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Beyond lymph nodes: ^{18}F -FDG PET/CT in detection of unusual sites of extranodal lymphoma

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Abstract

Background: The purpose of this study was to compare between contrast-enhanced computer tomography (CE CT) and ^{18}F -FDG PET/CT in the detection of extranodal involvement in lymphoma and to correlate between SUV_{max} of the extranodal lesion and the hottest LN. One hundred patients with pathologically proven lymphoma underwent whole body ^{18}F -FDG PET/CT and CECT scans. Images were compared regarding the ability of detection of extranodal lymphomatous sites. *Kappa* agreement was applied to find the degree of agreement between both modalities. Pearson's correlation was used for correlating SUV_{max} of the extranodal lesions and hottest LN. The degree of FDG uptake was correlated with histopathological type.

Results: There was a poor agreement between PET/CT and CECT in the detection of extranodal sites ($k = 0.32$). There was a significant positive moderate correlation between SUV_{max} of the extranodal lesions and hottest LN ($r = 0.45$). PET/CT study resulted in up staging of 10% and down staging of 5% of cases.

Conclusion: In lymphoma staging, FDG PET/CT enables more detection of extranodal involved sites that show normal morphology at CECT. It differentiates lymphomatous infiltration from benign causes of increased FDG uptake with subsequent proper disease staging.

Keywords: ^{18}F -FDG PET/CT, Extra nodal, Lymphoma, SUV_{max}

Background

Lymphoma is a malignancy that originates from the lymphatic system but can occur at extranodal sites [1]. Extranodal disease is commonly part of lymphomatous involvement (secondary lymphoma), but it can also be the primary site where lymphoma arises (primary lymphoma) [2]. Route of spread to the extranodal site is either regional spread from nodal disease or hematogenous dissemination [3].

The prevalence of lymphoma is increasing, so that extranodal forms are frequently seen. Primary lymphoma can involve any organs mimicking carcinomas or infection [2]. The aim of this work was to identify the added role of PET/CT over diagnostic CT in the detection of extranodal lymphoma.

Patients and methods

This prospective study was performed between January 2016 and May 2018 at Ain Shams University hospital (Nuclear medicine unit) and a private center. Approvals of the institutional review board were obtained. All patients provided written informed consent for doing the examination and for anonymous use of their data in research purposes.

Inclusion criteria

Patients with pathologically proven lymphoma having at least one extranodal site referred for staging.

Exclusion criteria

Exclusion criteria includes pregnant patients, patients with hypersensitivity to non-ionic contrast agents, or with high blood glucose level > 200 mg/dl.

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Patient preparation

Patients should be fasting for 4–6 h, blood glucose less than 200 mg/dl, avoidance of vigorous activity 24 h before the procedure to avoid physiologic background muscle uptake of the tracer, and avoidance of talking following injection of FDG.

Scanning technique and imaging parameters

PET/CT examination was performed using a CT machine (Philips® Ingenuity TF128 multislice PET/CT) and (General Electric (GE) 16 slice discovery I Q). All cases were injected with 5–10 mCi (1 mCi/10 kg) of ^{18}F -FDG about 1 h before the examination.

The examination started with a low dose non-enhanced routine CT scan from the skull base to the mid-thigh for attenuation correction. Then, PET imaging was performed at 1 mm/min in bed position, and a 512×512 matrix.

Following PET study, a diagnostic enhanced CT scan was obtained using 60–100 ml of non-ionic iodinated contrast material. 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.

Image analysis and data interpretation

Whole body PET and CT images were loaded on three-dimensional workstations for visual evaluation and data analysis (Philips Intellispace Portal) and (GE healthcare advantage workstation AW05). Non-attenuation corrected images, attenuation-corrected, as well as maximum intensity projections of CT, PET, and fusion PET-CT images were visually evaluated on the three planes (coronal, sagittal, and axial).

Based on CECT, the extranodal sites were identified as positive if there is a mass lesion or abnormal post contrast enhancement. Based on PET, the organ was positive if there is increased FDG uptake with SUV_{max} higher than physiologic hepatic background activity (SUV_{mean}).

Primary extranodal lymphoma is defined as extranodal organ affection with no lymph node involvement, while secondary lymphoma starts in nodal organ then the extranodal site is secondarily infiltrated.

A 3D region of interest (ROI) was drawn around each lesion at PET images. Image analysis software was used for calculation of SUV_{max} . (SUV = standardized uptake value) using the following formula: $\text{SUV} = \text{tissue radioactivity concentration (Bq/ml)} / (\text{injected dose [Bq]} / \text{body weight [g]})$ [2].

Extranodal organs showed different degree of FDG uptake according to histopathology type. Lowest SUV_{max} and highest SUV_{max} of each organ were listed. The SUV_{max} of the hottest lymph nodes and the extranodal organ were also quantified.

Statistical analysis

Collected data were coded and tabulated, then statistical analysis was done using statistical programs for social

science software version IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY, USA).

Descriptive analysis was done for numerical variables and was presented as mean \pm standard deviation. Categorical variables (qualitative data) were presented as number and percentage. **Kappa agreement** (κ) of CE-CT and PET-CT data for detection of extranodal lymphoma was measured. κ values were as follows: $k = 0$ –0.20 (very poor agreement); 0.21–0.40 (poor); 0.41–0.60 (fair); 0.61–0.80 (good); and 0.81–1.00 (excellent). **Pearson's correlation** analysis (r) was used to evaluate correlations between the SUV_{max} of the hottest lymph node and the SUV_{max} of extranodal sites of lymphoma, $r = 0$ –0.2 (poor correlation), 0.2–0.5 (moderate), 0.5–0.7 (strong), and 0.7–0.9 (very strong).

Results

Demographic data

Out of the 100 patients enrolled in our study, 70% were males and 30% were females. The age ranged from 9 to 93 years, mean 47 ± 21 SD.

Histopathological subtypes

Non-Hodgkin lymphoma (NHL) was detected in 79% of all cases while Hodgkin disease (HD) constituted the remaining 21%. The most frequent subtype in NHL was diffuse large B cell lymphoma (DLBCL) (63%), while in HD it was nodular sclerosis (5%) of all cases (Fig. 1a, b).

Primary and secondary extranodal lymphoma

Primary lymphoma was seen in 10% of cases (histopathologically confirmed) as follows: stomach 4%, small intestine 2%, thyroid 1%, lung 1%, muscle 1%, bone 1%. Secondary lymphoma was depicted in 90% of cases.

Regions of extranodal involvement in NHL and HD (Table 1)

The frequency of organ involvement in NHL were as follows: spleen (24% of all studied cases, focal infiltration 20% and diffuse 4%), head and neck (18%), GIT (15%) and Osseous lymphoma (14%). The axial skeleton was more commonly involved than the appendicular. The most commonly involved vertebrae were lumbar followed by dorsal. The humerus and tibia were the most commonly involved long bones. Regarding HD, the spleen was commonly involved (6%) of all cases, liver (3%), and marrow (2%).

The extranodal organs with hottest and lowest FDG uptake were the kidney and the pancreas SUV_{max} 73, 6 respectively. The relation between SUV_{max} and sites of extranodal involvement was demonstrated in Table 2. There was a wide range SUV_{max} in patients with similar lymphomas. Table 3 demonstrates the assessment of FDG uptake among the histological subtypes of lymphoma.

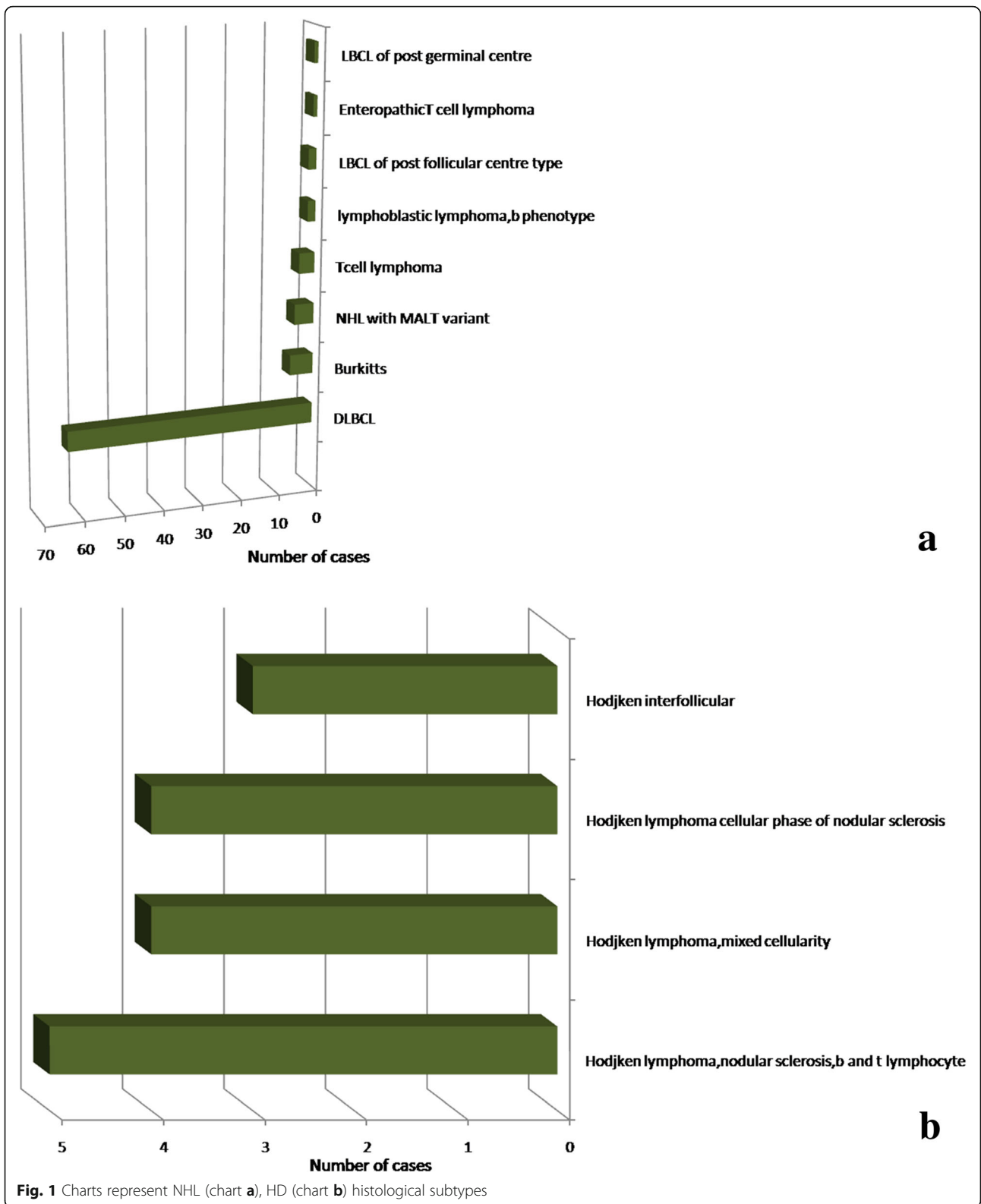


Table 1 The organs with extranodal lymphoma and related pathological subtypes in the study group

Organs with extra nodal lymphoma	Total number	Distribution	Pathological subtypes	
			NHL	HD
• Spleen	30	Focal	20	2
		Diffuse	4	4
• Head and neck	16	Tonsils	3	0
		Oropharynx	3	0
		Nasopharynx	3	0
		Orbits	2	0
		Thyroid	2	0
		Brain	2	0
		Parotid	1	1
• GIT	15			
		Stomach	7	1
		Small intestine	5	1
		Peritoneum	1	0
• Osseous	14		12	2
• Chest	12	Mass	6	0
		Nodule	3	0
		Consolidation	3	0
• Liver	7		4	3
• Cutaneous	5		5	0
• Muscle	4		2	2
• Kidneys	4		4	0
• Breast	2		1	1
• Pancreas	1		1	0
• Adrenal	1		1	0
• Heart	1		1	0
• Testicle	1		1	0
• Adnexa	1		1	0

The present study included 100 patients showing 122 extranodal organs with lymphomatous involvement based on both PET/CT and CECT. Agreement between both modalities was seen in 81 lesions. Based on PET/CT, 117 lesions were positive for lymphoma, whereas five lesions were negative excluding lymphomatous infiltration (confirmation was made by biopsy, MRI or follow up). Based on CECT, 86 lesions were positive, while PET/CT detected 36 extra lesions that were not detected by CECT.

Kappa agreement was done to evaluate the agreement between CECT and PET/CT study in the detection of extranodal lymphomatous infiltration (Table 4). It revealed a poor agreement (prevalence adjusted and **bias adjusted kappa coefficient** k , PABAK = 0.32).

Pearson's correlation between SUV_{max} of the hottest lymph node and the extranodal sites revealed significant positive but moderate correlation ($r = 0.45$).

Table 2 Relation between SUV and sites of extranodal involvement (listed according to SUV max)

Organ	Number	Lowest SUV_{max}	Highest SUV_{max}	Mean $SUV_{max} \pm SD$
Kidney	4	7	73	22.8 ± 23
Oropharynx	3	40	60	50 ± 10
Tonsils	3	18	40	29 ± 11
Thyroid	2	13	37	25
Stomach	8	28	36	17.7 ± 13.7
Spleen diffuse	8	5	33	10.6 ± 8.3
Liver	7	4	31	15.2 ± 9
Spleen focal	22	5	30	12 ± 7.6
Bone marrow	14	14	27	15.3 ± 7.7
Muscle	4	6	23	10.8 ± 7
Lung	12	5	22	9.8 ± 6.4
Intestine	6	12	21	16.5
Orbit	2	15	18	16.5 ± 2.2
Nasopharynx	3	6	18	12 ± 6
Cardiac	1	18	18	18
Testis	1	17	17	17
Adnexa	1	15	15	15
Breast	2	4	14	9 ± 5
Cutaneous	5	7.6	9.7	8.8 ± 0.9
Suprarenal	1	9	9	9
Peritoneum	1	8.2	8.2	8.2
Pancreas	1	6	6	6

Discussion

Identification of extranodal lymphomatous involvement is prognostically important in management [4]. PET-CT is a hybrid technique that provides both anatomical and functional data.

We aimed at this study to evaluate the added value of PET/CT over diagnostic CT in the detection of extranodal lymphomatous involvement. There was poor agreement between these two modalities ($k = 0.32$). This result denotes that CECT should not replace PET/CT in the staging of lymphoma. These results are different from Omur et al.'s study, where agreement was fair ($k = 0.6$). In the current work, disagreements were frequently depicted between these two modalities regarding the bone marrow, spleen, and liver, while in Omur et al.'s study, there was disagreement regarding spleen, marrow, thyroid, and prostate [5].

In the current study, PET study detected infiltration in 36 sites that were negative by CECT. Most of them showed either diffuse splenic or marrow uptake by PET images while were normal by CECT. This resulted in up

Table 3 Relation between SUV and histopathological subtypes

Type	No	SUV _{min}	SUV _{max}	Mean ± SD
NHL DLBCL	63	3.7	73	21 ± 16.6
Thyroid T cell lymphoma	4	4	37	15.5 ± 13.9
LBCL post germinal centre	1	12	36	24.4 ± 10
LBCL post follicular centre	2	20	26	23 ± 3
Burkitts	6	11.2	15	13 ± 1.9
MALT NHL variant	5	5.5	6	5.6 ± 0.4
Enteropathic T cell lymphoma	1	5	6	5.5 ± 0.3
HD HD interfollicular	3	20	27	23 ± 3.5
HD nodular sclerosis	5	18	22	20 ± 2
HD cellular phase of nodular sclerosis	4	18	20	19 ± 1
HD classic mixed cellularity	4	1.25	9	6.2 ± 3.3

NHL non-Hodgkin lymphoma, HD Hodgkin disease, DLBCL diffuse large B cell lymphoma, LBCL large B cell lymphoma, MALT mucosal-associated lymphoid tissue

staging in 10% of cases, because in the remaining cases there were other CT detected sites of extranodal involvement.

CECT showed five positive lesions at the liver and marrow; however, FDG uptake was only present in lymph nodes. Benign nature of these five lesions was confirmed by biopsy or MRI. Accordingly, PET/CT resulted in down staging of 5% of cases. This percentage was notably higher than that of Omur et al. where percentages of cases downstaged and upstaged based on PET-CT were 1.8% and 5.4% respectively [5].

In a prospective study made by Luminari et al. [6] that was conducted on 142 patients, PET/CT helped in upstaging and downstaging of 11% and 1% of patients respectively.

In Le Dortz et al.'s [7] study, which was a retrospective study on 45 patients, upstaged and downstaged cases were 8% and 0% respectively.

Cheson et al. [8] found that PET/CT resulted in a change in staging in 10–30% of cases.

If there is diffuse increased FDG uptake in any organ, it should be investigated for the presence of lymphoma either by MRI or biopsy [5].

SUV_{max} values for hottest LNs and extranodal organs were measured in patients with secondary lymphoma. Pearson's correlation was done and revealed significant positive moderate correlation ($r = 0.45$). On the other hand, in Omur et al.'s [5] study, they found a high positive correlation between SUV_{max} of highest FDG accumulating lymph node and extranodal sites ($r = 0.67$).

Table 4 Agreement between PET/CT and CECT in detection of extranodal lymphomatous involvement

Organ	Positive by PET CT	Positive by CE CT
Kidney	4	3
Adrenal	1	1
Muscle	4	3
Tonsil	3	1
Oropharynx	3	2
Nasopharynx	3	2
Thyroid	2	1
Parotid	2	2
Orbit	2	2
Brain	2	3
BM	14	6
Spleen diffuse	8	6
Spleen focal	22	4
Liver	7	9
Pancreas	1	0
Lung lesions	12	12
Effusion	0	2
Stomach	8	8
Small intestine	6	6
Peritoneum	1	1
Cutaneous nodule	5	5
Cardiac	2	2
Testicles	1	1
Breast	2	2
adenxa	1	1
Total	117	86

The importance of this data is that the highest SUV_{max} value of the lymph nodes can support the diagnosis of extranodal organ involvement by lymphoma over other benign conditions like inflammation or infection especially if the FDG is seen accumulated in the extranodal organ without mass effect. Organs with SUV_{max} that is close to the SUV_{max} of maximum 18FDG accumulating LN can be diagnosed as lymphomatous.

In the current work, the maximum FDG uptake was seen at NHL (DLBCL) followed by (large B cell lymphoma), while in HD, the maximum uptake was seen in HD interfollicular followed by HD nodular sclerosis. These results were in agreement with Schroder et al. [9], where the DLBCL, nodular sclerosis types showed the highest FDG avidity.

In NHL, the spleen is considered an extranodal organ while in HD, it is nodal. In the present study, the most commonly involved organ was the spleen (Fig. 2) seen in 30% of cases (22% focal and 8% diffuse infiltration). Ten

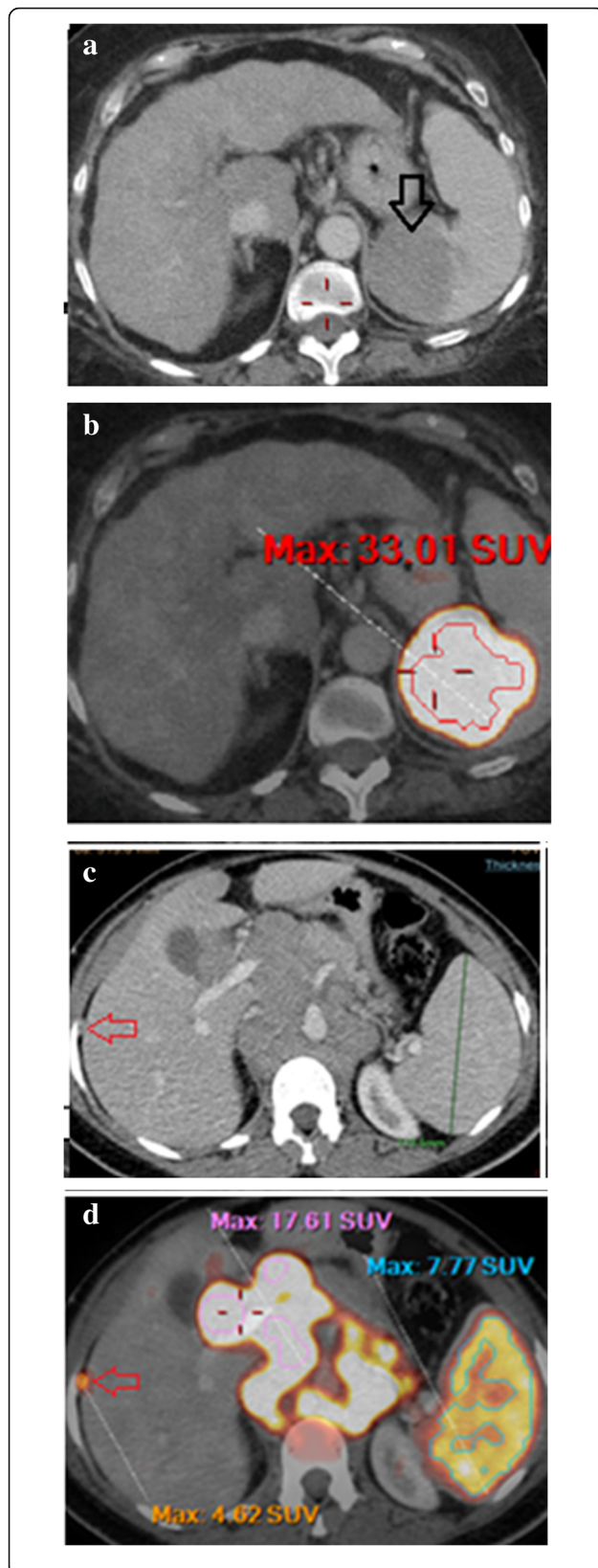


Fig. 2 Two different cases. **a, b** Focal splenic infiltration (black arrow). **c, d** Diffuse splenic infiltration in a patient with B cell lymphoma with normal size and attenuation of the spleen (**c**). Associated multiple retroperitoneal avid lymph nodes and a perihepatic peritoneal nodule (red arrow)

out of these 30 cases (30%) only were positive by CECT while the remaining were negative. These results clarify the importance of PET/CT in identification of splenic lymphoma in normal size and morphology spleen by CT. These results are keeping with the study made by Omur et al. [5] where CECT detected only 42% of all PET/CT detected cases.

In the current study, the second commonly involved extranodal after the spleen was head and neck. PET/CT discriminated between true infiltration and physiological FDG uptake at tonsils in two cases (2%) (physiological uptake is bilateral, symmetrical, of low grade, and without corresponding abnormalities on diagnostic CT). PET/CT depicts intense focal FDG uptake even in normal size tonsils and can differentiate between lymphoma and nasopharyngeal carcinoma, as the latter has predilection for transforaminal cranial extension. PET/CT can identify this extension [4].

Thyroid gland lymphoma was depicted in 2% of cases (1% secondary and 1% primary). The important differential is anaplastic carcinoma which has strong avidity to FDG and heterogeneous enhancement in diagnostic CT [1]. According to Sin et al. [1], diffuse but low-grade thyroid FDG uptake can be seen in other non-lymphomatous conditions such as reactive uptake, Hashimoto thyroiditis, and post-chemotherapy.

In the current study, the only involved salivary gland was the parotid (2%). There are FDG avid benign lesions in the salivary glands that show uptake even more than malignant lesions which are Whartins tumor and pleomorphic adenoma [10]. Sjogren's syndrome and lymphoepithelial sialadenitis predispose to lymphoma [4].

Orbital lymphoma was depicted in 2% of cases seen as FDG avid lesions involving the lacrimal glands bilaterally infiltrating the extraocular muscles sparing the optic nerve (Fig. 3). This agrees with Das et al.'s [4] study as they reported that optic nerve is not involved in lymphoma. Orbital lymphoma rarely erodes the bone [11, 12]. Interpretation of ocular lymphoma by PET/CT is challenging because of the physiological uptake of the nearby brain and the small volume of the lesion [13].

In the present study, 12% of cases showed pulmonary affection; all were NHL (Fig. 4a, b). This is keeping in agreement with Das et al. [4]; they reported that HD of the lung is rare and usually due to direct extension from a mediastinal or hilar mass. On the other hand, Metser et al. [14] found that lymphoma of the lung is three times more

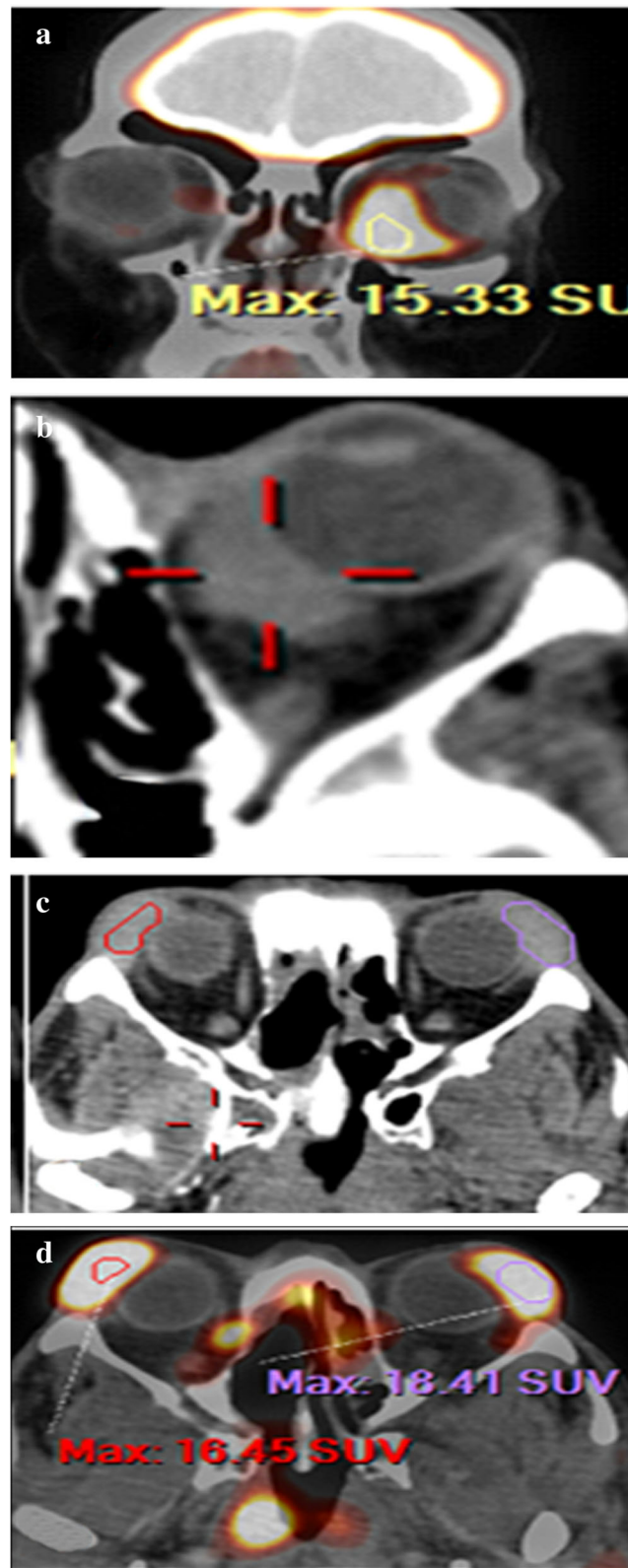


Fig. 3 Orbital lymphoma: two different cases. **a, b** A well-defined homogenous soft tissue lesion, pathologically proven NHL, occupying the infero-medial aspect of left orbital cavity, infiltrating the inferior and medial recti, sparing the optic nerve. **c, d** Bilateral intensely avid lacrimal gland infiltration

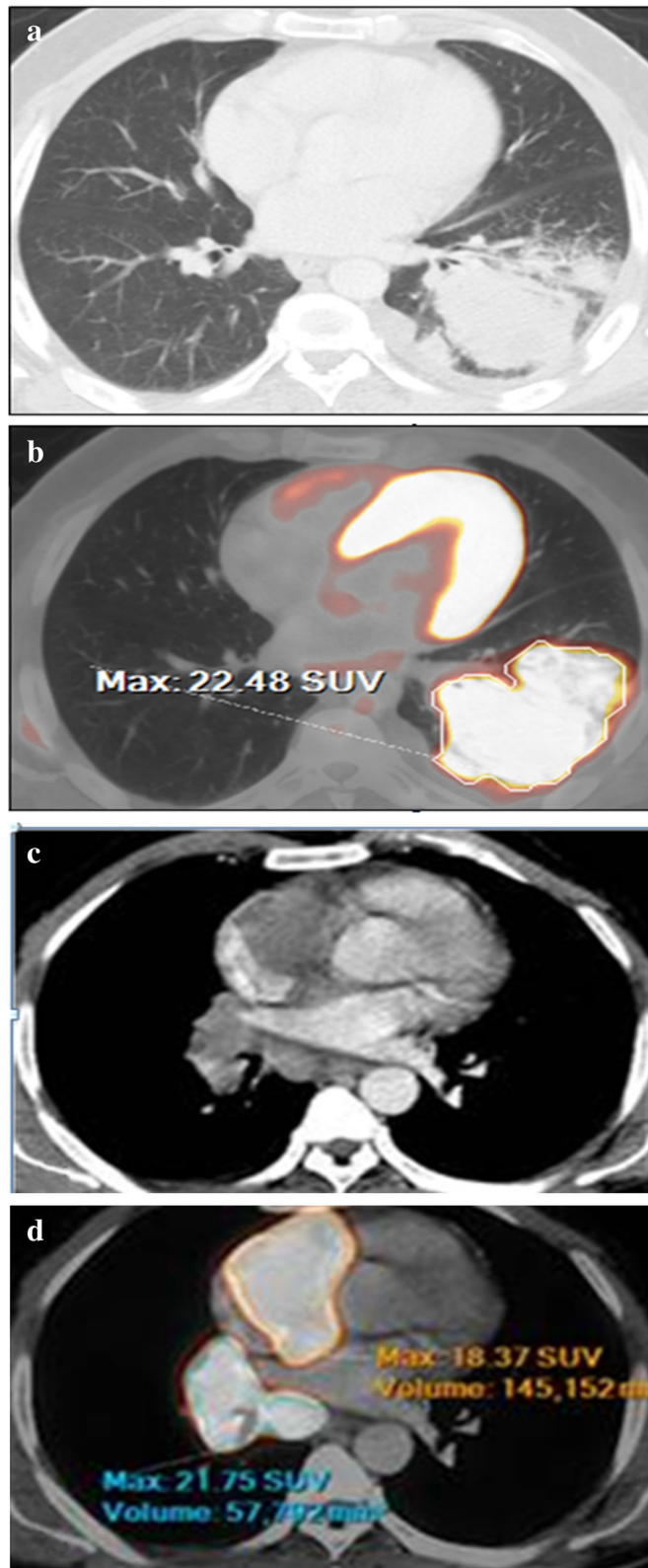


Fig. 4 a–d Thoracic lymphoma in two patients. Case 1 **a, b** lung lymphoma, B cell lymphoma **a** axial CT and **b** axial fused PET/CT image, showing a hypermetabolic lesion at the left lower lung lobe. Case 2 **c, d** cardiac lymphoma, DLBCL type **c** axial CT showing a large hypodense soft tissue mass within the right atrium presumed to be intra-atrial thrombus. In the axial fused PET/CT (**d**), it is intensely avid associated with subcarinal and right hilar avid lymphadenopathies

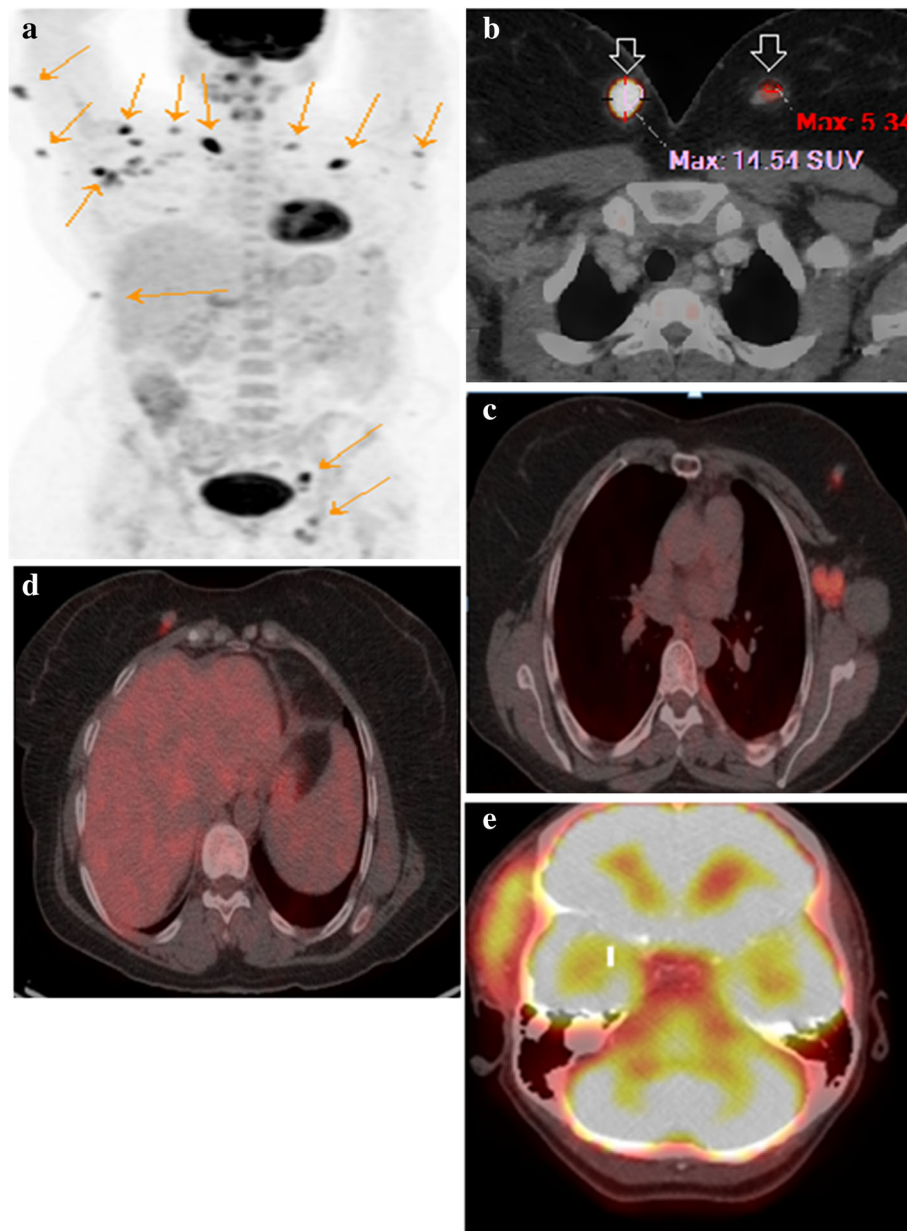


Fig. 5 a-d Breast lymphoma two different cases: case 1 **a, b** bilateral avid breast lesions (**b**, PET CT, white arrows), associated supra and infradiaphragmatic avid LNs and subcutaneous nodules (**a**, MIP image, orange arrows). Case 2 (**c, d**) showing bilateral small breast lesions with low-grade FDG uptake associated with avid axillary LNS and right temporal subcutaneous lesion (**e**)

frequent in HD more than NHL. Differentials include granulomatous disease or even second primary malignancy.

In the current study, PET/CT enabled discrimination between reactive and lymphomatous pleural effusion in 2% of cases. Active pleural effusion is seen as FDG avid focal pleural thickening, pleural plaques, or bulky masses. According to Sarah and Rodney [15], reactive effusion is more common and occurs secondary to lymphatic or venous obstruction by mediastinal lymph nodes and seen as a non-FDG avid pleural lining.

In the present study, we had 1% case with chest wall muscle lymphoma. According to Das et al. [4], chest wall invasion may be due to direct extension from internal mammary or mediastinal adenopathies [3, 4]. Chest wall lymphoma mandates aggressive treatment because of the high rate of recurrence [16].

One case (1%) presumed to have an intra-atrial thrombus; however, on combined PET/CT, it was seen as large hypermetabolic hypodense soft tissue mass within the right atrium encroaching upon the AV valve reaching the right

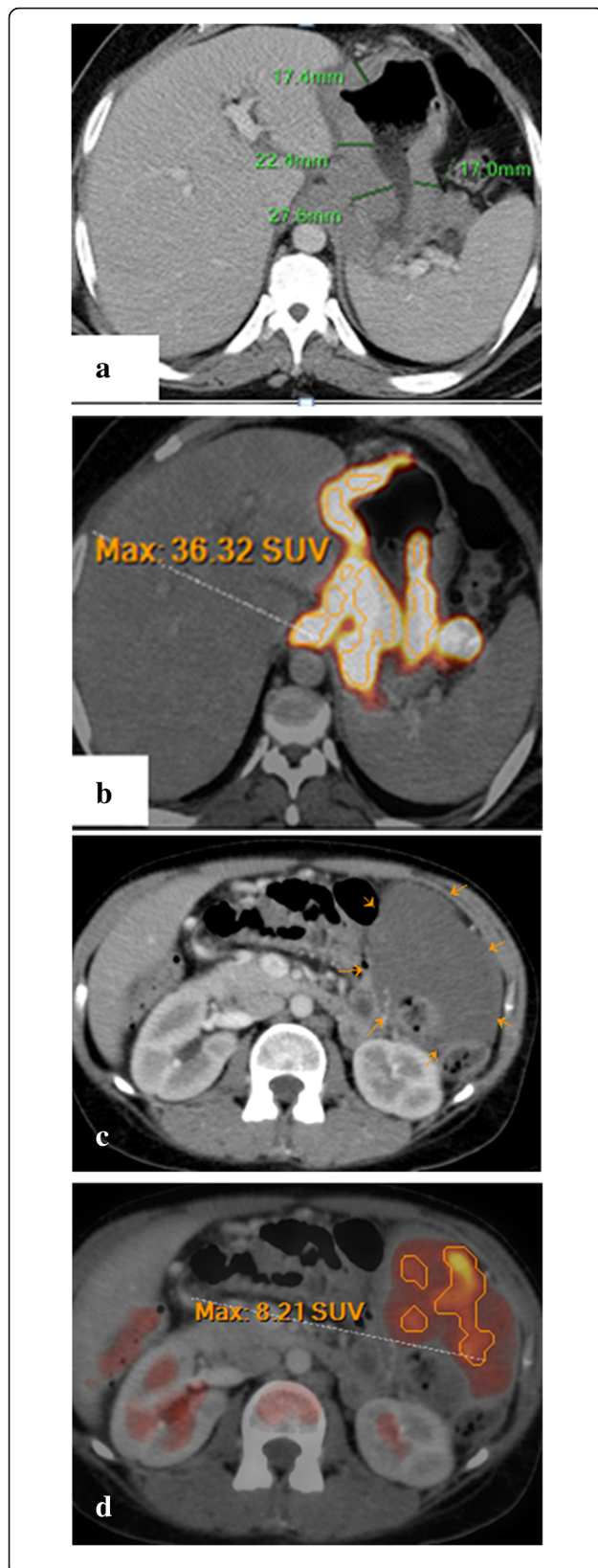


Fig. 6 a–d GIT lymphoma. **a, b** Gastric lymphoma: non-uniform soft tissue mural thickening of the gastric walls more pronounced at the lesser curvature. In PET CT images, **b** it is intensely avid, associated with small perigastric and gastrohepatic LNs having the same activity. **c, d** Peritoneal lymphoma: a large metabolically active left hypochondrial peritoneal soft tissue lesion [orange arrows] encasing the bowel anteriorly, the spleen and tail of pancreas posteriorly (not shown) (proven to be B cell lymphoma)

ventricle (Fig. 4c, d). These findings are in agreement with Mahajan et al., as they reported that the right atrium is most frequently involved. It is an oncologic emergency due to its rapid progression [17]. The interpretation of cardiac lymphoma is challenging as physiological uptake of FDG by the myometrium mask lymphomatous infiltration [18].

FDG avidity on PET/CT discriminates between cardiac lymphoma and other benign conditions including lipomatous hypertrophy of the interatrial septum, cardiac sarcoidosis, and myocarditis [17]. Presence of FDG avid pericardial effusion indicates lymphomatous infiltration [18].

The thymus is a nodal organ, so its involvement by lymphoma does not change the stage of the disease [2]. However, PET/CT is crucial in the differentiation between rebound thymic hyperplasia that develop following completion of chemotherapy (seen as low level FDG uptake anterior mediastinal mass with no active disease elsewhere in the body) from true active thymus lymphomatous infiltration (seen as focal intense FDG uptake). Thymic lymphoma retains the shape of the gland while enlarged mediastinal lymph nodes are lobulated [4].

In the current study, we found two cases (2%) of secondary breast lymphoma NHL (DLBCL subtype) seen as bilateral multiple masses associated with axillary lymph nodes and subcutaneous nodules (Fig. 5). According to Even et al., PET/CT is helpful in identification of breast lymphoma, because CT alone is not accurate for breast pathology and mammography is not routinely done in lymphoma staging [13]. According to Das et al. [4], age distribution of lymphoma has two peaks; one during pregnancy and lactation and is often high grade, the other is around the age of 50 and is usually solitary.

Normal physiological bowel uptake is a problem during interpreting PET/CT; however, higher uptake than the liver favors lymphoma [4]. GIT lymphoma is associated with risk factors like parasitic infection and inflammatory bowel disease [19]. In the current study, GIT was involved in 15% of cases. Four (4%) were primary lymphoma (3% NHL and 1% HD), and 11% were secondary lymphoma (10% NHL and 1% HD). These findings were in agreement with Sin et al. [1] who reported that secondary GIT lymphoma is relatively common while primary small bowel lymphoma is rare.

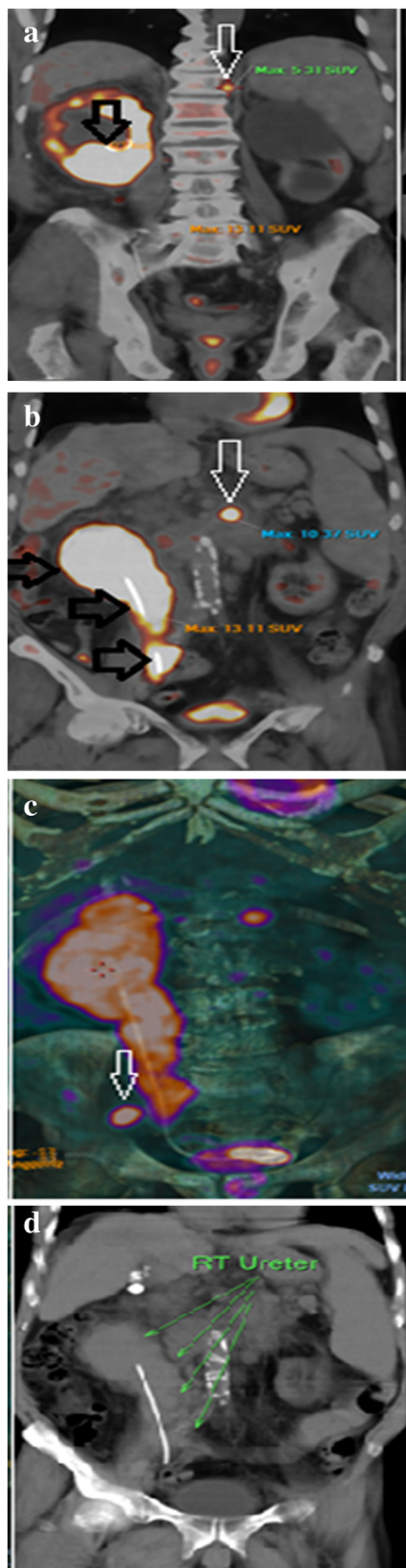


Fig. 7 RT renal and ureteric lymphoma: note intensely avid soft tissue mass lesion related to the lower pole of the right kidney and ureter. **a, b** PET CT images with corresponding 3D PET (**c**) and diagnostic component thick MIP (**d**), associated avid LT para aortic and LT retrocrural LNs (white arrows). Double J ureteric stent is seen

Gastric lymphoma was found in 8% of cases (7% NHL seen as diffuse mural thickening and 1% HD seen as exophytic masses) (Fig. 6a, b). This agrees with Paes et al. [2], who reported that the stomach was the most common involved part of the GIT.

In the current study, small bowel lymphoma was detected in 6% of cases [ileum (4%), jejunum (1%), and duodenum (1%)]. This was in agreement with Das et al. [4] who found that the incidence of involvement decreases proximally. Metser et al. reported that primary bowel lymphoma can be identified by intense FDG uptake in a short segment and in draining lymph node, while in secondary lymphoma, multiple segments are involved [3]. Peritoneal lymphomatous infiltration was seen in 1% of cases (Fig. 6c, d).

MALT lymphoma has predilection to the stomach while enteropathy-associated T cell lymphoma has predilection to the jejunum [1]. We encountered a case (1%) of the later type, which is commonly seen with celiac disease [20].

In the current study, all cases with hepatic lymphoma were secondary lymphoma. This is in agreement with Das et al. [4], where secondary lymphoma was more common. In the present study, two cases showed hepatic focal lesions based on CECT; however, no FDG activity was detected, and accordingly, these two cases were downstaged.

In the present study, we encountered one case (1%) with pancreatic lymphoma. According to Metser et al. [3], the presence of a large mass below the renal veins associated with peripancreatic lymph nodes suggests lymphoma rather than pancreatic adenocarcinoma.

Although the sensitivity of PET/CT for detection of renal lymphoma is low because FDG is normally excreted by the kidneys; however, the advantage of PET/CT is the ability to detect subtle lesions and the ability to diagnose lymphoma in diffusely enlarged kidney without focal lesions [4]. PET/CT detected lymphoma in 4% of cases (25% of these lesions were not detected on diagnostic CT) (Fig. 7). One case showed concomitant ureteric lymphomatous infiltration. Presence of renal affection indicates an aggressive form. Patterns of renal lymphoma are solitary, multiple hypodense masses, or diffuse infiltration [1].

In our study, PET/CT discriminated adrenal lymphoma from incidentaloma in 1% of cases. Lymphoma patients commonly have non-lymphomatous adrenal hyperplasia [3].

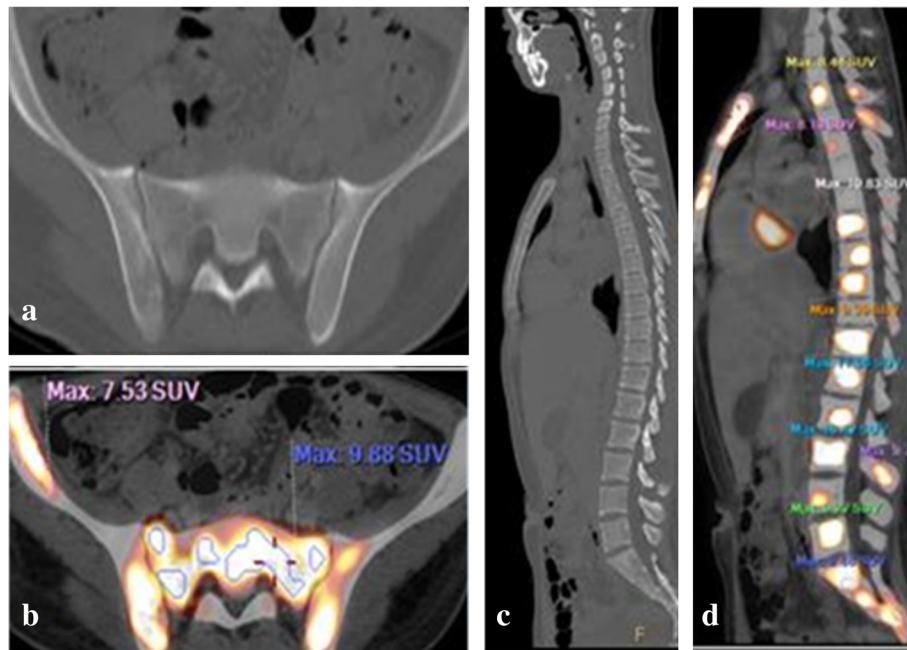


Fig. 8 a-d Hodgkin lymphoma cellular phase of nodular sclerosis (a, c) CT (b, d) fused PET/CT images showing hyper metabolic osseous lesions infiltrating the sacral ala, iliac bones (b) multiple vertebrae and sternum (d). The lesions were not detected in the diagnostic CT (a, c)

Lymphoma detection in the brain is challenging because of the physiological FDG uptake [4]. We depicted CNS lymphoma in (2%) of cases. Diagnosis of lymphoma is by MRI; however, PET/CT can differentiate it from non-FDG avid lesions like toxoplasmosis in immune-compromised patients and identify recurrence [12].

Primary osseous lymphoma is considered stage 1 disease, while secondary osseous lymphoma is considered stage 4 [2] (Fig. 8). In the current study, we encountered two cases (2%) of primary osseous lymphoma involving the appendicular system (patella 1% and tibia 1%) both were NHL. DLBCL was the most common histological subtype in both primary and secondary lymphoma.

Primary osseous lymphoma arises from flat bones and appendicular system while secondary lymphoma arises from the axial skeleton [4]. Bone marrow involvement is diffuse or focal, mono or polyostotic, the lesions could be lytic, sclerotic, or mixed. Sclerosis may be denovo or following radiotherapy [21]. Diffuse marrow uptake of FDG is seen after chemotherapy mainly by granulocyte colony-stimulating factor (G-CSF); this pattern is commonly associated with increased splenic uptake [21].

This study depicted cutaneous lymphoma in 5% of cases seen as FDG avid nodules. A pitfall in the diagnosis of cutaneous lymphoma is T cell lymphoma type, which is associated with mycosis fungoides that shows low FDG avidity [12].

Muscular lymphoma is focal or diffuse. Although Sin et al. found that primary lymphoma of the muscle is more common [1], in the current study, diffuse muscle affection was in 2% of cases and both were secondary lymphomas. The role of PET/CT is the identification of single or multiple foci that guide the biopsy. A pit fall in the diagnosis of muscle lymphoma is diffuse uptake due to vigorous muscle activity prior the study.

In the present study, we encountered testicular lymphoma in 1% of cases that was secondary lymphoma. Secondary lymphoma of the testis is more common than primary and indicates aggressive disease. The detection of testicular lymphoma is challenging due to the physiological uptake of FDG by the normal testis. However, concomitant affection of the spermatic cord, epididymis, skin, and CNS are common that may help the diagnosis of lymphoma [4]. In females, adenaxa is more commonly secondary affected by lymphoma than the uterus [4]. In the present study, 1% of cases had adnexal mass proved to be Burkitts lymphoma.

Conclusion

CECT should not replace PET/CT in lymphoma staging. ^{18}F -FDG-PET enables accurate detection of more unusual organs with extranodal lymphomatous infiltration that help in up or downstaging the disease. There is positive correlation between SUV_{max} of the extranodal lesions and hottest LN. Organ involvement and FDG avidity greatly depends on histopathological subtypes.

Abbreviations

CECT: Contrast-enhanced computer tomography; DLBCL: Diffuse large B cell lymphoma; FDG: Fluorodeoxyglucose; GCSF: Granulocyte colony stimulating factor; HD: Hodgkin disease; NHL: Non-Hodgkin lymphoma; PET: Positron emission tomography; SUV: Standardized uptake value

Acknowledgement

Not applicable

Ethical approval and consent to participate

The study was conducted according to the regulations of the ethical and scientific committee at our institute (Ain Shams University). Informed consents were obtained from all patients for participation with explanation of the procedure.

Authors' contributions

AA participated in data collection, image interpretations, statistical analysis, writing manuscript, editing, and supervision. MN participated in the design of study data collection and statistical analysis. MA participated in the design of study, data collection, and image interpretation. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to individual privacy but are available from the corresponding author on reasonable request.

Consent for publication

Consent for publication was obtained from all patients.

Competing interests

The authors declare that they have no competing interests.

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References

1. Sin KM, Ho SK, Wong BY, Gill H, Khong PL, Lee EY (2017) Beyond the lymph nodes: FDG-PET/CT in primary extranodal lymphoma. *Clin Imaging* 42:25–33
2. Paes FM, Kalkanis DG, Sideras PA, Serafini AN (2010) FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease. *Radiographics* 30:269–291
3. Metser U, Goor O, Lerman H, Naparstek E, Even-Sapir E (2004) PET-CT of extranodal lymphoma. *AJR* 182:1579–1586
4. Das J, Ray S, Sen S, Chandy M (2014) Extranodal involvement in lymphoma—a pictorial essay and retrospective analysis of 281 PET/CT. *Studies. Asia Oceania J. Nucl Med Biol* 2(1):42–56
5. Ömür Ö BY, Oral A, Ceylan Y (2014) Fluorine-18 fluorodeoxyglucose PET-CT for extranodal staging of non-Hodgkin and Hodgkin lymphoma. *Diagn Interv Radiol* 20:185–192
6. Luminari S, Biasoli I, Arcaini L, et al (2013) The use of FDG-PET in the initial staging of 142 patients with follicular lymphoma: A retrospective study from the FOLL05 randomized trial. *Ann Oncol* 24(8):2108–2112.
7. Le Dortz L, De Guibert S, Bayat S et al (2010) Diagnostic and prognostic impact of 18F-FDG PET/CT in follicular lymphoma. *Eur J Nucl Med Mol Imaging* 37:2307–2231
8. Cheson BD (2011) Role of functional imaging in the management of lymphoma. *J Clin Oncol* 29:1844–1854
9. Schöder H, Moskowitz C (2008) PET imaging for response assessment in lymphoma: potential and limitations. *Radiol Clin North Am* 46:225–241
10. Nassie DI, Berkowitz M, Wolf M, Kronenberg J, Talmi YP (2010) Parotid mass as presenting symptom of lymphoma. *Isr Med Assoc J* 12(7):416–418
11. Purohit BS, Vargas MI, Ailianou A, Merlini L, Poletti PA, Platon A et al (2016) Orbital tumours and tumour-like lesions: exploring the armamentarium of multiparametric imaging. *Insights Imaging* 7(1):43–68
12. Kashyap R, Mittal BR, Manohar K et al (2011) Extranodal manifestations of lymphoma on [18F] FDG-PET/CT: a pictorial essay. *Cancer Imaging* 11:166–174. <https://doi.org/10.1102/1470-7330.2011.0023>
13. Even-Sapir E, Liovshitz G, Perry C, Herishanu Y, Lerman H, Mester U (2007) Fluorine-18fluorodeoxyglucose PET/CT patterns of extra nodal involvement in patients with Non-Hodgkin lymphoma and Hodgkin's disease. *Radiol Clin N Am.* 45:697–709
14. Nieuwenhuizen L, Verzijlbergen FJ, Wiltink E, Grutters JC, Biesma DH (2008) A possible role of 18FFDG positron emission tomography scanning in the early detection of Rituximab-induced pneumonitis in patients with non-Hodgkin's lymphoma. *Haematologica* 93:1267–1269
15. Sarah JV, Rodney HR (2003) Reticuloendothelial disorders: lymphoma. In: Adam A (ed) Grainger & Allison's Diagnostic Radiology A textbook of Medical Imaging, 5th edn. Elsevier Limited, Philadelphia, pp 1733–1758
16. Guermazi A, Brice P, Kerviler ED, Ferme C, Hennequin C, Meignin V et al (2001) Extranodal Hodgkin disease: spectrum of disease. *Radiographics*. 21: 161–179
17. Mahajan SM, Maitra S, Singh N, Pereira M (2017) Extra nodal natural killer/T cell lymphoma with cardiac and abdominopelvic nodular deposits: unique presentation on 18-fluorodeoxyglucose positron emission tomography computed tomography scan. *Asian J Oncol* 3:74–77
18. Buchmann I, Wandt H, Wahl A, Reske SN (2003) FDG PET for imaging pericardial manifestation of Hodgkin lymphoma. *Clin Nucl Med.* 28:760–761
19. Ghimire P, Wu GY, Zhu L (2011) Primary gastrointestinal lymphoma. *World J Gastroenterol* 17(6):697–707
20. Zucca E, Conconi A, Cavelli F (2002) Treatment of extranodal lymphomas. *Best Pract Res Clin Haematol.* 15:533–547
21. Radan L, Fischer D, Bar-Shalom R, Dann EJ, Epelbaum R, Haim N et al (2008) FDG avidity and PET/CT pattern in primary gastric lymphoma. *Eur J Nucl Med Mol Imaging.* 35:1424–1430

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