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ORIGINAL ARTICLE

Role of Fluoro-2-Deoxy-D-Glucose Positron Emission Tomography with Computer Tomography (FDG-PET/CT) in Evaluation of Extranodal Lymphoma

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ABSTRACT

Background: Combined PET/CT using 18F could be very effective with minimal hazards as well as false findings compared to the use one of these components alone in assessment of lymphoma. The purpose of this study was to review the usefulness of FDG PET/CT in diagnosis and staging of lymphoma, assessment of response to therapy, follow up and assessment of remissions and relapses among patients who had extranodal lymphoma.

Methods: This cross-sectional study involved 36 patients who had pathologically confirmed lymphoma who underwent PET/CT study. A PET/CT in-line system was used to collect all of the data (General Electric PET CT Discovery). Prior to conducting a diagnostic enhanced whole-body CT scan, we conducted a low-dose enhanced CT scan, then a whole-body PET study.

Results: The study compared the efficacy of contrast-enhanced CT and PET/CT in detecting lymphoma manifestations in 36 patients. PET/CT showed high sensitivity (100%) in detecting lymph node involvement and other extranodal manifestations, with varying specificity. Treatment response was evaluated using International Harmonization Project (IHP) and visual assessment based on the Déauville Criteria, showing a high level of agreement between the two methods.

Conclusion: One promising oncologic imaging modality that could play a significant role in lymphoma care is a PET/CT combination that using 18F-FDG. In the early interim and after treatment ended, response assessments based on the Deauville criteria seemed to agree with IHP classifications to a reasonable degree.

Keywords: Fluoro-2-Deoxy-D-Glucose Positron Emission Tomography, Computer Tomography, Extranodal Lymphoma.

INTRODUCTION

Hematological malignancies like lymphomas can develop anywhere outside of lymph nodes. Lymphadenopathy, whether localized or widespread, with or without involvement of the spleen or bone marrow, is a common imaging result [1]. When lymphomatous infiltration occurs at locations outside of lymph nodes, this is called extranodal disease [2]. Extranodal lymphomas have been more common in Egypt during the past 20 years, contributing to the country's fifth-highest cancer incidence rate overall [3].

CT imaging captures anatomical details but can struggle to differentiate between healthy and diseased tissues with similar densities, limiting its sensitivity and specificity. In contrast, PET utilizes radioactive tracers to visualize metabolic activity, providing functional information that complements CT's anatomical data. By combining PET with CT, clinicians gain a more comprehensive understanding of disease processes [4]. Radiotracers are labeled

with a short-lived positron-emitting radioisotope. A number of radioisotopes have been used for PET imaging. Fluoro-2-deoxy-D-glucose (FDG) is the most widely used PET radioisotope [5]. FDG PET imaging detects tumor metabolism, aiding in identifying extranodal damage. PET/CT combines PET with CT, compensating for PET's limitations in discerning benign from inflammatory tissues by accentuating glucose metabolic activity. This integrated approach improves pathology detection and characterization for more accurate diagnoses [6]. Combining computed tomography (CT) with positron emission tomography (PET) increases sensitivity and specificity in tumor imaging, while enhancing specificity first and foremost [7]. Consequently, compared to the sum of its parts and, likely, to seeing pictures from both modalities side by side, PET/CT provides a more accurate assessment [8]. A more hardware-oriented method of image fusion, the combined PET/CT scanner has made it possible to obtain functional and anatomically registered pictures in a single examination [9]. Improving lesion characterization and localization enhances diagnosis accuracy, while the significance of disease staging and restaging accuracy lies in its potential to influence patient care by reducing invasive procedures when warranted [10].

The study aims to assess the utility of FDG PET/CT in the initial diagnosis and staging of lymphoma, evaluating treatment responses, monitoring progress, detecting remissions or relapses, and identifying recurrence. It emphasizes the advantages of integrating PET and CT modalities through an in-line PET/CT system, highlighting the benefits of combining both modalities rather than relying on either one independently.

PATIENTS AND METHODS

Patients:

This cross-sectional was carried out from first of January 2023 to the end of June 2023 at the Radio-diagnosis Department, Faculty of Medicine, Zagazig University to obtain a representative variety of cases. Patients included in our study were referred from the oncology department. Thirty-six cases were enrolled in the study, 24 males and 12 females, aged between 20 and 78 years old. Verbal and written informed consents were obtained from all participants after an explanation of the procedure and medical research. The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for human research. This study was carried out after the approval of the Institutional Review Board (IRB#10095/6-11-2022).

Our final sample size included 36 cases; 36 patients divided into four subgroups based on their pathological examination, PET/CT findings and treatment as follows: Group I included 8 patients with pathologically confirmed Lymphoma with primary extranodal involvement, came for initial staging by PET/CT exams, Group II included 5 patients with pathologically confirmed Lymphoma, came for pre-treatment staging, interim follow up assessment by PET/CT exams, Group III included only 15 patients whom underwent interim PET/CT for response assessment after mid treatment, Group IV included 8 interim patients that ended treatment and were seen in our institution for end of treatment PET/CT for relapse/response assessment.

Methods:

Patient population:

After reinterviewing the adult patients and reviewing the goal and end points of the study, all patients were subjected to Complete history taking, clinical examination.

Patient preparation: A six-hour fast was required of all patients before the scan. Before being given a gown to wear, patients were asked to remove any metallic objects from their bodies, such as jeans with zippers or belts. To administer 18F-FDG, an indwelling intravenous cannula was placed in the patient's arm. Serum glucose levels were regularly checked; The ideal fasting plasma glucose levels should range from 70 to 200 mg/dl, One hour prior to the examination. If plasma glucose was higher than 200 mg/dl, the FDG PET CT study was rescheduled. Patients with diabetes shouldn't take their regular insulin within four hours of having FDG administrated. Serum glucose was routinely measured prior to 18F-FDG injection and fasting levels should be 70–200 mg/dl. Usually, we did not inject insulin to reduce blood glucose level (this leads to greater muscle uptake), but in few cases insulin can be considered (depending on the trials being conducted). In this condition PET-CT study should be postponed and we inject rapid acting subcutaneous insulin. Each patient received one liter of a negative oral contrast agent containing 5% mannitol. Between 55 and 75 minutes prior to the examination, they were given 5MBq/Kg of 18F-FDG.

Patient Position: The optimal patient positioning depended on the area of interest. Generally, the patients were positioned arms up with head to

thighs in the gantry iso-center with arms down, we started with a low-dose, non-enhanced CT scan, then moved on to a whole-body PET scan, and finally finished with a diagnostic, enhanced CT scan of the entire body. The entire research process lasted about twenty to thirty minutes.

CT Technique

Patient weight (1ml/kg) was used to establish the contrast dose. The optimal method for administering intravenous contrast agent with a 20Gx1.16 catheter was a programmed fluid injector operating at 2.5 ml/sec (if located in the elbow).

In a standard PET-CT scan of the entire body (neck, chest, belly, and pelvis), the scanner moves from the base of the head all the way down to the level of the upper thighs (except if dedicated brain imaging was indicated). In a typical scanning setup, the gantry rotation time is 0.8 seconds, the field of view is 50 cm, the collimator width is 5.0 mm, and the pitch is 1.5. In a retroactive process, the helical data were reconstructed at one-millimeter intervals.

PET Technique:

After the CT scan, the patient shouldn't be moved for the PET scan. In three-dimensional acquisition mode, there are around six or seven planned bed positions for scanning the entire patient, with three to five minutes of acquisition time at each position.

PET/CT Fusion

The study began by generating hundreds of trans-axial PET and CT scans, which were then rearranged into sagittal and coronal formats for clarity. Fusion images were created by merging PET and CT data sets to facilitate interpretation. Integrated PET/CT scans required approximately 25 minutes for acquisition. Co-registered images were displayed using specialized software after PET image data sets were reconstructed using CT data for attenuation correction. Post-therapy PET scans were conducted 4-6 weeks after surgery or chemotherapy and 8-12 weeks after radiation therapy or immunotherapy.

Experienced observers from nuclear medicine and radiology reviewed all PET/CT scans, examining various lymph node groups for 18F-FDG-positive lymphoma, extra-nodal disease involvement, and structural residual soft-tissue abnormalities. Patients were categorized using the Ann Arbor system, and response evaluations were conducted using the Deauville criteria and updated Cheson's recommendations. Lesions visible on PET/CT scans, based on combined morphologic CT and 18F-FDG uptake criteria, were investigated for nodal and extra-nodal disease. Abnormal 18F-FDG uptake was determined by radiotracer accumulation exceeding background activity, excluding physiological uptake due to symmetry or normal positioning.

Interpretation of the PET/CT findings

According to the IHP (international harmonization project)

A PET scan was considered positive if a residual mass measuring 2 cm or larger in greatest transverse diameter (GTD) exhibited 18F-FDG activity visually greater than that of structures in the mediastinal blood pool. Residual masses measuring 1.1 to 1.9 cm were deemed positive only if their activity exceeded the surrounding background. Even smaller residual masses or lymph nodes of normal size (<1 × 1 cm) were considered positive if their activity surpassed the background. Liver or spleen lesions smaller than 1.5 cm on CT scans were deemed positive for lymphoma if their uptake equaled or exceeded that of the liver or spleen, otherwise negative. Lung nodules measuring 1.5 cm or larger were considered positive for lymphoma if their FDG uptake exceeded that of the mediastinal blood pool. A patient was classified as PET positive if the bone marrow showed a clearly multifocal increase in FDG uptake [11].

According to the modified Deauville Criteria definitions:

The National Comprehensive Cancer Network (NCCN) recommends FDG PET scans for both initial staging and assessing residual masses post-therapy. Additionally, the NCCN-modified Deauville scores primarily rely on reevaluation of initially avid sites [11].

Assessment of treatment response:

Complete response (CR): Complete metabolic response (CR) was defined as scores 1, 2, or 3 in the absence of FDG-avid bone marrow lesion(s), regardless of the presence or absence of a persisting mass on CT.

Partial response (PR): if the following conditions are met: there was no structural advancement on CT, or uptake was lower than baseline; or the Deauville score was 4 or 5.

Stable disease (SD), FDG uptake remained unchanged from baseline with a Deauville score of 4 or 5, also known as no metabolic response.

Progressive disease (PD): an FDG-avid focus that is new and/or a growing Beauville score of 4–5 relative to baseline or any intermediate scan, all of which are indicative of malignant lymphoma.

STATISTICAL ANALYSIS

Range, median, standard deviation, number of instances, and percentages were used for statistical data description when applicable. Using the Kruskal-Wallis analysis of variance (ANOVA) test, we compared the research groups on quantitative factors. In order to compare two sets of categorical data, the Chi-square test was used. For anticipated frequencies below 5, an exact test was substituted, and a p-value of less than 0.05 was deemed statistically significant. Data analysis and statistical computations were carried out using SPSS (Statistical Package for the Social Science) version 21 for Microsoft Windows and Microsoft Excel 2019 for Windows.

RESULTS

We included 36 patients, 24 patients were males (66.6 percent), while 12 patients were females (33.33 percent). At time of presentation of patients in each group, we found that 2.77% presented stage II-E, 5.55% presented stage II-S, 8.33% presented II-E, 11.11% presented stage III-S, 22.22% presented III-E, 11.11% presented III-SE and 38.88% presented stage IV. One of three possible locations for lymph nodes were either supra- or infra-diaphragmatic, or both. Involvement of supra-diaphragmatic lymph nodes was seen in 4 out of 36 patients, infra-diaphragmatic lymph nodes in 2 patients, and combined involvement of both supra- and infra-diaphragmatic nodes in 30 patients (Table 1).

In our study, twenty individuals had many extranodal affection sites, while sixteen patients had just one. Twelve patients developed splenic involvement, eleven had osseous involvement, nine had hepatic involvement, twelve displayed lung nodules, two had renal affection, four had muscle lesions, three had pleural affection, and four had gastrointestinal tract involvement, 4 patients showed cutaneous nodules, 4 patients had nasopharyngeal affection, 1 patient had salivary gland involvement, 2 patients showed tonsillar affection, and 2 patients had adrenal affection and finally only one patient had one of thyroid, breast, and CNS involvement, each extra nodal site was calculated separately in each study group (Table 2).

Comparison between CT only and PET-CT showed that PET-CT revealed high significant sensitivity of 100% (P-value <0.001) in detection of lymph node involvement, spleen involvement, bone marrow involvement, and other extra-nodal affection with specificity of 66.6%, 85.6 %, 93.7 %, and 76.9 % respectively (high specificity in all except for detection of lymph node) (Table 3).

On the basis of the IHP after early interim, overall, 16 out of 20 patients had concordant designations (87.5%, 100%, 71%, and 50%) and 4 patients had discordant designations. On the basis of the IHP after late interim, overall, 18 out of 20 patients had concordant designations (100%, 100%, 67%, and 50%) and 2 patients had discordant designations. On the basis of the IHP after end of treatment, overall, 18 out of 20 patients had concordant designations (100%, 100% and 80%) and only 2 patients have discordant designations (Table 4).

A 17-year-old male patient, presented with history of colonic lymphoma underwent right hemicolectomy, the patient performed last PET/CT 2 years ago, and now referred for PET/CT follow up (Figure 1).

A 53-year-old female patient, with pathologically proven gastric B-cell lymphoma, came with gastric pain and dyspepsia, she referred for assessment and staging by PET CT examination (Figure 2).

Table 1: Patient's characteristics, Type of lymphoma, staging of the patients at time of presentation Different sites of lymph nodes involvement in the studied groups

Characteristics	Patients group (n= 36)	
Age (years)		
Range	20-78	
Mean ± SD	51.47 ± 14.70	
Gender		
Female	12 (33%)	
Male	24 (67%)	
Type of lymphoma	**Frequency**	**Percentage**
NHL	27	75%
HD	9	25%
Total	36	100%

Staging	Group I	Group II	Group III	Group IV	Total no.	Percent
I-E	1	0	0	0	1	2.77%
II-S	1	0	1	0	2	5.55%
II-E	1	0	0	2	3	8.33%
III-S	0	0	2	2	4	11.11%
III-E	1	2	3	2	8	22.22%
III-SE	1	0	2	1	4	11.11%
IV	3	3	7	1	14	38.88%
Sites of lymph nodes groups	Number of patients					Percent %
Supradiaphragmatic and infra diaphragmatic	30					83.3 %
Infra diaphragmatic	2					5.5 %
Supradiaphragmatic	4					11.1%
Total lymph node affection	36					100 %
Total	36					100 %

SD: Standard Deviation, NHL: Non-Hodgkin lymphoma, HD: Hodgkin Disease

Table 2: The different sites of the extra-nodal disease in study groups

Sites of extra-nodal disease	No. of patients in Group I	No. of patients in Group II	No. of patients in Group III	No. of patients in Group IV	total Number of lesions	Percent %
Spleen	3	3	5	1	12	33.3
Bone marrow & osseous	1	4	5	1	11	30.5
Liver	3	2	3	1	9	25
Pulmonary nodules	2	1	6	3	12	33.3
Renal	1	0	1	0	2	5.5
muscular	0	1	2	1	4	11.1
pleural	1	0	2	0	3	8.3
GIT	1	1	2	0	4	11.1
cutaneous	0	0	4	0	4	11.1
nasopharyngeal	2	0	0	2	4	11.1
salivary Gland (Parotid gland)	1	0	0	0	1	2.8
Tonsils	0	1	1	0	2	5.5
adrenal	0	0	2	0	2	5.5
thyroid	0	0	1	0	1	2.8
breast	0	0	1	0	1	2.8
CNS	0	0	0	1	1	2.8

GIT: Gastrointestinal Tract, CNS: Central Nervous System

Table 3: Comparison between detection of lymph node, splenic involvement, bone marrow lesions, other extranodal affection by CT and PET CT in all patients included in the study

Detection of lymph nodes					
CT	**PET CT (Diagnostic test)**			**Kappa**	**P value**
	Positive	**Negative**	**Total**		
Positive	**30 (TP)**	**0 (FP)**	**30**	**0.254**	**0.0001****
Negative	**2 (FN)**	**4 (TN)**	**6**		
Total	**32**	**4**	**36**		
Detection of Splenic Involvement					
CT	**PET CT (Diagnostic test)**			**Kappa**	**P value**
	Positive	**Negative**	**Total**		
Positive	**8 (TP)**	**0 (FP)**	**8**	**0.610**	**0.001****
Negative	**4 (FN)**	**24 (TN)**	**28**		
Total	**12**	**24**	**36**		
Detection of Bone marrow Involvement					
CT	**PET CT (Diagnostic test)**			**Kappa**	**P value**
	Positive	**Negative**	**Total**		
Positive	**4 (TP)**	**0 (FP)**	**4**	**0.259**	**0.006****
Negative	**2 (FN)**	**30 (TN)**	**32**		
Total	**6**	**30**	**36**		
Detection of extranodal affection					
CT	**PET CT (Diagnostic test)**			**Kappa**	**P value**
	Positive	**Negative**	**Total**		
Positive	**10 (TP)**	**0 (FP)**	**10**	**0.254**	**0.037***
Negative	**6 (FN)**	**20 (TN)**	**26**		
Total	**16**	**20**	**36**		
	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
LN	30\30 (100%)	4\6 (67%)	30\32 (94%)	4\4 (100%)	**34\36 (94%)**
spleen	8\8 (100%)	24\28 (86%)	8\12 (67%)	24\24 (10%)	**32\36 (89%)**
BM	4\4\ (100%)	30\32 (94%)	4\6 (67%)	30\30 (100%)	**34\36 (94%)**
Other extranodal	10\10 (100%)	20\26 (77%)	10\16 (63%)	20\20 (100%)	**30\36 (83%)**

Data are expressed as number (percent).
TP: true positive; FP: false positive; TN: true negative; FN: false negative.
NS= p> 0.05= not significant.

Table 4: Different sites of lymph nodes involvement, Stages, and Extranodal affection in group II & III.

Characteristics	Patients group (n= 20)
Age (yrs)	
Range	20-78
Mean ± SD	51.47 ± 14.70
Gender	
Female	6 (30%)
Male	14(70%)

Characteristics	Number	Percent
II S	1	5
III E	5	25
III S	2	10
III SE	2	10
IV	10	50

Characteristics	No.	Percent
One site extranodal affection	9	45
More than one site extranodal affection	11	55

Table 5: Concordance of response designations between (IHP) and Deauville after early, late interim and after end of treatment in groups II & III

		IHP after early interim			
		CR (n= 8)	PD (n= 3)	PR (n= 7)	SD (n= 2)
Deauville after early interim	CR (n= 9)	7 (87.5%)	0(0%)	2 (29.0%)	0 (0%)
	PD (n= 4)	0 (0%)	3 (100%)	0 (0%)	1 (50%)
	PR (n= 6)	1 (12.5%)	0 (0%)	5 (71.0%)	0 (0%)
	SD (n= 1)	0 (0%)	0 (0%)	0 (0%)	1 (50%)
	Data are expressed as number (percent).				

		IHP after late interim			
		CR (n= 9)	PD (n= 6)	PR (n= 3)	SD (n= 2)
Deauville after late interim	CR (n= 9)	**9(100%)**	0 (0%)	0 (0%)	0 (0%)
	PD (n= 7)	0 (0%)	**6 (100%)**	0 (0%)	1(50.0%)
	PR (n= 2)	0 (0%)	0 (0%)	**2(66.6%)**	0 (0%)
	SD (n= 2)	0 (0%)	0 (0%)	1 (33%)	**1 (50%)**
	Data are expressed as number (percent).				

		IHP after end of treatment			
		CR (n= 11)	PD (n= 3)	PR (n= 5)	SD (n= 1)
Deauville after end of	CR (n= 11)	11(100%)	0 (0%)	0 (0%)	**0 (0%)**
	PD (n= 5)	0 (0%)	3 (100%)	1 (20%)	**1 (100%)**
	PR (n= 4)	0 (0%)	0 (0%)	4 (80%)	**0 (0%)**
	Data are expressed as number (percent).				

CR: complete remission, IHP: international harmonization project, CT: computed tomography, PR: partial remission, SD: stable disease, PD: progressive disease

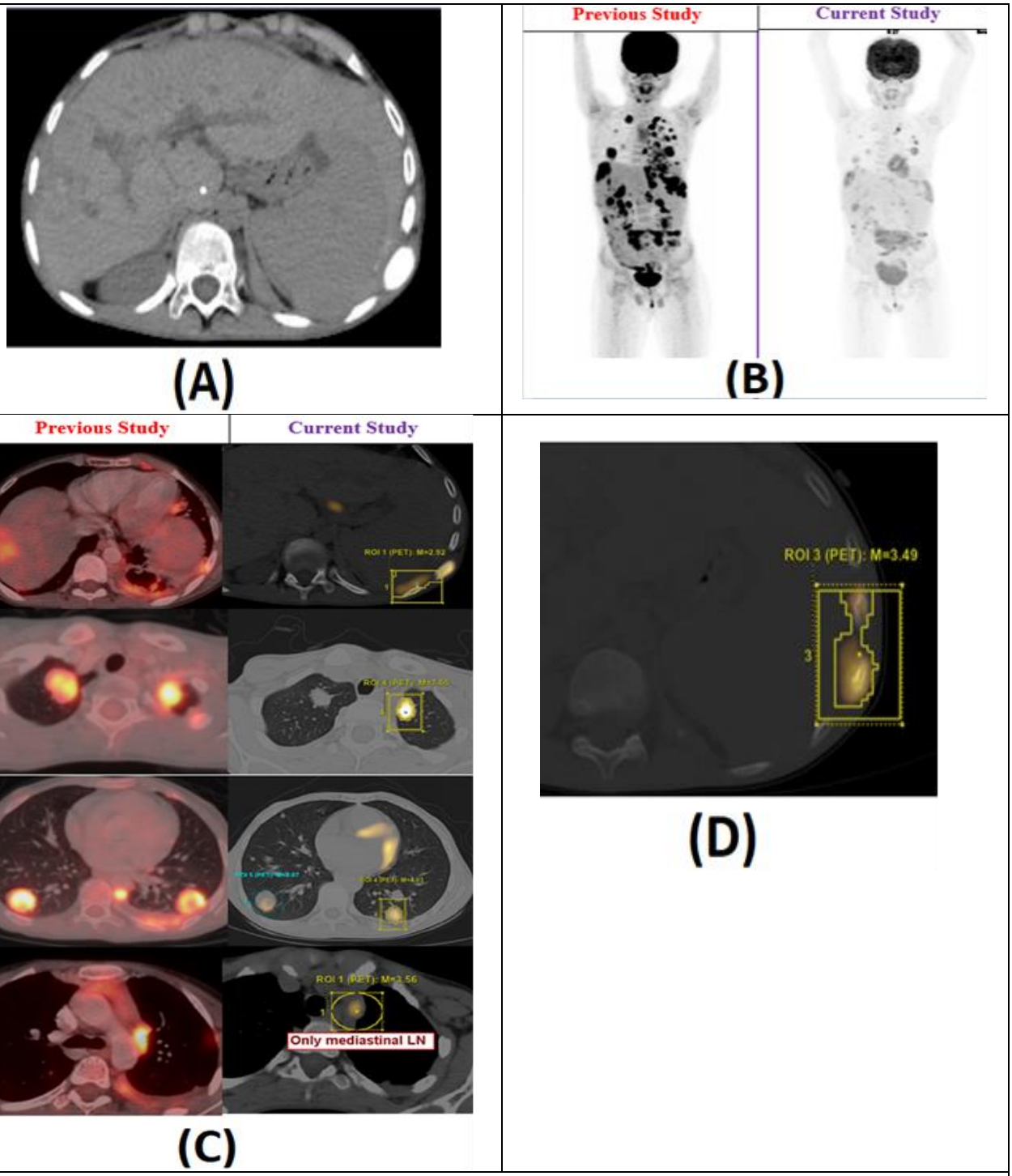

Fig. 1. (A) Axial CT chest shows hyperdense lesion at left 8th rib. (B, C) showing significant regression in the size and activity in comparison to the previous study denoting partial regression. (D) shows Newly developed two hypermetabolic sclerotic osseous lesions at left 8th and 9th ribs, the most active of them achieving SUV max up to 5 at left 9th rib (pathologically proven to be Non-Hodgkin's lymphoma).

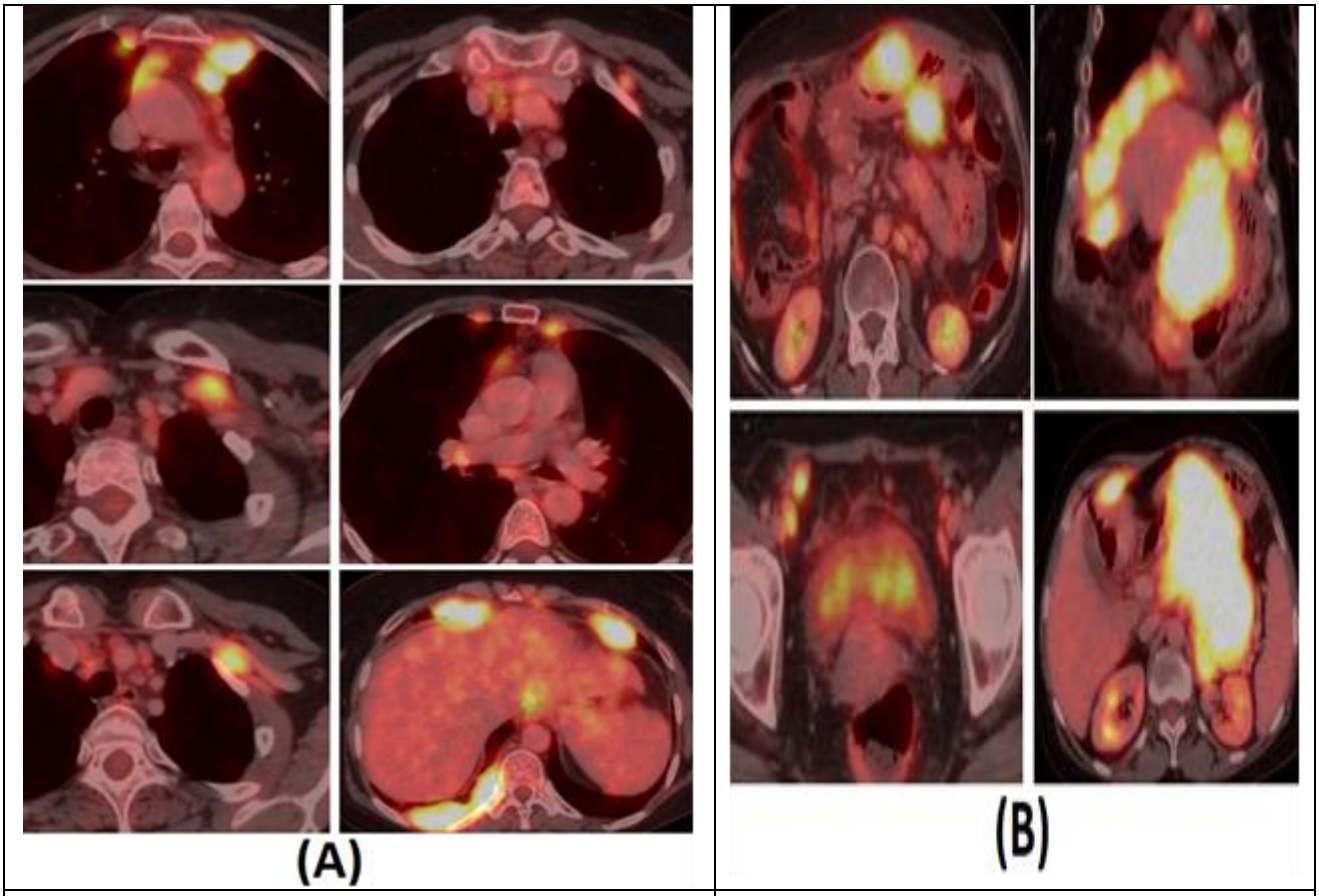

Fig. 2. (A) (A)Multiple enlarged hypermetabolic mediastinal lymph nodes are seen at bilateral retro clavicular, left infra-clavicular, pre-vascular, anterior mediastinal, bilateral internal mammary ,upper retro caval/pre tracheal) and bilateral cardiophrenic and epiphrenic as well as right hilar groups mounting to nodal masses formation (B) Positive PET/CT study for gastric antrum and proximal pylorus metabolically active polypoidal soft tissue mural wall thickening mounting to mass formation, seen encroaching upon the gastric lumen (measuring up to 6x3.7 cm and achieving up to 9.86 SUVmax) pathologically proven to be malignant B-cell lymphoma associated with supra sand infra-diaphragmatic hypermetabolic nodal lesions. (Deauville score 5).

DISCUSSION

Metabolic imaging provides unique benefits: it distinguishes between active tissue and scars, detects functional changes precluding size changes from treatment, and exhibits sensitivity linked to activity intensity rather than lesion size. [8].

In the present study, Different groups of lymph nodes can be located at either the supra- or infra-diaphragmatic locations, or perhaps both. Of the 36 patients analysed, 4 had lymph nodes involved above the diaphragm, 2 had lymph nodes involved below the diaphragm, and 30 had involvement in both areas.

According to. Metwally et al. [12] the upstaging by PET/CT for lymphoma included the identification of elevated 18F-FDG uptake in often small lymph nodes and in non-nodal locations, such as the skin, liver, spleen, cortical bone, bone marrow, and bones that diagnostic CT had previously missed.

In this study, there's concordance in 30 patients out of 36 patients between CT and PET-CT in lymph node involvement demonstrated 30 patients with positive lymph nodes affection, and discordance in 2 patients out of 32 that were positive in PET-CT and depicted as normal sized lymph nodes (false negative) by CT, and thus PET-CT allowed upstaging of them, We found in agreement with Wang et al. [13] studies that lymph nodes detection on PET-CT images showed high sensitivity of 100% with significant specificity 66.6%.

In our study, there's concordance in 32 patients out of 36 patients between CT and PET-CT in splenic

involvement showing concordance of 8 patients with positive splenic affection, and 24 patients with negative splenic affection. Discordance in 4 patients out of 36 between CT and PET-CT, that were positive in PET-CT and showed negative splenic affection by CT (false negative by CT), and thus upstaged by PET-CT, our study found that with agreement with Seban et al. [14] studies that PET CT had sensitivity of about 100% and specificity of about 85.6 % in detection of splenic involvement.

In our study, there's concordance in 34 patients out of 36 patients between CT and PET-CT in bone marrow involvement showing concordance of 4 patients with positive bone marrow affection, and 30 patients with negative bone marrow affection. Discordance in 2 patients out of 36 between CT and PET-CT, that were positive in PET-CT and showed negative affection by CT (false negative by CT), and thus upstaged by PET-CT, our study found that with agreement with Sollini et al. [15] that PET/CT is had high sensitivity (100%) and specificity (93.7%) for the evaluation of bone marrow and osseous involvement by PET CT than contrast enhanced.

In our study, 16 out of 36 patients in our study showed **other extranodal affection** by PET-CT, included hepatic, pulmonary nodules, renal affection, muscular lesions, pleural affection, GIT involvement, cutaneous nodules, nasopharyngeal affection, salivary gland involvement, tonsillar affection, adrenal affection thyroid, breast, and CNS involvement. 10 out of those patients showed agreement with CT and 6 out of them showed disagreement. Thus, PET CT upstaged those patients that were negative in CT. Our study agreed with Biggi et al. [16] studies that PET CT had high sensitivity and specificity in detection of other extranodal sites involvement in lymphoma.

In line with Biggi et al. [16], PET/CT may be especially useful in differentiating benign from malignant lesions, while both CT and PET/CT have shown good sensitivity for pulmonary lesions.

It is in line with the findings of the study by Ricard et al. [17], which demonstrated a small number of cases where lung lesions that were first diagnosed as benign on CT were later determined to be involved on PET/CT. Lymphoma patients who achieved full remission were found to have benign newly generated metabolically active lung nodules during response assessment and follow-up (inflammatory).

Also, our study findings agreed with Abdou et al. [18] who showed that PET/CT showed higher sensitivity and specificity than CT as follow: CT had specificity and sensitivity of 78%, 78 % respectively with PPV of 94 % and NPV of 47 %. PET/CT had sensitivity and specificity of 100 %, 83% respectively with PPV of 95% and NPV of 100%.

In our study, comparing contrast-enhanced CT (CECT) with PET/CT across all patients revealed significant sensitivity of PET/CT in detecting lymph nodes (LN), splenic, bone marrow, and other extranodal manifestations, with moderate to high specificity in other extranodal detections. While PET/CT enhances diagnostic confidence, some lesions remain indeterminate, necessitating confirmation through biopsy for accurate diagnosis. These findings align with a previous study conducted by Paes et al. [19]

In our study, patients underwent therapy response assessment at three stages: early interim assessment, between the first and third treatment cycles; late interim assessment; and end treatment assessment, typically one month post-chemotherapy completion. Early evaluation of treatment response is crucial for cancer patients, allowing for timely adjustment of chemotherapy regimens. This approach not only reduces costs by discontinuing ineffective medication but also minimizes unnecessary side effects associated with ineffective regimens. [20].

Lymphoma response evaluations primarily followed the International Workshop Criteria (IWC) (1999) and the International Harmonization Project's (IHP) updated response criteria (IHP) [20], **Modified Deauville Criteria**, **PERCIST** (Positron Emission tomography Response Criteria in Solid Tumors) and the **EORTC PET (European Organization for Research and Treatment of Cancer).**

We found that 18F-FDG PET following 1-3 cycles of chemotherapy was a good predictor of the ultimate response to treatment, which is in agreement with the findings of Mistry et al. [21]. In line with this, Rendl et al. [22] found that out of 28 patients, 23 demonstrated CR on interim PET/CT scans and all remained 18F-FDG negative on end-treatment PET/CT.

There was strong evidence from Mistry et al. [21] that poor outcome was linked to persistent 18F-FDG uptake after two to four cycles of treatment.

In concordance with Evens & Kostakoglu. [23] studies, we observed that the Deauville criteria for response assessment, when applied to the early and late stages of treatment, showed strong agreement with the IHP criteria for classification. This suggests that the Deauville criteria could serve as a

useful framework for intermediate PET CT follow-up.

In our study, we aimed to assess the relationship between maximum 18F-FDG uptake (SUVmax) in affected lymph nodes and extra-nodal sites with treatment response, hoping to establish a predictive cut-off value for response. However, the wide range of SUVmax values and various influencing factors rendered our findings statistically non-significant. Limitations included the lack of biopsy validation for all positive FDG-PET readings due to patient-related factors, a small sample size subdivided into smaller groups, and the need for a larger dataset to improve response measures and prognostic indicators.

CONCLUSION

When it comes to lymphoma treatment, the gold standard oncologic imaging modality right now is a PET/CT scan with 18F-FDG added. There seems to be good congruence between the Deauville criteria classification and the IHP classification in response assessment, particularly in the early interim and after the conclusion of therapy. Using the Deauville criterion, we recommend using PET-CT results in staging and response evaluation reports.

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