

Role of ^{18}F -FDG PET versus CT Scan in Evaluation of Extra-Nodal Lymphoma

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Abstract

Purpose: To compare findings in fluorine 18-fluorodeoxyglucose (FDG) positron emission tomography (PET) and computed tomography (CT) in patients with extra-nodal lymphoma by using a combined PET/CT scanner.

Methods and Materials: Between 2011 and April 2013, seventy seven patients with confirmed pathology of Hodgkin (32 patients) and Non Hodgkin lymphoma (45 patients) with extranodal involvement diagnosed at Nasser Institute Cancer Center (NICC), ministry of health, Cairo, Egypt. After collection of the two reports separately, combined reading was allowed afterwards, and the differences were recorded for our study.

Results: PET-CT is very effective in detection of lesions in the bone and bone marrow, few patients may have CT finding without corresponding FDG uptake, CT without PET may be very effective in detecting recurrences in soft tissue, renal and GIT extranodal lymphoma.

Conclusion: PET scan is more sensitive than the CT used alone, and the combination PET-CT can be considered the standard of care for detection of extranodal lymphomas excluding soft tissue, renal and GI lymphomas.

Keywords: Extranodal lymphoma; PET; CT; Hodgkin; Non-hodgkin

Patients characteristics

Thirty six male [mean age=46 years, (range: 24–83 years)] and 41 female [mean age=39 years, (range: 30–72 years)]. Only 31 patients returned for follow-up studies. None of the patients had inflammatory or infectious disease of unknown origin.

Introduction

Malignant Lymphoma (ML) is a highly curable disease, and very responsive to chemotherapy, extra-lymphatic involvement is not uncommon [1] and accurate staging is very crucial in its management, more critical is the restaging; as salvage treatment is usually more aggressive and carry a lot of side effects and consequences. Residual masses or enlarged lymph nodes are commonly found at Computer Tomography (CT) after treatment of lymphoma, which may or may not contain viable tumor, and this may represent the PET challenges, also extralymphatic sites may be difficult to interpret with CT only. In developing countries PET scan is economically very difficult to provide for all patients, the aim of this study is to assess the value of PET scan in the detection of extra-lymphatic disease site and its value in comparison to the commonly used in assessment of lymphatic and extra-lymphatic sites, so that we can define the type of patients that benefit most from this type of expensive investigation.

PET-CT technique

Patients were not allowed to consume any food or sugar for at least 6 hours prior to the start of the study, adequate hydration was encouraged. After injection patient remained seated, recumbent and silent to minimise extra-tumor FDG uptake, patient kept warm 30–60 min before the injection of FDG and throughout the whole procedure. No sedatives were administered. All patients had blood glucose level measured before the scan. Dose used was 1.4 mCi/10 Kg administered intravenously. After the PET scan is complete, intravenous contrast was administered for the CT scan. Machine used was SIEMENS Biograph™ TruePoint™ PET•CT. FDG PET images were interpreted by both nuclear medicine and radiologists consultants separately and each was blinded for the other study. After collection of the two reports separately, combined reading was allowed afterwards, and the differences were recorded for our study. The location of positive FDG uptake was reported in 6 anatomic extranodal sites (bone and bone marrow, pleuro-pulmonary; hepatic; renal; supra renal, GIT and soft tissues). Concordant findings at both CT and FDG PET were regarded as actual locations of disease; discordant results were resolved on the basis of PET-CT combined reading results or follow-up when possible.

Methods and Materials

Between 2011 and April 2013, seventy seven patients with confirmed pathology of Hodgkin (32 patients) and Non Hodgkin lymphoma (45 patients) with extranodal involvement diagnosed at Nasser Institute Cancer Center (NICC), ministry of health, Cairo, Egypt. Patients referred to us for initial PET- CT assessment and later after treatment for follow-up.

Statistical analysis

PET scan considered as our golden standard in our study and the concordance and discordance between two modalities was calculated with Kappa test.

Results

Bone and bone marrow

In initial images PET scan were negative for metabolic activity in 37(48%) patients, 33 (89.2%) of which were negative for any morphological changes in CT scans and positive in only 4 (10.8%) patients. In 40 patients (51.9% out of 77 patients) reported by PET to be positive, discordant and concordant results were found in 16 (40%) patients and in 24 (60%) patients respectively, all differences were in patients with bone marrow infiltration that was not reported in CT scan, (Kappa test= 0.486, P<0.001), (Table 1 and Figure 1).

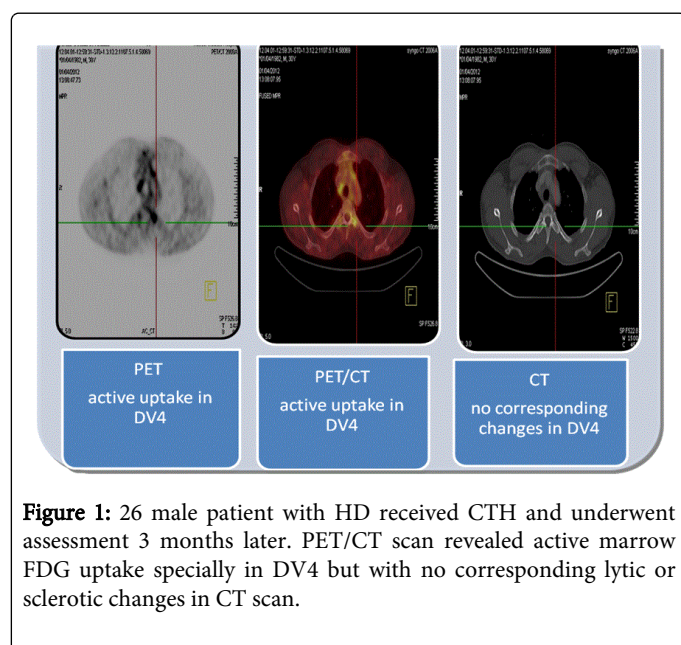


Figure 1: 26 male patient with HD received CTH and underwent assessment 3 months later. PET/CT scan revealed active marrow FDG uptake specially in DV4 but with no corresponding lytic or sclerotic changes in CT scan.

Follow-up images (second reading)

In the follow-up images for 31 patients, PET scans were negative for metabolic activity in 23 patients and CT scans reported to be negative in 21 patients (91.3%), discordant results were in only two patients with lytic bone lesions without corresponding FDG uptake. Both PET and CT scans were positive in the remaining 8 patients, (Kappa test=0.844 P<0.01), (Table 1).

Pleuro-pulmonary lesions

PET scans were negative for metabolic activity in 66 patients (85% of 77 patients), 60 patients had negative CT (90%) with discordant positive findings in CT scan and no corresponding PET activity in 6 (9.1%) patients attributed to be old granulomas in 4 patients and fibrotic changes in two. There were positive PET scan results in 11 patients, with corresponding CT findings in 10 patients (90.9%) and in one patient (9.1%) CT study didn't show any lesions, which was attributed to be masked by the lung hilum, (Figure 2). (Kappa test=0.668, p<0.001).

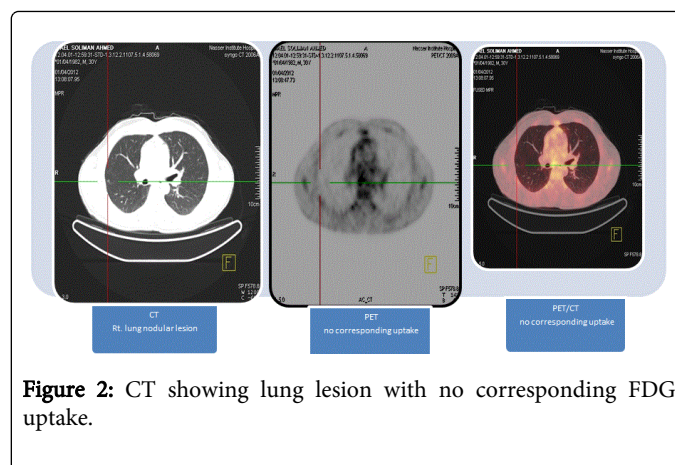


Figure 2: CT showing lung lesion with no corresponding FDG uptake.

For Follow-up images

In follow-up images for 31 patients, PET scans were negative for metabolic activity in 28 patients, with concordant findings in the CT scan readings. In 3 patients PET scan was positive with one patient had negative CT results. Two patients showed CT findings with corresponding PET activity, (Kappa test=0.518, and P value<0.001).

Hepatic lesions

In 64 patients (83.1%) PET scans were negative for metabolic activity, with concordant CT findings in 54 patients, while in 10 patients there was CT findings without a corresponding FDG activity. In 13 patients with positive PET findings, CT could not detect the lesions in 3 patients (23%) which may be attributed to the diffuse nature of the lesions, (Kappa test=0.505 and P value<0.001).

For Follow-up imaging

PET scan was negative for metabolic activity in 27 patients with concordant finding in the CT scan in 22 (81.4%) patients. In 4 patients with PET scan lesions uptake, CT detected the lesions in 3 and couldn't detect it in one patient, (Kappa test=0.495 and P value<0.001).

Renal lesions

PET /CT scans were negative for metabolic activity in 74 patients (96.1%) and positive in only 3 patients (3.9%). CT images showed the same results.

For Follow-up imaging

In thirty one patients, Both PET and CT scans detected lesions in 4 patients (100%) and were negative in 27 patients (100%) (Kappa test=1).

Gastrointestinal lesions

PET scans were negative for metabolic activity in 71 patients, while CT scans were negative in 72 patients (98.6%) both PET and CT images were able to detect lesions in 5 patients, except one patient had positive PET scan that could not be seen in CT. (Kappa test=0.902).

For Follow-up imaging

PET scan was negative for metabolic activity in 30 patients with concordant negative results in CT scans however, PET scan detected FDG uptake in one patient with no corresponding CT finding, (Kappa test=0.651 and P value<0.001).

Soft tissue

PET scans were negative for metabolic activity in 61 patients (79.2%) but positive in 16 patients (20.8), with CT scan showed exactly same results.

Site		PET -ve (N=37)	PET +ve (N=40)	Kappa result (P value)	Site		PET -ve (N=66)	PET +ve (N=11)	Kappa result (P value)
Bone and B.M. First reading	CT -ve. (N=49)	33(89.2%)	16(40%)	0.486(p<0.001)	Pleuro-Pulmonary First reading	CT-ve. (N=61)	60(90.9%)	1(9.1%)	0.668(p<0.001)
	CT +ve. (N=28)	4(10.8%)	24(60%)			CT+ve. (N=16)	6(9.1%)	10(90.9%)	
		PET -ve (N= 23)	PET +ve (N=8)				PET -ve (N= 28)	PET +ve (N=3)	
Bone and B.M. Second reading	CT -ve. (N=21)	21(91.3%)	-		Pleuro-Pulmonary Second reading	CT-ve. (N=29)	28(100%)	1 (33%)	
	CT +ve. (N=10)	2(8.6%)	8(100%)			CT+ve. (N=2)		2 (66.7%)	
		PET-ve (N=64)	PET+ve (N=13)				PET-ve (N=71)	PET +ve (N=6)	
Hepatic lesion First reading	CT-ve. (N=57)	54(84.4%)	3(23.1%)	0.505(p<0.001)	Gastro-Intestinal First reading	CT -ve. (N=72)	71 (98.6%)	6 (100%)	0.902(p<0.56)
	CT +ve. (N=20)	10(15.6%)	10(76.9%)			CT +ve. (N=5)	6(9.1%)	5(83%)	
		PET-ve (N=27)	PET+ve (N=4)				PET-ve (N=30)	PET+ve (N=1)	
Hepatic lesion Second reading	CT-ve. (N=23)	22(81.4%)	1(25%)		Gastro-Intestinal Second reading	CT-ve. (N=31)	30(100%)	1(100%)	0.651(P<00.1)
	CT +ve. (N=8)	5(18.6%)	3(75%)			CT +ve. (N=0)	0	0	

Table 1: Concordance and Dis-concordance results between PET and CT scans both in initial and follow-up imaging.

Discussion

Extranodal involvement by extension from lymph node disease to such sites as the lung, bone, pleura, or skin may occur in stages I–III and does not increase the disease to stage IV. Such disease is designated by the subscript “E”(i.e., IE, IIE, and IIIE). However detection of lesions in nodal or extranodal sites may be more difficult using CT scan compared to FDG-PET [2]. According to a metaanalysis, the median sensitivity of FDG-PET is 90% per patient unit and 97% per lesion unit [3]. Especially in case of Hodgkin’s lymphoma, FDG-PET has been reported to have a higher sensitivity for the detection of extranodal lesions and bone marrow lesions compared to conventional methods, and patients may be upstaged in

15–25% of cases [4-8]. Better detection of initial tumor or recurrence can change treatment plan in 10 to 20% of patients according to Pelosi and Rigacci et al. [2,9]. The combined PET and CT scanner used in our study offers precisely fused images, as well as PET and CT images, obtained at the same location, and thus allows direct comparison of PET and CT findings. We compared PET and CT findings at six main anatomic sites, which may be difficult to interpret certain lesions in CT and we thought that PET scan may be needed to confirm the diagnosis. A main finding in our study was that PET and CT provided accurate results in renal, soft tissue, and gastro-intestinal lesions in a very good manner with agreement approaching the 100%, which may raise the question of the need of PET in patients with a lesion in such sites, this is was confirmed by others, [5,10], however the number of

our patients still small to make a final conclusion, Rodriguez et al. [11] reported high FDG uptake in six high-grade and one of two low-grade primary gastric lymphoma. No abnormal tracer uptake was seen in the patient with low-grade gastric NHL of the MALT type, they found more tumor extension compared to endoscopy but they didn't report the CT finding. Jerusalem et al. reported that PET plus a bone marrow biopsy compared to conventional staging procedures (also including a bone marrow biopsy) observed the same stage in 37 patients, a higher stage by PET in two patients [12], in our study PET detected bone marrow disease in 16 patients could not be caught by CT scan alone, and this was confirmed by bone marrow biopsy results, taking into consideration that the Jerusalem series was for patients with low grade lesions. Diffuse high FDG uptake of the bone marrow can occur due to the reactive changes of chemotherapy or the use of Colony-stimulating Growth factors (CSGF), in our study we insisted that the patient do not receive chemotherapy or CSGF at least two weeks prior to their PET scan. On the other hand, minimal bone marrow disease may be missed by FDG-PET, and thus FDG-PET should not be considered a replacement for bone marrow biopsy [13-15]. Conversely, mass lesions identified by CT may present as negative by PET. It is clear that PET alone cannot replace CT for the purposes of pretreatment staging of lymphoma. Positive predictive value of FDG in aggressive NHL and HL are middle-range of value (80 and 50%, respectively), these values are substantially higher than the corresponding values for CT (about 40 and 20%, respectively [14-17], suggesting that FDG-PET is more accurate than CT in the response assessment of lymphoma. The low accuracy of CT is mainly due to the fact that CT cannot distinguish residual active tumor from inactive fibrosis or necrosis.

Conclusion

PET scan is more sensitive than the CT used alone, and the combination PET-CT can be considered the standard of care for detection of extranodal lymphomas excluding soft tissue, renal and GI lymphomas.

Conflict of Interest

No conflict of interest to be declared

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