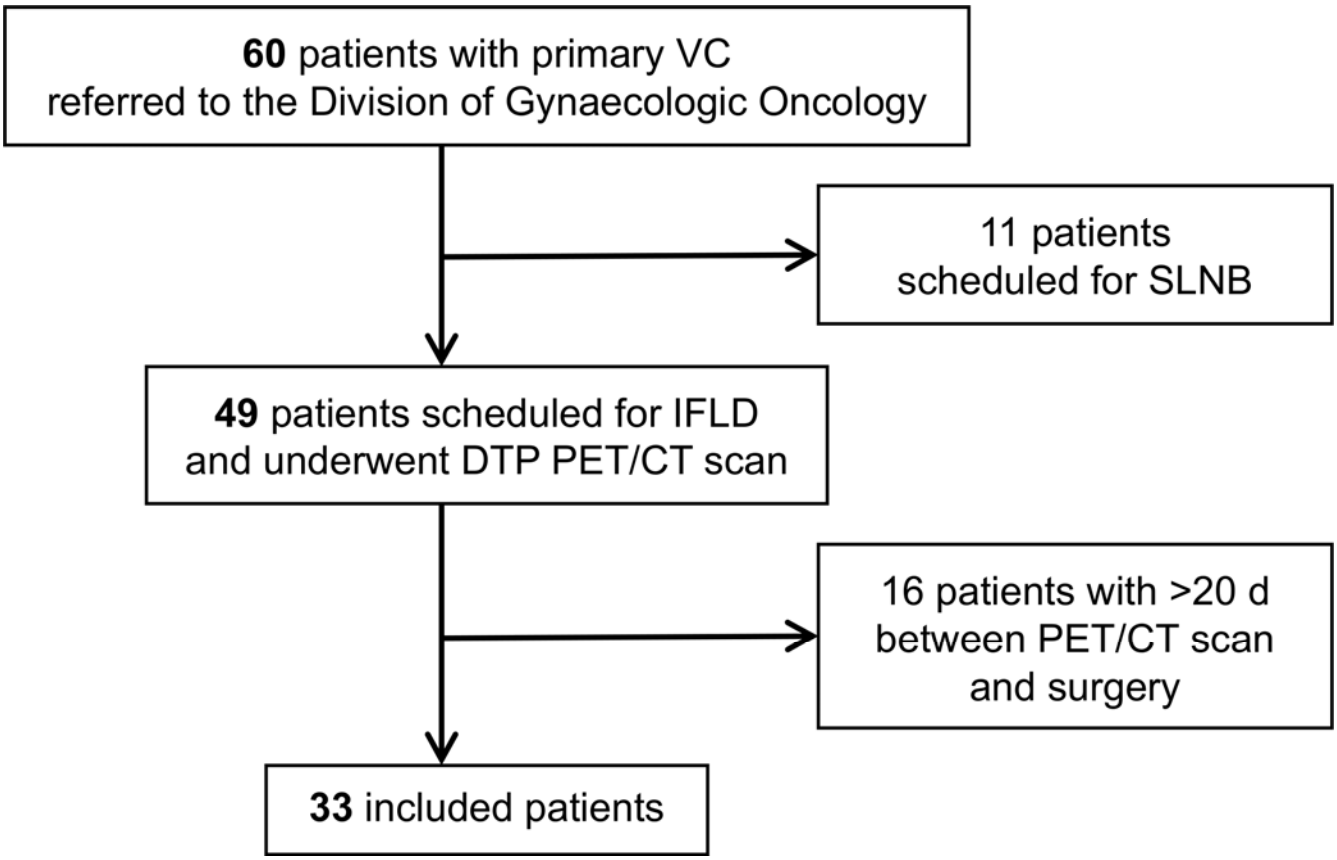
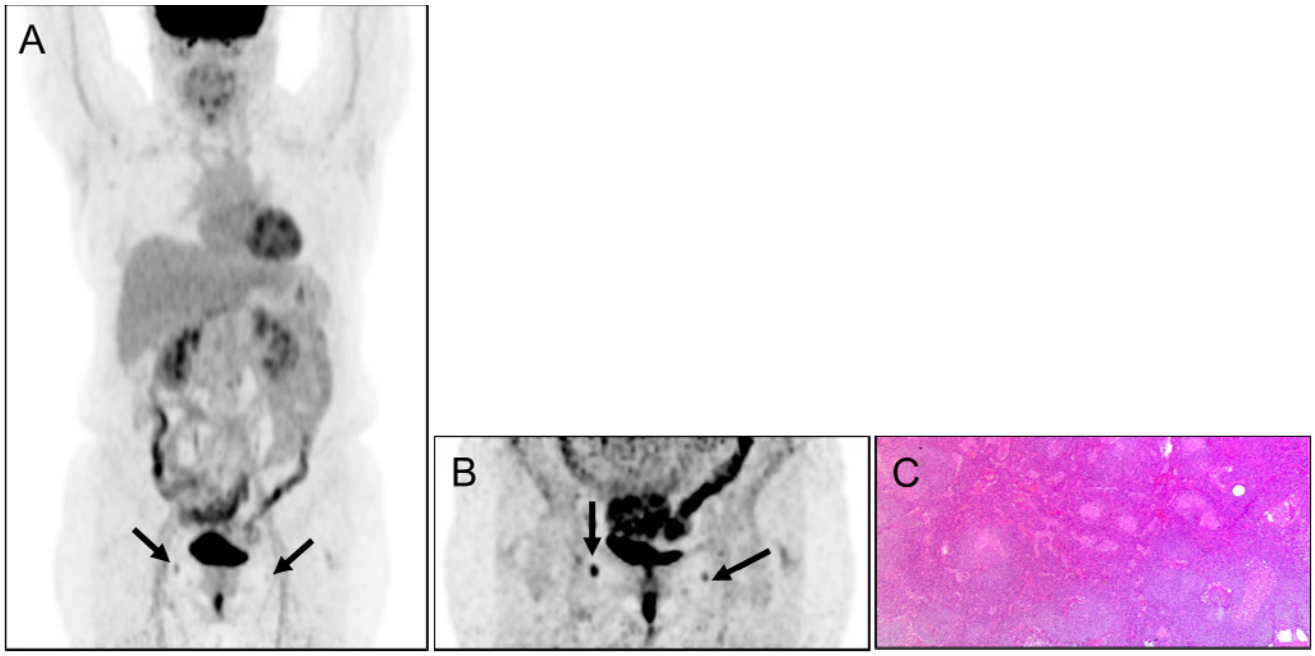
FIGURE 1

Flow chart of patients' selection



Legend: VC = vulvar cancer; SLNB = sentinel lymph node biopsy; IFLD = inguinofemoral lymph node dissection; DTP = dual time point; PET/CT = positron emission tomography/computerized tomography

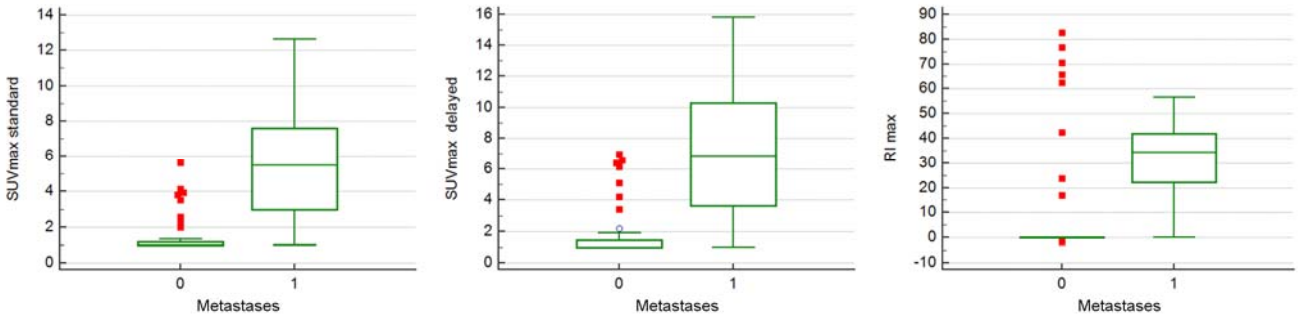
FIGURE 2



A 60 years old woman with midline tumour. (**A**) Maximum-intensity projection (MIP) of standard ^{18}F-FDG-PET/CT showing focus uptake in the right groin (SUV_{max} 3.5) as well as in the left groin (SUV_{max} 2) (arrows). (**B**) MIP of delayed scan showing increase of the focal uptake in the right groin (SUV_{max} 6.39) and in the left groin (SUV_{max} 3.41) (arrows). (**C**) Pathological exam showed no metastatic LNs in both groins.

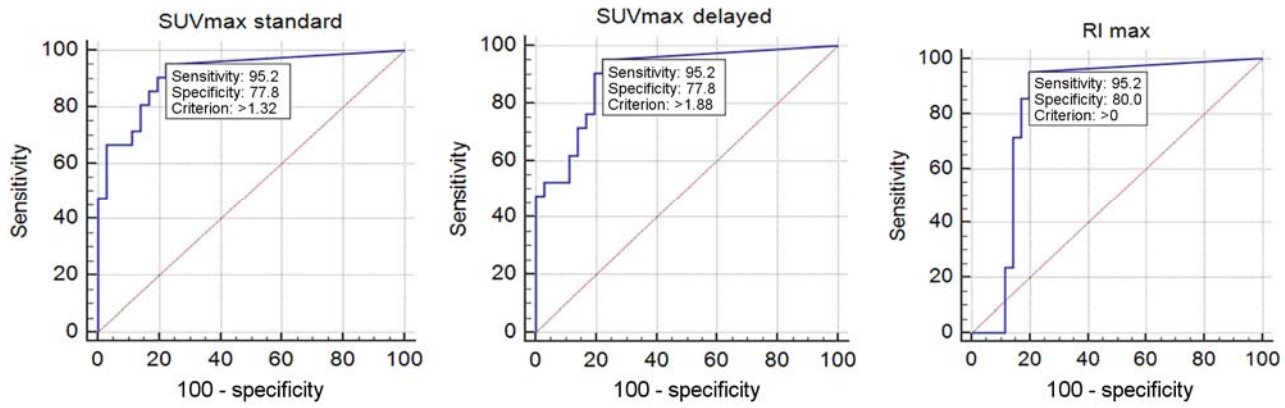
FIGURE 3

Box plots showing distribution of SUV_{max} standard, SUV_{max} delayed and RI_{max} for metastatic and non-metastatic groins.



Legend: 0 = absence of metastases; 1= presence of metastases.

FIGURE 4



The ROC curves of SUV_{max} on standard scan, delayed scan and Retention Index (RI).

TABLE 1

Title: Patients' characteristics

Number of Patients	33	
Age		
mean ±SD	69±13.4	
BMI		
mean (range)	24 (21-42)	
Tumour site		
Central	16	48%
Monolateral	11	34%
Multifocal	6	18%
Vulvar surgical procedure		
Partial vulvectomy	11	33%
Radical vulvectomy	22	67%
IFLD		
Monolateral dissection	9	27%
Bilateral dissection	24	73%
Tumour size		
< 4 cm	25	76%
≥ 4 cm	8	24%
Grading		
G1	4	12%
G2	24	73%
G3	5	15%
Figo Stage [a]		
Ib	15	45.5%
II	3	9%
III	15	45.5%

Legend: SD= standard deviation; BMI = body mass index; IFLD = inguinofemoral lymph node dissection; a = 2009 revised FIGO staging system.

TABLE 2

Title: Qualitative (visual score) results of standard ^{18}F-FDG PET/CT and delayed ^{18}F-FDG PET/CT

		Pathological evaluation		
	Visual score	**LN metastasis**	**No LN metastasis**	**Total**
Standard PET/CT	0	1	27	28
	1	20	9	29
	Total	***21***	***36***	***57***
Delayed PET/CT	0	1	28	29
	1	20	8	28
	Total	***21***	***36***	***57***

Legend: score 0 = uptake ≤ than background; score 1 = uptake > than background; LN = lymph node.

TABLE 3

Title: Qualitative analysis

		Pathological evaluation							
		LN metastasis	**No LN metastasis**	**Total**	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**Accuracy (95% CI)**	**PPV (95% CI)**	**NPV (95% CI)**
	Standard PET/CT								
Per groin	pos	20	9	29	**95.2%** (85.2-99.8)	**75%** (61.5-85.1)	**82.5%** (72.7-92.3)	**69%** (55.2-80.2)	**96.4%** (86.7-99.4)
	neg	1	27	28					
	Total	21	36	**57**					
	Delayed PET/CT								
Per groin	pos	20	8	28	**95.2%** (85.2-99.8)	**77.8%** (64.5-87.3)	**84.2%** (74.8-93.6)	**71.4%** (57.7-82.2)	**96.6%** (86.9-99.4)
	neg	1	28	29					
	Total	21	36	**57**					

Legend: LN= lymph node; 95% CI= 95% confidence interval; pos= positive; neg= negative; PPV=positive predictive value; NPV= negative predictive value.

TABLE 4

Title: Mean and Median of SUV_{max} value on standard scan, on delayed scan and RI for metastatic and non-metastatic group.

	SUVmax standard	***p***	**SUVmax delayed**	**RI (%)**
Metastatic LNs (group 1)		**0.11**		
Mean ± SD	**5.43**±3		**7.17**±3.9	**31.42**±15.61
Median (range)	**5.51** (1-12.62)		**6.88** (1-15.82)	**34.39** (0-56.49)
Non-metastatic LNs (group 0)				
Mean ± SD	**1.56**±1.2	**0.3**	**1.94**±1.9	**12.21**±25.75
Median (range)	**1** (1-5.64)		**1** (1-6.98)	**0** (-1.79-82.57)
p	**<0.0001**		**<0.0001**	**0.003**

Legend: LNs = lymph nodes; SUV_{max}= maximum standardized uptake value; RI=retention index; SD= standard deviation.