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Utility of Positron Emission Tomography-Computed Tomography Imaging in The Management of Patients with Non-Hodgkin's Lymphoma

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Abstract

Introduction: Non-Hodgkin's Lymphoma is the most common hematologic malignancy worldwide, accounting for a significant portion of all lymphomas. Because FDG PET/CT can give accurate, non-invasive anatomical and functional data, it has recently become the standard clinical management imaging modality. Objective: To determine the role that positron emission tomography/computed tomography (PET/CT) performs in the initial staging and evaluation of treatment response in NHL patients. **Patient and Methods:** This was A retrospective cross-sectional monocentric observational study in which 109 patients where the diagnosis of non-Hodgkin lymphoma have been pathologically confirmed. All patients were examined using Siemens Bio-graph true point PET/CT scanner. These dedicated systems integrate a PET scanner with multi-slice helical CT scanners permit the acquisition of co-registered CT and PET images in one session. **Results:** Most of the samples were male, amounting to 68.5%. with a mean age of 43.43±15.03 years old. PET/CT detected 109 total involved different sites with sensitivity 94 %, specificity 87%, and accuracy 98 % which was larger than sites detected by CT. Regarding to treatment response assessment, PET/CT detected complete regression (83.5%), partial regression (17 %) stationary course (0.9%) and progression (0 %) while CT detected complete regression (80.7%), partial regression (18.3 %) stationary course (0.9%) progression (0%). **Conclusion:** Compared to CT, PET/CT showed better sensitivity and specificity. PET/CT's primary advantage was its improved capacity to identify additional lymphoma nodal sites and rule out active disease in nodal mass lesions that remained after follow-up.

Keyword: Non-Hodgkin's Lymphoma, positron Emission Tomography, Computed Tomography, Fluorodeoxyglucose

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INTRODUCTION

Non-Hodgkin lymphomas (NHLs) represent a heterogeneous group of lymphoproliferative disorders characterized by different clinical courses, varying from mild to highly aggressive [1]. Approximately 5% of all cancer cases are non-Hodgkin lymphoma cases. Most cases are non-Hodgkin lymphomas, which also tend to spread more widely to places other than nodes [2]. People with lymphoma still often do not have a response to treatment, which leads to relapses, despite significant advancements in this area [3]. The CT-

based response assessment, the FLIPI (prognostic score for follicular lymphoma), and other pre-treatment prognostic indices are not very good at identifying these patients. New prognostic and predictive indicators that enable the early identification of patient categories at high risk are therefore urgently required [4,5]. Pretreatment staging, restaging, therapy monitoring, post-therapy surveillance, and transformation assessment are the several recent PET/CT applications in lymphoma [6]. Finally, prognostication and early treatment escalation or de-escalation in response-adapted or risk-adapted treatment are frequently achieved with interim PET/CT, which is essential for evaluating treatment response between therapeutic cycles [7]. Few recent studies have assessed the lesion SUV max of early-stage interim FDG PET/CT in the management of lymphoma diagnostically; the results are still unclear and call for more research [8]. This study aimed at highlighting the role of PET/ CT performs in the management of lymphoma and determining the initial staging and evaluation of treatment response in NHL patients.

Patients and Methods

This study was conducted in the Department of Hematology, Baghdad Teaching Hospital Medical City, Baghdad, Iraq. It was a retrospective cross-sectional analysis. A review was conducted on the non-Hodgkin lymphoma (NHL) patient data from September 2023 to April 2024. Patients with NHL who were admitted to the hospital made up the study sample. Any patient who met the inclusion criteria had to undergo a medical examination and have their lymphoma tested in a laboratory. To diagnose lymphoma pathologically, biopsies were performed on each instance. Table 1 presents demographic information such as age range, gender, and risk factors. Pregnant women, patients with hepatic or renal failure, severe acute or chronic respiratory or circulatory failure, and general contraindications for a CT scan (e.g., allergic reaction to contrast material) were excluded. Out of 126 NHL patients, 100 were selected based on meeting the inclusion and exclusion criteria.

The following details were included in the prepared questionnaire that the researchers created using the data that the registered patients provided, which was gathered from their recorded hospital records: NHL features (stage, histology, hemoglobin (Hb), and white blood cell [WBC] count), as well as basic patient characteristics (age and gender), interim PET/CT scan results (positive or negative). The doctor used the WHO criteria to diagnose NHL based on a lymph node biopsy [9].

Image Analysis

Every PET/CT scan was examined by two qualified observers who work as radiologists and nuclear medicine doctors. During the initial trials, the PET and CT images were analyzed for residual/recurrent abnormalities during/after therapy, as well as for the presence and extent of 18F-FDG in different nodal and extra-nodal regions. The maximum standardized uptake value (SUV max) of FDG was measured at lesions that were discovered by applying a circular ROI with an average diameter of approximately 2 cm over the lesion's most active region. The CT criteria for lymph nodal involvement were defined as short-axis diameter greater than 10 mm and/or long-axis diameter greater than 15 mm; the CT criteria for extra-nodal involvement were defined as the presence of any mass lesions or changes in focal density. Using fused PET/CT images, all lesions found on CT scans were reevaluated for SUV max estimation and association with FDG uptake.

Statistical Analysis of Data

Version 26 of the Statistical Package for Social Science (IBM SPSS) entered, coded, and modified the data. For the quantitative data with parametric distribution, the data were given as mean, standard deviations, and ranges; for the qualitative data, the numbers and percentages. The Chi-square test was used to compare two groups with qualitative data. The paired sample t- test was used to compare two groups with quantitative data and one way ANOVA was utilised to compare two groups with quantitative data and parametric distribution. ROC curve was used in measuring sensitivity, specificity, and accuracy of each technique of NHL patients. The margin of error allowed was set at 5%, and the confidence interval was set at 95%. So, the P-value was considered significant as $P > 0.05$.

Results

During the study period, 109 patients with varying ages and stages of various kinds of NHL were gathered. In this study, there were more male patients than female patients (69% vs. 31%). A majority of the research subjects (65%) were in stage II. The age distribution was 3–78 years old, with a mean age of 42.89 ±15.48 years (Table 1). Pre-treatment, during chemotherapy, and post-planned treatment CT and PET-CT were performed on all 109 patients.

Table 1: Demographics of the patients

Variables	
Age (Mean±SD)	43.43±15.03
Gender (n%)	
Male	75(68.8%)
Female	34(31.2%)
Stage (n%)	
Stage I	24(22.0%)
Stage II	74 (67.9%)
Stage III	10 (9.2%)
Stage IV	1 (0.9%)

A significant change ($p \leq 0.05$) was observed in the SUV max range of 0.0 – 30.0 with a mean value of 7.74±4.41 SD in the follow-up examination of the patients referred for follow-up assessment, whose SUV max of the initial PET/CT examination ranged from 3 – 27 with a mean value of 13.51±5.59 SD (Table 2).

Table 2: Descriptive of the studied cases according to SUV max value

	SUV Baseline	**SUV Follow-Up**	**t**	**P**
SUV max			17.501	0.000*
Min. – Max	3-27	0-20		
Mean ± SD	13.51±5.59	7.74±4.41		

t, p: t and p values for **paired sample t- test** for comparing between baseline and follow up

*: Statistically significant at $p \leq 0.05$

The most common NHL pathology subtypes in the group under study were follicular (40.4%) and large B cell (56.9%) (Table 3).

Table 3: Histopathological classification of NHL cases in study

Subtypes of NHL	**Frequency**	**Percent**
Large B Cell	62	56.9
Follicular	44	40.4
Small Lymphocytic	1	0.9
Marginal Zone	0	0.0
Mantel Cell Lymphoma	2	1.8
Total	109	100

Compared to indolent follicular and marginal zone lymphomas, large B cell lymphoma exhibited a high SUV max in almost all instances recorded (Table 4).

Table 4: Relation between NHL subtypes and SUV uptake

Subtypes of NHL	Mean SUV max
Large B Cell	19.00
Follicular	8.76
Small Lymphocytic	5.71
Marginal Zone	0
Mantel Cell Lymphoma	15.50

PET/CT indicated greater sensitivity 94%, specificity 87%, and accuracy 98% for the detection of total lesions compared to CT's sensitivity 91%, specificity 81%, and accuracy 93%, respectively (Table 5) (Figure 1).

Table (5): Diagnostic performance of CT and PET/CT scans

Parameters	CT			PET/CT		
	Sensitivity	Specificity	Accuracy	Sensitivity	Specificity	Accuracy
Total Mean	91	81	93	94	87	98

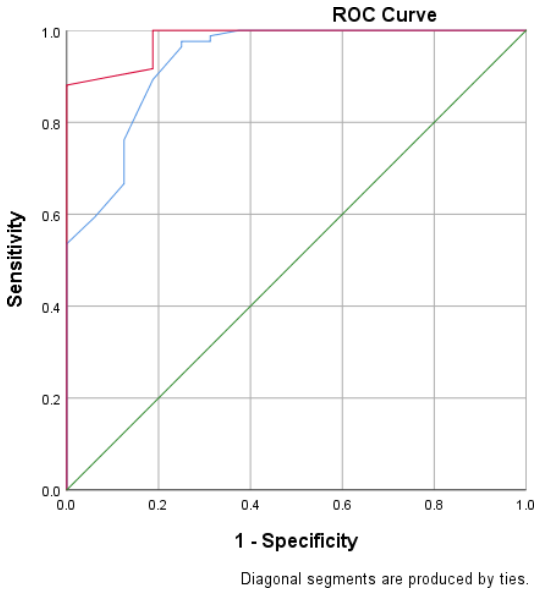


Figure 1: Receiver operating characteristic curve of maximum standard uptake value (red solid line) in distinguishing accuracy of PET/CT from CT in non-Hodgkin lymphoma patients. The green solid line is the reference line.

Twenty-four patients were classified as stage I by CT, while two patients were diagnosed as stage II by PET-CT. Seventy of the patients had stage II CT diagnoses, while two had stage III PET-CT diagnoses. Nine of the patients had stage III diagnoses from CT; these same individuals had stage III diagnoses from PET-CT. Between NHL stages, there was a statistically significant difference between PET/CT and CT (Table 6).

Table 6: Changes in staging according to Lugano classification between CT and PET/CT

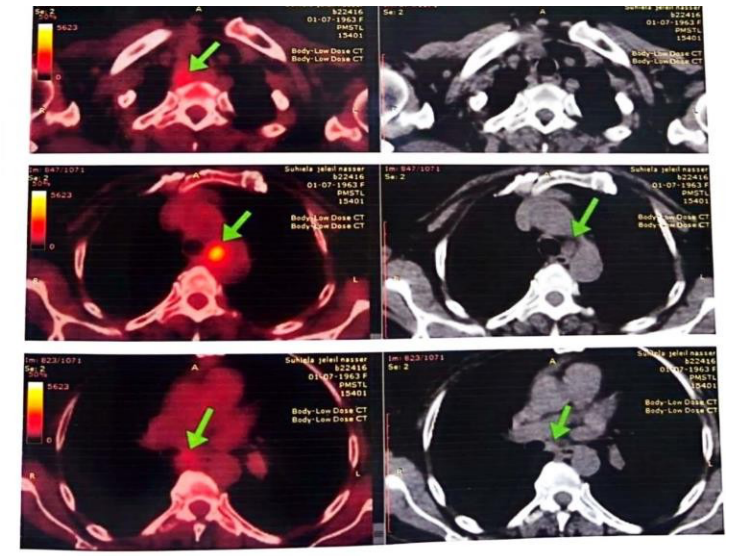
		CT STAGE			Total	Chi square test	P-value
		Stage I	Stage II	Stage III		X^2	
PET/CT STAGE	Stage I	24	0	0	24	176.80	0.000*
	Stage II	2	70	2	74		
	Stage III	0	1	9	10		
	Stage IV	0	0	1	1		
Total		26	71	12	109		

X^2: Chi square test p: p value for comparing between PET/CT and CT

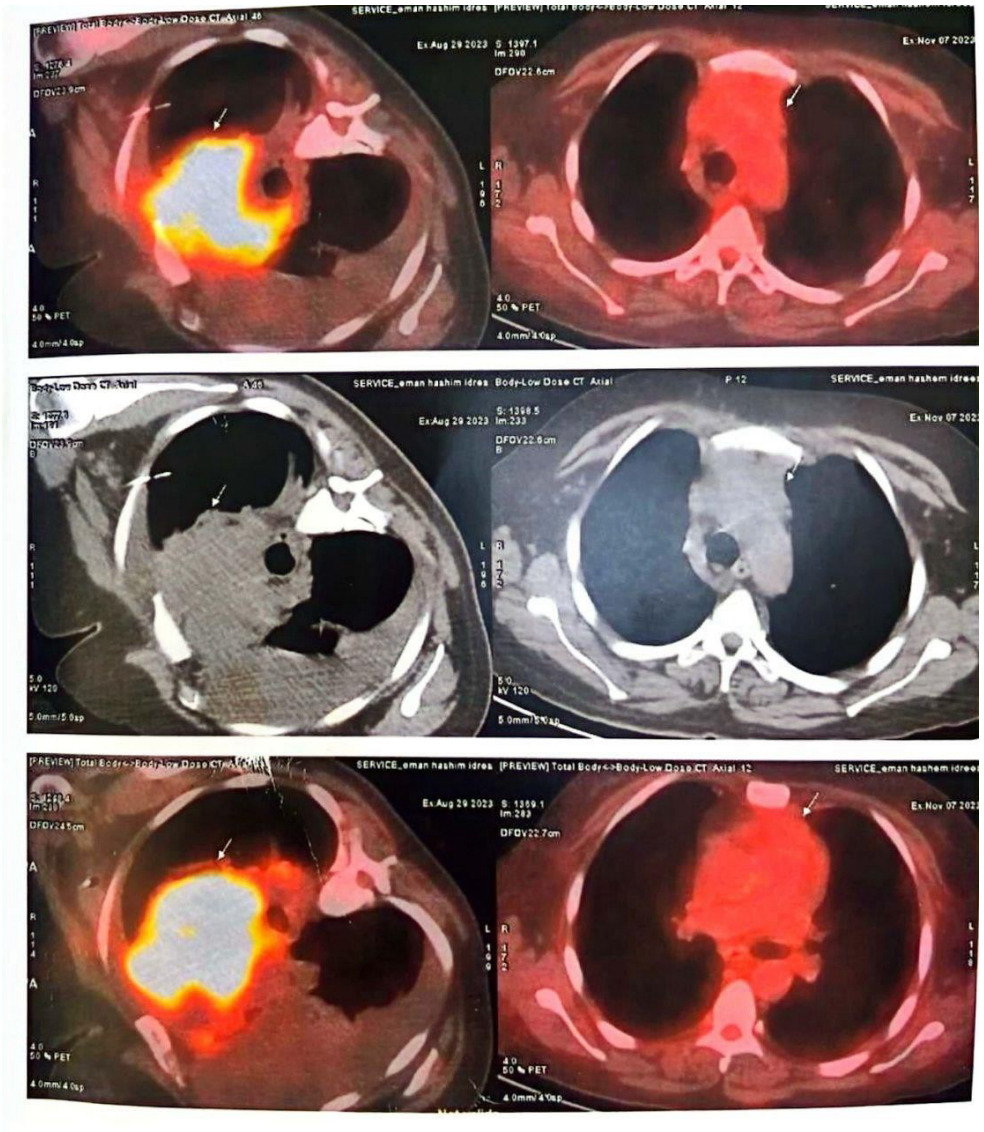
In contrast to PET/CT, which showed entire regression (83.5%), partial regression (15.6%), stagnant course (0.9%), and progression (0%), CT detected complete regression (80.7%), partial regression (18.3%), and progression (0%) (Table 7).

Table 7: PET/CT and CT results in the assessment of treatment response

Treatment Response CT			Treatment Response PET/ CT		
	Frequency	Percent		Frequency	Percent
Complete regression	88	80.7	Complete regression	91	83.5
Partial regression	20	18.3	Partial regression	17	15.6
Stationary course	1	0.9	Stationary course	1	0.9
Progression	0	0.0	Progression	0	0.0
Total	109	100.0	Total	109	100.0



Case 1: 61 years old female with FDG avid right superior mediastinum, left paratracheal and bilateral hilar lymph nodes are seen, largest measuring 12x11mm, SUVmax 4.1 -no interval change in size.



Case 2: resolution of metabolic activity with regression in size of previously seen large lobulated soft tissue mass in anterior and superior mediastinum involving right upper paratracheal, paraaortic, perivascular, pre and paracardial region. in present study metabolically inactive ill define soft tissue lesion is seen in perivascular and paraaortic region score I measuring 3.9x3.7x3.3cm previously 10x8.4x15.4 cm

Discussion

Approximately 4% of adult cancer cases are lymphomas, which are the most common primary haematological malignancy. 18F-FDG Both nodal and extra-nodal lymphomatous infiltration could be found with PET/CT, which made it possible to precisely stage, plan treatment, evaluate patient response, and alter therapy. The management of malignant lymphoma has made accurate, non-invasive anatomical and functional data from PET a gold standard due to efforts to standardise its acquisition and reporting. Efforts to standardize PET acquisition and reporting have enabled it to become a gold state of the art in the management of malignant lymphoma providing accurate, non-invasive anatomical and functional data [10]. Numerous studies have evaluated the usefulness of PET/CT in assessing the treatment response in lymphomas. In this study, we assessed the usefulness of PET/CT and CT in assessing response in lymphoma patients both during and after treatment. The current study included 109 patients who were referred for an initial assessment of non-Hodgkin lymphoma. The baseline SUV max ranged from 3.0 to 27.0, with a mean value of 13.51±5.59 SD; the follow-up SUV max ranged from 0.0 to 20.0, with a mean value of

7.74±4.41 SD. All NHL types were statistically significant ($p \leq 0.05$). It was observed that there was a significant change (p 0.046) in the SUV max range from 0.0 – 28.0 with a mean value of 11.73 9.25 SD in the follow-up examination, which was not in line with the findings of ELsheikh, Attia, and Kotb (2022). Their baseline SUV max PET/CT examination ranged from 3–49.0 with a mean value of 11.73 ± 9.25 SD [11].

The majority of big B cell lymphoma cases in our analysis had high SUV values, whereas the mean SUV max for indolent follicular and marginal zone lymphomas was 19, the mean SUV max for large B cell lymphoma was 8.76, and the mean SUV max for follicular lymphoma was 15. This was consistent with the findings of Halfawy, Ebrahim, and Mohamed (2023), who discovered that aggressive and indolent B-cell non-Hodgkin lymphoma differed markedly in their SUV max values of FDG [12]. In comparison to those diagnosed by CT, which had sensitivity of 91%, specificity of 81%, and accuracy of 93%, our study's conforming PET/CT discovered 109 implicated regions overall with sensitivity of 94%, specificity of 87%, and accuracy of 98%. According to Zytoon et al. (2020), 545 involved regions were diagnosed by PET/CT, which was higher than the number of regions detected by CT. Of these, 439 involved regions had sensitivity of 87.5%, specificity of 85.7%, and accuracy of 88% [13]. In this study, all of the cases were coming in for initial staging; in 75% of the cases, 18F-FDG PET/CT and CT agreed on the staging, while in 25% of the cases, 18F-FDG PET/CT disagreed with CT. Our study's concordant staging between 18F-FDG PET/CT and CT were very similar to that found by Omar, Alotaify, and Abolela [14]. When it comes to lymphoma staging, PET/CT tends to upstage rather than downstage tumours, which has an impact on both the staging and the therapy protocol [15]. According to Othman et al. (2019), following PET/CT, 10% of the patients were upstaged and 5% were downstage. [16].

In our study, the results of PET/CT and CT were discordant in 18% of cases and concurrent in 82% of cases. Whereas PET/CT detected complete regression in 83.5%), partial regression in 15.6%, stationary course in (0.9%), and no progression, CT detected entire regression in (80.7%), partial regression in 18.3%, and no progression. ELsheikh, Attia, and Kotb (2022) evaluated the early response to chemotherapy in their study; in 33.3% of them, the results of the CT and PET/CT were not consistent: 29.4% of them had false positive results on the CT, while the PET/CT revealed complete remission [11].

Ninety percent of patients who underwent an 18F-FDG PET scan showed concurrent positive results from CT and PET. Only ten percent of patients showed both positive and negative results from PET/CT, and all of these patients had lymphoma relapse confirmed by histological analysis. In HL and aggressive NHL, with or without residual masses on CT, 18F-FDG PET conducted after treatment is significantly predictive of progression free survival and overall survival, according to numerous studies. Functional imaging using 18F-FDG PET appears to be able to distinguish between viable lymphoma cells and necrosis or fibrosis in residual masses following treatment, as well as evaluate the earlier metabolic alterations rather than the morphological changes of the lymphoma. These results led to the development of the International Harmonisation Project PET scan review standards, which were based on visual interpretation and meant for end-of-treatment assessment [17]. First of all, our study is small-scale and monocentric, which limits its applicability. Second, the scans were quite expensive, and the recompense from health insurance was insufficient. Lastly, the availability of FDG isotope tracer is restricted.

Conclusion

In patients with NHL, PET/CT has a greater sensitivity and accuracy. In follow-up trials after chemotherapy, PET/CT was statistically more effective because the standard uptake value (SUV), which measures the functional activity of remaining tumour cells rather than the tumor's size, was more closely correlated with the former.

Abbreviations

18F-FDG	18F-Fluorodeoxyglucose
PET	Positron emission tomography
CT	Computed tomography

SUV	Standardized uptake value
ROC	Receiver operating characteristic
NHL	Non-Hodgkin lymphoma
AUC	Area under the ROC curve
CI	Confidence interval
Hb	Haemoglobin
WBC	White Blood Cell
WHO	World Health Organization
IBM SPSS	Statistical Package for Social Science
ANOVA	Analysis of Variance
SD	Standard Deviation

Declarations

Ethics approval and consent to participate

No ethics approval was required as this was a retrospective study based on previously published database. No subjects were involved in the study this no consent was required.

Consent for publication

Not applicable.

Availability data and materials

The datasets supporting the conclusions of this article is available in data repositories.

Competing of interest

The authors declare that they have no competing interests to this work.

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Author contributions

Shahad A. Ibraheem and Abdullah Dhaifallah Almutairi and khalid Mohammed kelis are contributed to the study concepts and design. Abdullah Dhaifallah Almutairi and Shahad A. Ibraheem contributed to the literature research. Shahad A. Ibraheem contributed to the data analysis and statistical analysis, manuscript preparation and manuscript editing. All authors have read and approved the final manuscript.

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The authors declare that they had full access to all of the data in this study and the authors take complete responsibility for the integrity of the data and the accuracy of the data analysis.

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