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## PET-CT Diagnostic and Evaluation Role in Patients with Nodal Lymphoma

Ahmed Shaaban Hussain Muhammad

*Radio diagnosis department, Faculty of medicine, Al-azhar University, Cairo, Egypt., aatia91@yahoo.com*

Mahmoud Kadry Elguindy

*Radio-diagnosis department, Faculty of Medicine, Al-azhar University, Cairo, Egypt*

Muhammad Abol wafa Ahmed Amin

*Radio-diagnosis department, Faculty of Medicine, Al-azhar University, Cairo, Egypt*

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## ORIGINAL ARTICLE

# PET-CT Diagnostic and Evaluation Role in Patients with Lymphoma

Ahmed Shaaban Hussain Muhammad<sup>a,\*</sup>, Mahmoud Kadry Elguindy<sup>b</sup>,  
Muhammad Abol Wafa Ahmed Amin<sup>b</sup>

<sup>a</sup> Department of Radiodiagnosis, Nasser Institute Hospital, Egypt

<sup>b</sup> Department of Radiodiagnosis, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

## Abstract

**Background:** The most prevalent hematological malignancy is malignant lymphoma, which makes up ~8% of all adult malignancies. Non-Hodgkin lymphoma and Hodgkin disorder are two types of lymphoid neoplasms.

**Aim:** To examine how positron emission tomography/computed tomography (PET/CT) may be used to diagnose nodal lymphoma, analyze the effectiveness of 18-FDG-PET/CT in the first staging of nodal lymphoma, analyze the function of PET-CT in patient monitoring both during and after the therapeutic course, and examine the function of PET-CT in foretelling and spotting relapses.

**Patients and methods:** A total of 30 patients (12 females and 18 males; 11 Hodgkin disorder and 19 non-Hodgkin disorder) with histologically confirmed malignant lymphoma were enrolled in this investigation. They were split into three groups judging by the outcomes of the PET/CT examination.

**Results:** CT for diagnosis was compared with PET/CT results. The current study demonstrated the critical relevance of PET/CT in lymphoma staging, monitoring therapeutic response, and follow-up. The present investigation demonstrated the significance of 18F-FDG. When it comes to the early staging of lymphomas, PET/CT has shown to be a valuable tool in the treatment of lymphomas. PET/CT exhibited substantial effects on early and delayed therapy response evaluation.

**Conclusion:** The outcomes of the present research highlighted the value of 18F-FDG PET/CT as a technique for the first staging of lymphomas. Comparing PET/CT with diagnostic CT has major consequences for early and delayed evaluation of therapy response.

**Keywords:** Lymphoma, Nodal, Positron emission tomography/computed tomography

## 1. Introduction

Malignant lymphoma is the most frequent hematological malignancy, accounting for ~8% of all adult malignancies, whereas malignant pediatric lymphoma accounts for 10–15%.<sup>1,2</sup>

Modern imaging for lymphoma is positron emission tomography (PET) coupled with computed tomography (CT) in a single operation (PET/CT).<sup>3</sup>

For the diagnosis of nodal and extra-nodal lymphoma, FDG-PET/CT is crucial.<sup>4</sup>

Lately, PET/CT systems that allow for PET/CT data gathering in the same environment without repositioning the patient have been made available for use in clinical settings. On the fused PET/CT,

lesions are identified based on their anatomical characteristics and metabolic state. Such fusion may also help differentiate between physiologic and tumoral FDG uptake locations.<sup>5</sup>

For patients with early-stage lymphoma (stage I or stage II) who are managed with involved field radiation treatment, accurate staging is essential. Patients with early-stage lymphoma may benefit most from PET/CT before treatment; chemotherapy is administered to those with more advanced stages.<sup>1</sup>

The aims were to examine how PET/CT may be used to diagnose nodal lymphoma, analyze the effectiveness of 18-FDG-PET/CT in the first staging of nodal lymphoma, analyze the function of PET-CT

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\* Corresponding author.

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in patient monitoring both during and after the therapeutic course, and examine the function of PET-CT in foretelling and spotting relapses.

## 2. Patients and methods

**Type of study:** this was a prospective study.

**Study setting:** patients in the research underwent PET/CT scans for lymphoma staging and treatment evaluation at Nasser Institute Hospital in Cairo.

**Study population:** 30 cases of lymphoma had PET/CT scans for staging and treatment evaluation.

**Inclusion criteria:** all patients should have visible pathologically enlarged lymph node or mass lesion in initial CT examination; patients should undergo a physical examination; patients should undergo laboratory tests for lymphoma, including Lactate Dehydrogenase Enzyme (LDH), Erythrocyte Sedimentation Rate (ESR), and Complete Blood Count (CBC); and patients should have a histopathological diagnosis of lymphoma following biopsy, whether surgically or image-guided, to confirm the diagnosis and in situations where there is a possibility of disease relapse.

**Exclusion criteria:** patients who previously had surgery, radiation treatment, or chemotherapy for their lymphoma condition, women who were pregnant, and women of reproductive age who were suspected to be pregnant (they were advised to take a pregnancy test if they had any reason to suspect they could be pregnant).

**Ethical consideration:** no fabrication, falsification, or misinterpretation of authorship, evidence, data, findings, or conclusions of the patient was done. The findings and the practical significance of the study were communicated in clear, straightforward, and appropriate language. No influence was used on the patients to compel them to participate in the research, and before collecting any data or conducting any investigations, we obtained the patients' explicit written agreement.

**Consent forms** were signed after the following directives: all information was regarded as private and would not be utilized outside of this study without patient consent. All samples were used in the research exclusively. The study's objectives were explained in a way that the patients could understand. Participants were given the researcher's phone number and other contact information, and they had the right to withdraw from the study at any time without providing a reason. This would not have any bearing on their ability to receive the best care. All participants were informed of the study's findings.

**Study procedures** were performed after an informed consent.

Each patient was subjected to personal history taking, such as name, age, parity, profession, and any unique behaviors that are crucial for health; past history, such as information on current and former drug usage, history of any surgeries, and/or therapeutic head or neck irradiation, as well as information about family history (in first-degree and second-degree relatives) and/or other autoimmune disorders; and present history such as associated symptoms and current disease or medications.

**General examination:** vital signs (body temperature, breathing rate, pulse rate, and BMI, and blood pressure), weight, height, and abdominal circumference of participants were measured. BMI ( $\text{kg}/\text{m}^2$ ) was determined according to the following formula: body weight in kg divided by length in meter squared. BMI was determined for each participant, and physical tests of the limbs, chest, and heart were performed.

**Abdominal evaluations:** inspection and superficial palpation were performed.

**Methods:** the machine used was combined PET/CT (Siemens mCT 20, Cairo, Egypt, Germany) high-definition high-resolution (HiRez) machine.

**Imaging protocol:** we initially did a low-dose, nonenhanced CT scan to adjust for attenuation, then a whole-body PET study, then a diagnostic, fully-enhanced CT scan of the whole body.

### 2.1. Imaging technique

#### 2.1.1. Patient preparation

Before the scan, the patient was instructed to fast for 6 h. The patient was stripped of all metallic jewelry, including dentures, zippered trousers, bra, belts, bracelets, etc. For the administration of  $^{18}\text{F}$ -FDG, we placed an IV catheter (18 G cannula) in the patient's anti-cubital fossa. We also gave all our patients instructions to abstain from caffeine and alcohol. To prevent physiologic muscle absorption of FDG during this time, only water was permitted, and they were also told to refrain from any form of intense exercise in the days leading up to the test and immediately after the radioisotope injection. Additionally, the patient was instructed to urinate before scanning if they had diabetes. This is because diabetes competitively inhibits the uptake of FDG into cells, which uses a common transporter (glucose transporters) for enabling easier delivery into both healthy and cancerous cells. Serum glucose was routinely assessed before  $^{18}\text{F}$ -FDG administration, and it should be below 180–200 mg/dl. Regular insulin should not be given to diabetic individuals subcutaneously within 4 h after receiving FDG.

The contrast media was used to help distinguish between bowel loops and any lymph nodes or tumors in the abdominal and pelvic region. The bowel wall should be stretched. Oral contrast material was used on all patients in this research, and intravenous contrast material was used on 30 patients.

#### 2.1.2. 18F-FDG dosage administration

The patient received the 18F-FDG injection at a dose of 0.14 mCu/kg or as directed by the doctor. For the patient's cells to receive the FDG and be adequately biodistributed and delivered, the patient had to wait for 45–60 min after FDG administering. During this time, which is known as the uptake phase, patients were urged to keep their movements minimal and to relax in a quiet environment without any distractions, including talking, to a minimum. As a result, less FDG is physiologically absorbed into skeletal muscle, which might affect how the scan is interpreted.

#### 2.1.3. Patient position

They were shown how to use the PET-CT machine while laying on their back with their arms either at their sides or over their heads.

#### 2.1.4. Examination time

An improved whole-body CT examination is performed after a full body PET study (neck through pelvis). The CT scan takes around 60–70 s, whereas the PET scan takes about 20–30 min.

#### 2.1.5. Computed tomography technique

The level of the skull base is where a normal whole-body PET-CT investigation (neck, chest, belly, and pelvis) begins and terminates caudally, at the level of the symphysis pubis. Single-phase contrast material-enhanced images were obtained after 125 ml of a low-osmolality iodinated contrast medium (ioversol; Optiray 350) was injected at a rate of 4 ml/s using a power injector. The research is conducted with the patient breathing gently, and the total number of bed configurations scanned during the collection of PET data is crucial to the entire length of CT coverage. At 2.4-mm intervals, the helical data are retroactively rebuilt.

#### 2.1.6. Positron emission tomography technique

The same extended-length gantry houses the PET scanner, which is placed beneath the CT scanner. Without moving the patient, a PET scan is carried out after the CT scan. Six to seven bed positions are planned in the three-dimensional acquisition mode to scan the complete patient, with an acquisition

time of 5–7 min at each position. The table travels 11.5 cm after data capture at each bed position, and the greatest length of the patient that can be scanned with the current PET-CT scanner is 145 cm. Each bed position (in the cranio-caudal direction) is 15.5-cm long.

#### 2.1.7. Positron emission tomography/computed tomography fusion

Following the completion of the PET acquisition, the recreated attenuation-corrected PET images, CT images, and fused images of corresponding pairs of PET and CT images are accessible for review in axial, coronal, and sagittal planes and in maximum-intensity projections, three-dimensional cine mode, using the manufacturer's review station.

#### 2.1.8. Positron emission tomography/computed tomography interpretation

The original tumor, the existence of lymph nodes and distant metastases, and fused PET-CT and CT images were analyzed, and patients were staged utilizing TNM staging system's seventh edition.

### 3. Results

The Nasser Institute Hospital in Cairo served as the study's location. The research comprised 30 patients with lymphoma who had PET/CT scans between June 2020 and December 2021 (Tables 1–16).

Table 1. Sex of the studied group.

Sex	Frequency	Percent
Male	18	60
Female	12	40
Total	30	100

Table 2. Types of lymphoma of studied group.

Type of lymphoma	Frequency	Percent
HD	11	37
NHL	19	63
Total	30	100

HD, Hodgkin disorder; NHL, non-Hodgkin lymphoma.

Table 3. Histopathological classification of Hodgkin disorder cases in this study.

Subtypes of HD	n (%)
Nodular sclerosis	6 (55)
Mixed cellularity	2 (18)
Lymphocytic predominance	1 (9)
Lymphocytic depleted	1 (9)
Lymphocytic rich	1 (9)

HD, Hodgkin disorder.

Table 4. Histopathological classification of non-Hodgkin lymphoma cases in study.

Subtypes of NHL	n (%)
Large B cell	10 (53)
Follicular	5 (26)
Small lymphocytic	2 (11)
Marginal zone	1 (5)
Mantel cell lymphoma	1 (5)
Total	19 (100)

NHL, non-Hodgkin lymphoma.

Table 5. Relationship between non-Hodgkin lymphoma subtypes and SUV uptake.

Sub types of NHL	Mean SUV max
Large B cell	20
Follicular	6.5
Small lymphocytic	6.5
Marginal zone	6
Mantel cell lymphoma	11

NHL, non-Hodgkin lymphoma.

Table 6. Relation between Hodgkin disorder subtypes and SUV uptake.

Sub types of HD	Mean SUV max
Nodular sclerosis (NS)	25
Mixed cellularity (MC)	22
Lymphocytic predominance	11
Lymphocytic depleted	12
Lymphocytic rich	12

HD, Hodgkin disorder.

Table 7. Initial staging by computed tomography as opposed to positron emission tomography/computed tomography within the study group.

	PET/CT stages				Total
	1	2	3	4	
CT stages					
1	1	0	0	0	1
2	0	3	1	1	5
3	0	0	1	1	2
4	0	0	1	0	1
Total	1	3	3	2	9

PET/CT, positron emission tomography/computed tomography.

Table 8. Staging results of positron emission tomography/computed tomography in relation to computed tomography.

	N = 9 [n (%)]	P value
Down staging	0	
No change	7 (77.8)	0.004 <sup>a</sup>
Upstaging	2 (22.2)	

<sup>a</sup> Statistically substantial ( $P < 0.01$ ).

Table 9. Initial staging by computed tomography as opposed to positron emission tomography/computed tomography within the study group.

Stages	CT (N = 9)	PET-CT (N)
I	1	1
II	5	3
III	2	3
IV	1	2

PER-CT, positron emission tomography/computed tomography.

Table 10. Positron emission tomography/computed tomography results in the treatment assessment.

	Frequency	Percent
Complete regression	4	26.67
Partial regression	2	13.33
Stationary	0	0
Progression	9	60
Total	15	100

Table 11. CECT results in the treatment assessment.

	Frequency	Percent
Complete regression	4	26.67
Partial regression	2	13.33
Stationary	3	20
Progression	6	40
Total	15	100

Statistically substantial ( $P < 0.05$ ).

Table 12. Positron emission tomography/computed tomography results in follow up.

	Frequency	Percent
Complete regression	2	33.33
Disease relapse	4	66.67
Total	6	100

Table 13. PET-CT extra-nodal assessment in all studied group.

	N = 9
Spleen	3
Lung	1
Cautanouse	1
Suprarenal	1
Hepaic	2
Renal	1

Table 14. CECT results in follow up.

	Frequency	Percent
Complete regression	3	50
Partial regression	2	33.3
Stationary	1	16.67
Total	6	100

Table 15. Follow up results of positron emission tomography/computed tomography in relation to computed tomography.

	N = 6 [n (%)]	P value
Missed findings	0	
No change	2 (33.33)	0.006 <sup>a</sup>
Additional findings	4 (66.67)	

<sup>a</sup> Statistically substantial (P < 0.01).

Table 16. Positron emission tomography/computed tomography extra-nodal assessment in all studied group.

	N = 9
Spleen	3
Lung	1
Cutaneous	1
Suprarenal	1
Hepatic	2
Renal	1

#### 4. Discussion

A histologically diverse collection of malignancies arising from immune system cells is referred to as lymphoma. The growth and development of secondary lymphoid tissues or lymph nodes are the disease's defining features. Nearly every organ of the human body may be the source of either non-Hodgkin lymphoma (NHL) or Hodgkin disease. This unusual kind of lymphoid malignancy, in which neoplastic growth occurs at locations other than the anticipated native lymph nodes or lymphoid tissues, has been referred to as extra-nodal lymphoma.<sup>6,7</sup>

In patients with Hodgkin disease and NHL, FDG-PET has been routinely utilized for disease staging, recurrence identification, and therapy response monitoring. Contrast-enhanced CT may, however, only identify a small percentage of lymphomatous involvement in extra-nodal tissues, bone marrow, and lymph nodes that are normal in size. FDG-PET/CT has been useful for staging, restaging, and therapeutic monitoring, according to many studies.<sup>8,9</sup>

Age and sex: of the cases, we had 18 (60%) male cases and 12 (40%) female cases, with age between 14 and 79 years old. There were no substantial variations in results regarding age and sex.<sup>11</sup>

##### 4.1. Types and subtypes of lymphoma

Patients in the studied group were divided as follows: Hodgkin disease was present in 11 (37%) cases: nodular sclerosis (55%) and multiple cellularity (18%) were the most represented Hodgkin

disorder (HD) pathology subtypes in the studied groups. Other subtypes were lymphocytic predominance (9%), lymphocytic depleted (9%), and lymphocytic rich (9%). Non-Hodgkin's disease was present in 19 (63%) cases: large B cell (53%) and follicular (26%) were the most represented NHL pathology subtypes in the studied groups. Other subtypes were small lymphocytic (11%), marginal zone (5%), and mantle cell lymphoma (5%).

On initial staging, it was noted that when compared with CT alone, PET/CT was beneficial in detecting mostly advanced disease. This was shown primarily for NHL and Hodgkin Disease (HD) stages I and II. If the illness was previously classified as an advanced diagnostic stage III or stage IV, PET/CT may not have any extra benefit, just as CT.

Of the 30 patients in this study, nine cases came positive on initial staging. 18 F-FDG-avid subcentimetric lymph nodes were detected in two patients; these additional sites of lymphomatous involvement would have been missed if staging was done using CT alone. In seven patients, there were no changes in the staging as they were already stages I, III, and IV, whereas in two patients, the detection of the 18F-FDG-avid subcentimetric lymph nodes resulted in restaging of these patients from stage II into III and stage III.

PET-CT and CECT agreed on the first staging of seven (77.8%) of the nine cases in our research. However, PET-CT differed with CECT in the early stage of two (22.2%) instances; upstaging of two cases from stage II to stage III and IV was done. As in the previously reported research, the added utility of PET-CT in all of the upstaged patients was not in the discovery of active subcentimetric lymph nodes but rather in the identification of extra-nodal locations of illness that were not identified by CECT.

In our investigation, PET-CT outperformed CECT in terms of sensitivity and specificity. The primary advantage of PET-CT over CECT was its improved capacity for the identification of lymphoma extra-nodal locations. Results from the first staging PET-CT were statistically substantial (P = 0.004).

Evaluating response to therapy: PET is useful in assessing the effectiveness of treatment. It is often carried out after the end of treatment. An increasingly common practice in the treatment of patients with HD and histologically aggressive NHL is earlier evaluation. FDG uptake changes may occur quickly after the start of treatment and come before changes in tumor volume that are visible on morphological imaging modalities.<sup>2</sup>



In our research, PET/CT and CECT outcomes were concordant in nine of the 15 patients at initial follow-up during chemotherapy (60%) and discordant in the remaining six (40%) cases, detailed as follows:

CECT found stagnant course in three instances (20%), partial regression in two (13%) cases, total regression in four (26.6%) cases, and advancement in six (40%) cases, whereas PET/CT found steady course in 0 (0%) instances, advancement in nine (60%) cases, partial regression in two (13.3%) cases, and full regression in four (26%) cases. In the follow-up PET-CT scan conducted during therapy, the variation was less statistically substantial. On follow-up, in our research, CECT revealed total regression in three instances (50%) and partial regression in two (33.3%) cases, whereas PET/CT identified two (33.3%) cases of total regression, and disease return in four of six (66.67) cases.<sup>11</sup>

Regarding cases of relapse, the follow-up PET-CT scan months after the conclusion of treatment produced statistically substantial outcomes ( $P = 0.006$ ). In our investigation, PET-CT outperformed CECT in terms of sensitivity and specificity, which was consistent with the findings of previous comparable studies.<sup>11,12</sup>

The primary advantages of PET-CT over CECT were its greater capacity to identify and exclude active disease, as well as its capacity for early identification of relapse sites, which may also assist in guiding the biopsy operation in situations when histopathology is required.<sup>13,14</sup>

PET-CT nodal and extra-nodal assessment:

Similar to initial staging, the added usefulness of PET-CT in all patients was not in the identification of the active subcentimetric lymph nodes as in the previously reported research but in the identification of the extra-nodal sites of illness which were not identified by CECT. Of 30 cases in our study that came for initial staging, assessment of treatment, and follow-up, although PET-CT could detect additional number of subcentimetric FDG-avid lymph nodes than CECT only, yet it was not significant in all cases because of associated larger sized lymph nodes either in the same or other groups that could be detected also by CECT, hence no change in staging, CTH evaluation, or follow up, and therefore no change in strategy of treatment. In contrast, PET-CT can detect<sup>15,16</sup> extra-nodal additional findings than CECT in nine cases as follows: diffuse splenic infiltration in three cases, pulmonary infiltration in one case, suprarenal infiltration in one case, diffuse renal infiltration in one case, focal cutaneous involvement in one case, and hepatic involvement in two cases.<sup>17</sup>

## 4.2. Conclusion

The outcomes of the present research highlighted the value of 18F-FDG PET/CT as an effective technique for the first staging of lymphomas. In comparison with diagnostic CT, PET/CT has important implications for both early and delayed evaluation of therapy response. Owing to its great specificity, PET/CT enables reliable residual mass characterization and identifies active tumor tissue inside residual masses. In this age range, PET/CT was also helpful in identifying recurrent lymphoma in both HD and NHL.

## Conflict of interest

None declared.

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