Int J Colorectal Dis (2011) 26:201–210
DOI 10.1007/s00384-010-1080-9

ORIGINAL ARTICLE

Impact of FDG PET/CT in the staging and the follow-up of anal carcinoma

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Accepted: 21 October 2010 / Published online: 9 November 2010

Abstract
Purpose The purpose of the study was to assess the diagnostic performance of positron emission tomography/computed tomography and fluorodeoxyglucose (18F) (FDG PET/CT) for the staging and the follow-up of anal carcinoma, and to evaluate the impact of FDG PET/CT on patient management.
Materials and methods Patients with anal carcinoma were referred to our department from October 2004 until July 2008. The diagnostic performance was evaluated on a per-examination basis and on a per-site basis, together with impact of PET/CT on patient management. The standard of truth was histology when available and, in all cases, follow-up data during at least 6 months.
Results Fifty-eight FDG PET/CT performed in 44 patients were analysed—22 for initial staging and 36 during follow-up. The detection rate of non-excised tumours on initial examination was 93%. During post-treatment follow-up, FDG PET/CT had, on a per-examination basis, sensitivity for the detection of persistent or recurrent disease of 93% and specificity of 81%, and on a per-site basis, 86% and 97%, respectively. Its negative predictive value was 94% on a per-examination basis and 98% on a per-site basis. FDG PET/CT had an impact on management in nine patients out of 44 (20%), which was relevant in eight of them (89%).
Conclusion FDG PET/CT is an accurate imaging modality in anal cancer. It has an interesting added value during post-treatment follow-up, especially when persistence or recurrence of disease is suspected. Further studies are needed to evaluate whether surveillance by means of FDG PET/CT might have a positive impact on overall survival.

Keywords Anal carcinoma · FDG · PET/CT · Diagnostic performance · Impact on management

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Introduction

Anal canal carcinoma is relatively rare, but its incidence increased over the last decades [1, 2]. Known risk factors are HIV and human papillomavirus infections [3, 4]. Staging is based on clinical examination and endorectal ultrasonography (EUS), determining the tumour depth and invasion of perirectal lymph nodes (LN) [5]. Computed tomography (CT) and magnetic resonance imaging (MRI) can provide additional information about inguinal and iliac lymph node involvement or presence of distant visceral metastasis [6, 7]. Sentinel lymph node procedure could permit a better N staging [8]

Initial treatment is based on chemoradiotherapy or radiotherapy alone [4]. Radiotherapy treatment fields include pelvic LN, but prophylactic radiotherapy on inguinal LN remains discussed, particularly in early tumour stage [9, 10]. Despite good results obtained with this treatment, persistent or recurrent disease is observed in up to 30% of patients, and salvage abdominoperineal resection can then be effective [11, 12]. Follow-up is classically performed by physical examination and imaging modalities such as EUS, CT and sometimes MRI [7, 13]. But, all these modalities encounter difficulties in differentiating local recurrences from changes induced by radiotherapy. The definitive proof of persistent disease or recurrence is based on biopsy, which can be deleterious on irradiated tissue. Hybrid positron emission tomography/computed tomography and fluorodeoxyglucose (18F) (FDG PET/CT) is now widely used in the management of patients with cancers, for staging, restaging and treatment follow-up [14]. Few studies have investigated its impact on management of patients suffering from anal cancer. Most studies addressed its role for staging, radiotherapy treatment planning and immediate post-therapy response [15–20].

This study aimed to evaluate:

- The diagnostic performance of FDG PET/CT for staging and monitoring anal carcinoma;
- The impact of FDG PET/CT in anal carcinoma, by the rate of induced changes in patients' management and to confirm the adequacy of the decisions, thanks to a long-lasting follow-up.

Materials and methods

Patient population

From October 2004 until July 2008, we included patients referred to FDG PET/CT for evaluation of an anal carcinoma. Criteria of inclusion were as follows: no current chemotherapy or radiotherapy at the time of positron emission tomography/computed tomography (PET/CT) and a follow-up of at least 6 months available. Since fluorodeoxyglucose (18F) (FDG) is registered in France for diagnosis in oncology, patients gave their consent orally. Similarly, with the procedure used by Californian teams for the determination of the rate of change in patient management [21], the clinician prospectively indicated on the inclusion questionnaire which patient management was scheduled before PET/CT.

Image acquisition and reconstruction

A Philips Gemini Dual with GSO crystals PET/CT camera was used. Well-hydrated patients fasted for 6 h before undergoing PET/CT. An activity of 5 MBq/kg of body weight of FDG was administered intravenously 1 h before imaging. CT images (5-mm slices) were obtained from the skull base to the mid-thigh at 120 kVp and 30 mAs, without injection of intravenous contrast medium. Next, positron emission tomography (PET) acquisition was performed over the same anatomic extent, with imaging time of 3 min per bed position. The CT transmission map was used for attenuation correction, and the PET whole-body images were reconstructed using a 128×128 matrix, by means of the 3D RAMLA iterative algorithm.

Image interpretation

The original reports of PET/CT examinations formed the bases for data analysis. PET/CT images were interpreted on site by an experienced nuclear physician, with knowledge of the patient's clinical history and of the results of previous imaging studies, according to the standard procedure in our centre, separately for PET (attenuation-corrected and non-corrected images), for CT and for fused images. Further blind reading would have been of no use and even misleading, since the management decisions were taken by the referring physician in view of this on-site reading.

Any abnormal focus of increased FDG uptake recorded in the report was classified as probably malignant or benign, based on its intensity of uptake, shape and the patient's clinical history (infection, inflammation...) and was attributed to one of eight “sites”. Sites consisted in anal region, pelvic, abdominal and inguinal LN, liver, peritoneum, other abdominal structures and lung. A PET/CT examination showing at least one site of abnormal FDG uptake considered as probably malignant was defined as positive. A PET/CT examination was considered negative when no FDG abnormal focus was visible or when all visible FDG foci were interpreted as probably non-pathologic or of a benign origin.

Standard of truth, determination of the diagnostic performance and impact on patient management

The standard of truth corresponded to the determination of the presence or absence of malignant tissue at the date of PET/CT examination. It was derived, for each site of each PET/CT examination, from the data of post-surgical or post-biopsy histology when available and, in all cases, from the data of follow-up during at least 6 months after the PET/CT examination. Follow-up data included physical and proctologic examinations and serial imaging studies such as CT, MRI, US or subsequent FDG PET/CT examinations. By comparing the content of the report of each PET/CT examination with the standard of truth, the result of PET/CT was classified for each site as true positive, true negative, false positive or false negative.

Sensitivity, specificity, accuracy, positive and negative predictive values of FDG PET/CT were then calculated on a per-examination and on a per-site basis.

The impact of PET/CT was determined as follows: The referring physician had to fulfil prospectively a form (French translation of the one used by Meta et al. [21] studying the impact of FDG PET in colorectal carcinoma) reporting the scheduled management option before PET (watchful waiting, chemotherapy, surgery, radiotherapy or performing additional diagnostic investigations). This was compared with the management which was actually performed, knowing the results of PET/CT. The adequacy of the actual patient management was checked, thanks to the data of the long-lasting follow-up.

Results

Characteristics of patients

Patient's characteristics are summarised in Tables 1 and 2. There were 44 evaluable patients, 31 women and 13 men (sex ratio 2.4:1). Mean age was 62 years (range, 38–85 years). Eleven patients were HIV-positive. Mean follow-up duration was 13.5 months (range, 7–23 months) after PET/CT performed for initial staging and 13 months (range, 4–44 months) after PET/CT performed during follow-up.

Clinical indications for FDG PET/CT

Fifty-eight PET/CT examinations were analysed, 22 performed for initial staging, ten for systematic evaluation after treatment, four for restaging of a proven recurrence and 22 for suspected recurrence or persistence of cancer, based on clinical findings in 12 cases, on conventional imaging anomalies in eight cases and on rising serum levels of squamous cell carcinoma antigen (SCC) in two cases. Thirteen patients had PET/CT for staging and then later during follow-up. One patient (#5) was considered twice during follow-up because he developed a second cancer.

Diagnostic performance of FDG PET/CT

Twenty-two examinations were performed for initial staging. Eight anal tumours had been excised before imaging. Of the 14 remaining anal tumours, PET/CT identified 13, the detection rate being 93%; the false-negative result corresponded to an 8-mm malignant tumour. FDG-positive LN were detected in five cases (23%; pelvic LN in one patient, inguinal in three patients and iliac LN in one case),

Table 1 Characteristics of patients referred for staging

Number of patients	PET/CT findings	PET/CT result (anal region)
1	Anal lesion	TP
2	No uptake in anal region	TN
3	Suspicious inguinal LN, no anal uptake	FN
4	Anal lesion, left inguinal LN	TP
5	No pathological uptake	TN
6	Anal lesion	TP
7	Anal lesion, pelvic LN	TP
8	No pathological uptake	TN
9	Anal lesion	TP
10	Anal lesion	TP
11	No pathological uptake	TN
12	Anal lesion, right inguinal LN	TP
13	No pathological anal uptake	TN
14	No pathological uptake	TN
15	Anal uptake, iliac LN	TP
16	No pathological uptake	TN
17	Anal uptake	TP
18	Anal uptake	TP
19	No pathological uptake	TN
20	Anal uptake	TP
21	Anal uptake	TP
22	Anal uptake	TP

LN lymph nodes, *TP* true positive, *TN* true negative, *FP* false positive, *FN* false negative

Table 2 Characteristics of patients referred after treatment

Number of patients	PET/CT Indication	PET/CT findings	Standard of truth	PET/CT result	Evaluable sites and site-based results
23	Suspicious imaging findings	Pulmonary uptake, but not considered secondary	Follow-up	TN	4 sites 4TN
24	Restaging before surgery for recurrence	Anal lesion	Histology	TP	8 sites 1TP 7 TN
1	Systematic	No pathological uptake	Follow-up	TN	7 sites 7 TN
25	Clinical suspicion of recurrence	Right inguinal LN, pulmonary lesion	Histology and follow-up	TP	3 sites 1TP1FP 1TN
3	Systematic	No pathological uptake	Follow-up	TN	7 sites 7 TN
4	Clinical suspicion of recurrence	Anal lesion, inguinal, pelvic and abdominal LN	Histology	TP	4 sites 4 TP
5	Systematic	No pathological uptake	Follow-up	FN	1 site 1 FN
5	Suspicious imaging findings	Anal uptake	Histology and follow-up	TP	3 sites 1 TP 2 TN
26	Clinical suspicion of recurrence	Pelvic LN	Follow-up	TP	4 sites 3TN 1TP
27	Restaging before hepatectomy for hepatic metastasis	Hepatic lesion, pelvic LN	Follow-up	TP	7 sites 2TP 5TN
6	Clinical suspicion of persistent disease	No pathological uptake	Follow-up	TN	3 sites 3TN
7	Systematic	No pathological uptake	Follow-up	TN	7 sites 7 TN
28	Clinical suspicion of recurrence	No pathological uptake	Histology	TN	3 sites 3TN
11	Systematic	No pathological uptake	Follow-up	TN	6 sites 6 TN
29	Suspicious imaging findings	No pathological uptake	Follow-up	TN	3 sites 3TN
12	Clinical suspicion of persistent disease	Inguinal uptake	Follow-up histology	TP	2 sites 1 TP 1 TN
30	Systematic	No pathological uptake	Follow-up	TN	4 sites 4 TN
13	Systematic	No pathological uptake	Follow-up	TN	8 sites 8 TN
31	Suspicious imaging findings	Pathological uptake in lung lesion	Histology	TP	8 sites 1TP 7TN
32	Suspicious imaging findings	Retroperitoneal infiltration	Follow-up	TP	7 sites 1 TP 6 TN
14	Systematic	No pathological uptake	Follow-up	TN	7 sites 7 TN

Table 2 (continued)

Number of patients	PET/CT Indication	PET/CT findings	Standard of truth	PET/CT result	Evaluable sites and site-based results
33	Suspicious imaging findings	Inguinal and abdominal LN	Follow-up	TP	7 sites 1TP 6TN
34	Restaging before abdominoperineal amputation for recurrence	Anal uptake	Histology hepatic metastases	TP	8 sites 1TP 1FN 6TN
35	Elevated SCC	No pathological uptake	Follow-up	TN	8 sites 8 TN
36	Elevated SCC	Anal uptake	Histology	TP	7 sites 1TP 6 TN
16	Systematic	No pathological uptake	Follow-up	TN	2 sites 2TN
37	Suspicious imaging findings	No pathological uptake	Follow-up	TN	2 sites 2 TN
38	Clinical suspicion of recurrence	Anal uptake	Histology	FP	3 sites 1 FP 2 TN
18	Clinical suspicion of persistent disease	Anal uptake	Histology	TP	4 sites 1TP 1FN 2 TN
39	Suspicious imaging findings	No pathological uptake	Follow-up	TN	4 sites 4 TN
40	Restaging before surgery for ureter invasion	Inguinal and iliac LN	Follow-up	TP	8 sites 2 TP 6TN
41	Clinical suspicion of recurrence	Inguinal LN No anal uptake	Cytology Follow-up	FP	6 sites 1 FP 5TN
42	Suspicious imaging findings	No pathological uptake	Follow-up	TN	7 sites 7TN
43	Clinical suspicion of persistent disease	Anal uptake	Histology	FP	2 sites 1 FP 1TN
44	Clinical suspicion of recurrence	Anal uptake	Follow-up	FP	3 sites 1 FP 2 TN
20	Systematic	No pathological uptake	Follow-up	TN	2 sites 2 TN

but no histological proof was obtained. In all cases, this nodal involvement had been suggested either clinically or by other imaging modalities. No focus evocative of visceral metastases was detected.

Thirty-six examinations were performed during post-treatment follow-up and PET/CT was positive in 18 cases. The positive findings were confirmed in 14 cases, but four examinations yielded false-positive results. Of the 14 true-positive examinations, none was performed for systematic evaluation.

The false-positive results corresponded to the following cases: In one HIV-positive patient with a suspected local

recurrence, no anal FDG uptake was visible, but FDG uptake was detected in an inguinal LN which prompted fine-needle aspiration that did not reveal any pathologic cells. After an 11-month follow-up, the patient was disease-free. Two patients referred because of a clinical suspicion of local recurrence had visible FDG uptake in anal canal—in one case, histology did not find any disease and the patient was disease-free 10 months later; the other patient was also disease-free 11 months after the examination. The fourth patient was treated for an inflammatory anal ulcer and PET/CT showed a positive anal uptake; clinical symptoms prompted surgery, but histology found no recurrence.

PET/CT was negative in 18 examinations, which corresponded to 17 true-negative results. The patient with a false-negative result (#5) was referred for systematic PET/CT, which was negative, but he presented, less than 6 months later, with a second cancer developed on an intraepithelial anal neoplasia that became invasive shortly afterwards.

On a per-examination basis, sensitivity of PET/CT for the detection of recurrent or persistent anal cancer tissue was 93% (14 out of 15), specificity was 81% (17 out of 21), accuracy was 86% (31 out of 36), positive predictive value (PPV) was 78% (14 out of 18) and negative predictive value (NPV) was 94% (17 out of 18).

Among the 17 patients with a true-negative PET/CT result, five were T1 stage, seven were T2, five T3 and none T4 stage. Among the 14 patients with a true-positive examination, one was T1, one T2, ten T3 and two T4.

At the last follow-up, seven patients had died (patients 4, 18, 25, 26, 27, 32 and 37), respectively 4, 10, 10, 11, 22, 17 and 12 months after PET/CT. All of them had positive FDG PET/CT.

Eight sites were defined for each PET/CT examination. For the 36 examinations performed during follow-up, 288 sites could have theoretically been assessed, but the standard of truth could only be determined for 179 sites.

There were 24 FDG-positive sites, corresponding to 19 true-positive and five false-positive results. Four corresponded to the false-positive examinations already described above. The fifth false-positive site corresponded to a FDG focus in the lung, in patient #25 with a histology-proven inguinal recurrence accurately diagnosed by FDG PET/CT (Fig. 1), but whose lung focus spontaneously disappeared afterwards and was considered as benign.

There were 152 FDG-negative sites—149 true-negative, three false-negative. One of the false-negative sites was observed in patient #5 reported above. The local recurrence of patient #34 was correctly assessed on PET/CT, but histologically proven multiple hepatic metastases (the largest measuring 1 cm) were only discovered at surgery. Of note, this patient had an elevated glycaemia at 11 mmol/L when PET/CT was performed, which may be responsible for the false-negative result. The third false-negative result on a per-site basis was observed in a patient whose local recurrence was also correctly assessed on PET/CT, but whose perirectal metastatic LN was only discovered during the abdominoperineal excision that followed.

On a per-site basis, sensitivity was 86% (17 out of 22), specificity 97% (150 out of 155), accuracy 96% (167 out of 175), PPV 79% and NPV 98%.

Impact of FDG PET/CT on patient management

FDG PET/CT results induced a change in patient management in nine patients (nine out of 44=20%), and the modification was relevant in eight of them (eight out of nine=89%). All these patients were referred for a suspected or proven recurrence and none of them for staging or for systematic post-treatment evaluation. Patients' details are given in Table 3.

It allowed avoiding unnecessary biopsies in two patients in a post-radiotherapy scar tissue. Chemotherapy was indicated in two patients with clinical or morphological findings suspicious for recurrence confirmed by pathologic foci on PET/CT, whereas no therapy was planned beforehand. Surgical intervention was indicated in two patients after PET/CT and found persistent disease after initial treatment. In two cases, scheduled surgery was replaced by chemotherapy because PET/CT showed that the disease was more extensive than expected. The case of one of them (patient #27) is reported in Fig. 2.

In one patient (#41), PET/CT prompted unnecessary cytology and the modification of management was not relevant.

In 35 patients, FDG PET/CT had no impact on patient management. It did not induce any change in management in patients referred for staging, even though it provided complementary data in two of them. In patient #3, abnormal uptake was found in inguinal nodes, but she received the scheduled radiotherapy dose on inguinal LN without any boost. As the patient was disease-free 23 months after this examination, there is no evidence of relevance of the PET/CT findings. In patient #15, PET/CT showed pathologic uptake in iliac LN, but she was, nonetheless, operated on, and histology confirmed PET/CT findings.

Among the patients referred during follow-up, 11 had positive PET/CT examinations. Eight were true-positive. In four patients, it confirmed known lesions. In two patients, PET/CT assessed correctly a local recurrence, but failed to spot perirectal LN in patient #18 and multiple hepatic lesions in patient #31. In two patients, PET/CT detected unknown lesions but had no direct impact on management because PET results were not taken into account and confirmation was obtained only months later (Fig. 3).

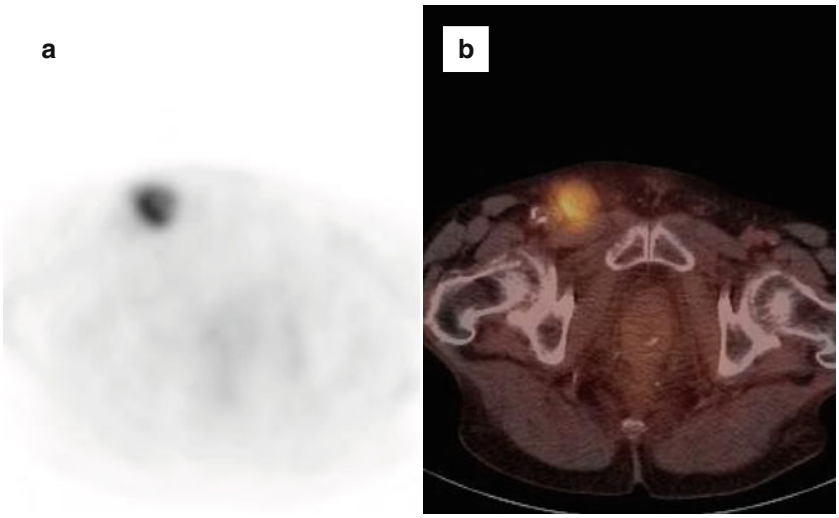

Fig. 1 Patient #25: In this patient referred for suspicion of inguinal recurrence, FDG PET/CT showed a right inguinal uptake, and the presence of disease was confirmed by histology. **a** Transaxial slice FDG PET, **b** transaxial slice FDG PET/CT fusion

False-positive results occurred in patient #38 with a suspicion of recurrence who, anyway, was scheduled to undergo anal biopsy; in patient #44, who was managed by a simple surveillance though PET/CT was positive, and in symptomatic patient #43 who was anyway scheduled for surgery.

Sixteen patients had a negative PET/CT with no impact on patient management. Fifteen were true-negative cases. One of them (patient #3) was referred because of elevated SCC serum levels and was doing well 2 years after a negative PET/CT, while SCC serum levels were still elevated and stable.

Table 3 Patients for whom FDG PET/CT had an impact on management

Number of patients	PET/CT indication	PET/CT findings	Scheduled management	Actual management	Relevance
4	Suspicion of persistent disease after treatment	Uptake in anus, pelvic, inguinal and abdominal LN	No treatment	Surgery (abdominoperineal amputation)	Yes Died 4 months after PET (sepsis shock)
5	Suspicion of inguinal nodal involvement after completion of treatment	Anal pathological uptake, without abnormal uptake in inguinal LN	No treatment	Biopsies and then surgery (abdominoperineal amputation)	Yes Free of disease 7 months later
27	Restaging before local treatment of a hepatic metastasis	Disseminated pelvic LN	Hepatectomy	Chemotherapy	Yes Died of disease progression
29	Suspicion of recurrence	No pathological uptake	Biopsy in post-radiotherapy scar tissue	No biopsy	Yes Free of disease 19 months later
32	Suspicion of recurrence	Retroperitoneal uptake	No treatment	Chemotherapy	Yes Initial stabilisation then disease progression
33	Suspicion of recurrence	Inguinal and abdominal LN	No treatment	Chemotherapy	Yes Stability with chemotherapy
39	Suspicion of recurrence	No pathological uptake	Biopsy in post-radiotherapy scar tissue	No biopsy	Yes Free of disease 21 months later
40	Restaging before surgery (nephro-ureterectomy) for recurrence in the left ureter	Inguinal and abdominal LN	Surgery	Chemotherapy	Yes Died of disease 12 months after PET
41	Clinical suspicion of local recurrence (bleeding of the anal margin)	No pathological anal uptake, but suspicious inguinal uptake	No treatment, no further examination	Fine-needle biopsy aspiration of inguinal LN, negative for disease	No Free of disease 11 months later

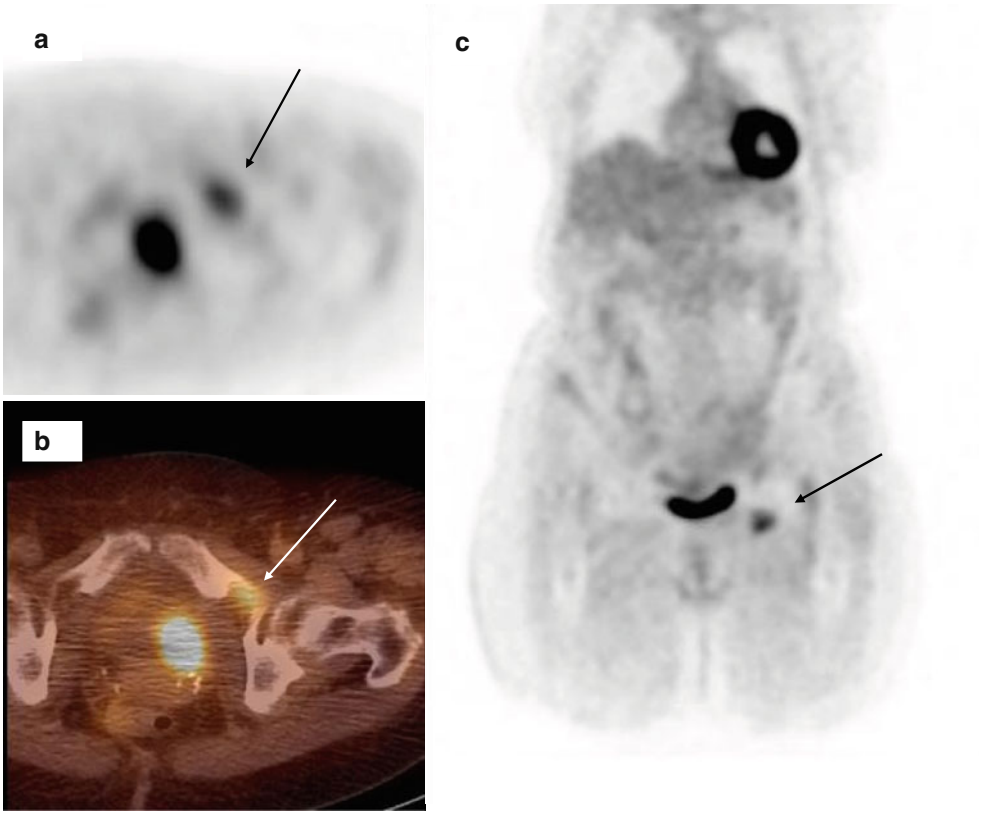

Fig. 2 Patient #27: FDG PET/CT was performed after neoadjuvant chemotherapy and before scheduled metastasectomy of a single hepatic metastasis, but FDG was taken up not only by the hepatic metastasis (not shown here), but also by LN in the left part of the pelvis, subsequently confirmed on MRI, and the patient was then treated by chemotherapy. **a** PET transaxial slice, **b** Fused PET/CT transaxial slice, **c** PET coronal slice

Discussion

Rather limited experience has been published until now on the performance and the impact of FDG PET or PET/CT in anal cancer. To the best of our knowledge, only seven studies including a total of 273 patients have been reported, four included post-therapy examinations and only one addressed its use in suspected recurrence (Table 4).

In our study, FDG PET/CT detected the non-excised primary tumours in 93% of patients, which is consistent with previous studies where PET identified the primary more often than CT, 91% versus 59% according to Cotters et al. and 98% versus 58% according to Nguyen et al. [17, 18]. De Winton et al. reported a 100% detection rate [19]. However, this detection had no clinical impact, since the visualisation of the primary tumour does not change the therapy management.

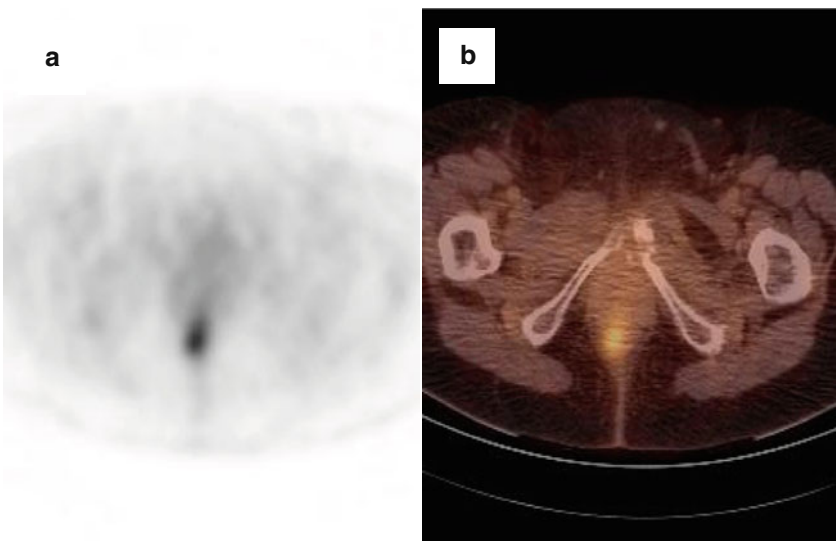

Fig. 3 Patient #36: FDG PET/CT, performed for rising SCC serum levels, was evocative of anal recurrence, requiring further examinations. The biopsy of the right posterior–lateral nodule confirmed recurrence of the disease, but it was only performed 8 months after FDG PET/CT. **a** Transaxial PET slice, **b** transaxial fused PET/CT slice

Table 4 Previous studies on FDG PET and anal cancer

Publication year	1st author (reference)	Imaging modality	Number of patients	PET indication	Number of PET examinations per indication
2005	Trautmann [15]	PET	21	Staging	21
				Post-therapy	18
2006	Cotter [17]	PET/CT	41	Staging	41
2008	Nguyen [18]	PET	50	Staging	48
				Post-therapy	25
				Follow-up	30
2008	Schwarz [20]	PET/CT	53	Staging	53
				Post-therapy	53
2009	de Winton [19]	PET	61	Staging	61
2009	Mai [25]	PET	39	Staging	39
2009	Iagaru [26]	PET	8	Staging	8
				Post-therapy	6
	Present study	PET/CT	44	Staging	22
				Post-therapy	14
				Follow-up	22

In the study by Cotter et al., FDG PET identified positive inguinal LN in 17% of groins considered as negative on both CT and clinical examination [17]. In the study by Nguyen et al., PET found previously unknown FDG-avid sites of nodal disease in nine patients [18]. It resulted in a change of radiotherapy planning in nine patients (19%), with an increased dose in PET-upstaged LN regions, but no changes in radiotherapy fields. In the study by de Winton et al., FDG PET was superior to conventional imaging for the detection of LN involvement [19]. The results of PET changed patient management in 16% of patients, mostly by modifying radiotherapy fields or irradiation protocol and treatment intent in two cases. In five of 61 patients, FDG PET results were ignored.

However, a recent study compared FDG PET/CT and sentinel LN biopsy for detection of inguinal involvement, which is not widely used at this moment in anal cancer. FDG PET/CT had a lesser accuracy, mainly due to false-positive results [22].

In our study, initial FDG PET/CT did not induce any management change. All the FDG-positive LN had already been suspected, either on clinical examination or on other imaging modalities. Moreover, the radiotherapist took other elements into account to decide to boost radiotherapy or change radiotherapy fields, such as tumour size, patient age and tolerance to treatment.

Results of previous studies are discrepant about the utility of performing post-therapy FDG PET. Trautmann et al. found that PET performed 1 month after completion of treatment was of little value in predicting durability of response [15]. Nguyen et al. performed post-treatment PET after a median 17-week delay, though it correctly identified persistent disease in two patients, it also yielded false-positive findings in three of 25 patients [18]. On the contrary, in a prospective study assessing the predictive value of post-therapy PET, Schwarz et al. showed that a partial metabolic response in the anal tumour was predictive of significantly decreased progression-free and cause-specific survival after chemoradiotherapy, compared with that of patients with complete metabolic response [20]. In this study, FDG PET was performed at a median of 2.1 months after treatment completion.

Nguyen et al. also performed follow-up examinations in 15 patients [18]. In seven of them, PET confirmed a suspected recurrence and it detected unsuspected recurrence in two patients [18]. In our study, post-therapy examinations were performed at a median of 3.5 (range, 1.5–6) months after the end of treatment. Follow-up examinations were performed at a median of 22 months with a large range (6–116). Our study confirms the risk of false-positive results, due to post-radiotherapy inflammation or infection, or radiation-induced ulcer that can occur later during follow-up. In our series, there were four false-positive examinations; among them, three patients had symptoms which could correspond to local recurrence as well as to local ulcer or inflammation. It is well known that FDG is taken up by activated leukocytes in these conditions, with intensity similar to that of malignancies [23]. Another false-positive finding was observed in a HIV patient with FDG-positive inguinal LN that proved to be devoid of malignancy.

Grigsby recently insisted on the need for a non-invasive assessment of tumour response, avoiding unnecessary biopsies in patients with complete metabolic response and guiding biopsies in case of incomplete metabolic response [24]. The demonstration of clinical utility of FDG PET/CT in patients with anal cancer suspicious for persistence or

recurrence is the major result of the present study. However, the design of our study does not permit assessment of whether this accurate restaging leading to salvage therapy increased overall survival. This would require a randomised dual-arm study.

In our series, PET/CT especially showed an interesting NPV, 94% on a per-examination basis and 98% on a per-site basis. This suggests that FDG PET/CT should be part of the imaging workup before salvage therapy of anal cancer, and especially surgical operation, to prevent the realisation of futile surgery. PET/CT induced a relevant impact in overall 18% (eight out of 44) of patients and in 22% of patients referred for follow-up, in our unselected population, corresponding to an everyday practice. Impact rate might have been higher, since in three patients, the referring physician did not take into account positive PET/CT results, which later proved to be relevant.

Conclusion

FDG PET/CT is accurate in anal cancer. Our study demonstrated that the added value of PET/CT was best during follow-up. Its excellent negative predictive value permits to avoid unnecessary biopsies or surgery in patients with irradiated tissue. Besides, PET/CT can be useful for diagnosis of recurrence or restaging, especially when a salvage surgery is scheduled. Even though foci of FDG uptake can be due to post-therapy infection or inflammation, they should be considered as warning for persistence or recurrence of cancer. In contrast, performing systematic FDG PET/CT examination during post-therapy follow-up yielded no impact.

Acknowledgements We would like to thank the clinicians who referred the patients and also provided us with valuable follow-up information Drs. Atienza, Bourguignon, Etienney, Meary and Mory, from Groupe Hospitalier Diaconesses Croix Saint-Simon, Drs. Huguet and Pene from Hôpital Tenon. We thank Pr Meignan for his review of the draft.

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