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Comparison of Contrast-Enhanced Computed Tomography with Positron Emission Tomography-Computed Tomography in Assessing Extra-Nodal Involvement in Lymphoma

Sana Ahmed Khan, Rizwan Bilal, Atiq Ur Rehman Slehria, Mobeen Shafique*, Shaista Nayyar, Hafsa Sadiq**

Department of Radiology, Armed Forces Institute of Radiology & Imaging, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan, *Department of Radiology, Combined Military Hospital, Pano Aqil/National University of Medical Sciences (NUMS) Pakistan, **Department of Radiology, Pakistan Air Force Hospital, Islamabad Pakistan

ABSTRACT

Objective: To compare the sites of extra-nodal involvement by Contrast-Enhanced Computed Tomography (CECT) and Positron Emission Tomography-Computed Tomography (PET-CT) in lymphoma patients

Study Design: Cross-sectional study

Place and Duration of Study: Armed Forces Institute of Radiology & Imaging, Military Hospital, Rawalpindi Pakistan, from Aug to Dec 2021.

Methodology: A total of 216 patients were included in the study who were diagnosed with lymphoma and presented with suspicion of extra-nodal metastasis. CECT and PET CT were performed in these patients, and a comparison of CECT and PET CT was made in the detection of sites of extra-nodal involvement.

Results: A total of 216 patients were included in the study, and the ability of CECT and PET CT was compared to detect the sites of extra-nodal involvement. The sensitivity, specificity, PPV, and NPV for 18-FDG PET-CT were calculated as 92.7%, 100.0%, 100.0% and 95.7% respectively, which was significantly more than CECT.

Conclusion: PET CT has proven to be a superior diagnostic tool for identifying sites of extra-nodal involvement as compared to CECT. It plays a significant role in guiding effective disease management.

Keywords: CECT, Extra nodal, Lymphoma, PET-CT.

How to Cite This Article: *Khan SA, Bilal R, Slehria AUR, Shafique M, Nayyar S, Sadiq H. Comparison of Contrast-Enhanced Computed Tomography with Positron Emission Tomography-Computed Tomography in Assessing Extra-Nodal Involvement in Lymphoma. Pak Armed Forces Med J 2025; 75(4): 640-644. DOI: https://doi.org/10.51253/pafmj.v75i4.9164*

INTRODUCTION

Lymphoma involves immune cells of the system and is a histologically heterogeneous group of malignancies with variable presentations and areas of involvement. They can arise in any organ of the body, and the term extra nodal lymphoma represents involvement of sites other than the lymphoid organs. It can be primary in origin at some other site, or it can be a secondary spread of a lymphomatous malignancy from primary nodal disease.[1] Cancer statistics state that approximately 81,560 people (45,630 males and 35,930 females will be affected by non-Hodgkin lymphoma, out of which about 20720 fatalities have been reported in the United States.[2]

Staging remains the most important prognostic factor in the management of any disease process, and accurate detection of all the lesions is an important step in staging the disease. Accurate staging guides the treatment process and prevents under- or over-treatment of the disease.[3] Presence of extra nodal involvement upstages the disease process and shows increased disease load. The treatment regimen changes according to the stage of the disease. It is important to identify the stage of the disease, whether the patient has been diagnosed of lymphoma and is coming for follow-up or for initial staging.

CT has been playing an important role in staging the disease process for decades, but it is limited by the fact that CT only detects structural changes and provides limited information about the early stage of the disease, in which structural changes are minimal.[4] Fludeoxyglucose F18 (FDG) is a positron-emitting radiotracer used with positron emission tomography (PET) to diagnose and monitor various conditions. F-18 FDG PET also provides functional information of the disease process and identifies the involvement of the organ before any structural change is evident.[5]

PET/CT is already used in staging numerous tumors and in assessing disease burden, as well as in the correct identification of disease stage and response to treatment. The principle of PET/CT is to evaluate metabolic changes in malignant tissue, which differ from normal tissues.[6] An additional advancement in the use of F-18 FDG PET is its combination with low-dose computed tomography, which further enhances

Correspondence: Dr Sana Ahmed Khan, Department of Radiology, Armed Forces Institute of Radiology & Imaging, Rawalpindi Pakistan
Received: 06 Aug 2022; revision received: 22 Nov 2022; accepted: 23 Nov 2022

its value by improving image detail and resolution, as images obtained solely from PET are noisy with low spatial resolution.[8] Images are acquired during the same visit with the patient in the same position. A low dose of radiation is used, and the images are then fused with those taken after administration of F-18 FDG. This technique provides improved anatomical details and also offers CECT images for better correlation. In this way, both the anatomical details and the metabolic activity of the disease are evaluated.

The primary objective of this study is to assess diagnostic accuracy through comparison between Contrast-Enhanced Computed Tomography (CECT) and Positron Emission Tomography-Computed Tomography (PET-CT), specifically for the detection of extra-nodal lymphomatous involvement. This investigation will focus on assessing how well each imaging modality identifies lymphomatous lesions outside of the lymphatic system and will include a detailed analysis of sensitivity, specificity, and overall efficacy of the tool. Additionally, the study will explore the implications of these findings for patient management and treatment planning in lymphoma patients.

METHODOLOGY

It was a cross-sectional study conducted at the Armed Forces Institute of Radio Imaging (AFIRI), Military Hospital, Rawalpindi, Pakistan, from Aug to Dec 2021. Approval from the ethical review committee (IERB certificate number: 0056) was obtained. A total of 216 patients were included in the study using non-probability consecutive sampling.

Inclusion Criteria: All patients of both genders, aged 20 years and above, who were histologically diagnosed with lymphoma, were included in the study. These patients presented either for the staging or for restaging of the disease after the initial treatment phase.

Exclusion Criteria: Patients who were not histologically diagnosed with lymphoma and the patients who refused to be a part of the study were not included.

The enrolled subjects were subsequently evaluated for extra-nodal involvement using both contrast-enhanced CT (CECT) and whole-body FDG PET–CT scans.

A PET machine that acquires PET images as well as low-dose CT images and merges them in a single session. Patients were instructed to fast for 4–6 hours before the administration of 18F-FDG. An intravenous dose of 250–450 MBq of 18F-FDG was then administered. Imaging was performed one hour after contrast injection, following the assessment of blood glucose levels. CT scans and PET images were taken of mid-thigh region. Images were displayed on a workstation that uses the software to merge the images of CT and PET and make it possible to interpret them side by side. Images were interpreted by a qualified radiologist and a nuclear medicine specialist.

The areas that appeared FDG avid were detected and noted, and were compared with CECT images for any structural changes indicating the disease process. The sites of extra nodal involvement were documented and were further evaluated by the clinician either by biopsy or by laboratory examination.

The data was entered in an MS Excel sheet and was evaluated by SPSS. Percentages, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated and are displayed in tables.

RESULTS

A total of 216 patients were evaluated for extra-nodal spread of disease process by lymphoma (both Hodgkin's and non-Hodgkin types). The mean age of the patients was 42.75±18.87 years.

Table-I describes qualitative variables, i.e., gender, frequency of subtypes of lymphoma (Hodgkins and non-Hodgkins's type), and frequency of their further subtypes, which shows that extra nodal involvement by the disease process was more common in patients with non-Hodgkin's lymphoma with Diffuse Large B-cell Lymphoma (DLBCL) subtype.

Frequency of sites where the extra nodal involvement was detected either by CECT or by PETCT is also tabulated, which shows spleen as the most common site involved by the disease process.

All the sites of extra nodal involvement were evaluated on CECT and PET CT, and a comparison of both was made to find out which modality is superior in detecting the extra nodal disease process. A 2*2 table for the calculation of sensitivity, specificity, PPV, and NPV for 18-FDG PET-CT is presented in Table-II, which was calculated as 92.7%, 100%, 100% and 95.7% respectively.

Table-I: Descriptive Statistics (n=216)

Characteristics		Frequency (%) (n=216)
Gender	Male	138 (63.9%)
	Female	78 (36.1%)
Type of Lymphoma	Non-Hodgkin's lymphoma	42(71.2%)
	Hodgkin's lymphoma	17(28.8%)
Subtypes of Lymphoma Non-Hodgkin's Lymphoma: DLBCL		
Follicular Lymphoma		108 (54.0%)
Lymphoblastic Lymphoma		14 (5.0%)
T-cell Lymphoma		01 (6.0%)
Mantle Cell Lymphoma		04 (5.0%)
Hodgkins Disease:		04 (5.0%)
Mixed Cellularity		45 (12.0%)
Nodular Sclerosis		28 (12.0%)
Lymphocyte Rich		04 (2.0%)
Lymphocyte Predominance		08 (3.0%)
Extra-nodal Involvement on F18-FDG PET/CT		
Yes		83(38.4%)
No		133(61.6%)
Extra-nodal Involvement on CECT		
Yes		76(35.4%)
No		140(64.8%)
Sites of Extra-nodal Involvement		
Spleen		22(26.5%)
lung		14(16.9%)
Liver		11(13.3%)
Bone		13(15.7 %)
Soft tissues		6(7.2%)
Kidney		5(6.0%)
Small intestine		4(4.8%)
Pleura		2(2.4 %)
Breast		1(1.2%)
Heart		1(1.2%)
Scalp		1(1.2%)
Peritoneum		1(1.2%)
Paranasal sinuses		1(1.2%)

**DLBCL - Diffuse Large B-cell Lymphoma*
CECT - Contrast-Enhanced Computed Tomography
F18-FDG PET/CT - Fluorine-18-labeled Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography

Table-II: Comparison of Extra-nodal Involvement between CECT and PET-CT (n=216)

Extra-nodal Involvement on CECT	Extra-nodal Involvement on PET CT	
	Present on PETCT	Absent on PET CT
Positive on CECT (Seen on CECT Image)	True Positive 76	False Positive 0
Negative on CECT (Not Seen on CECT)	False Negative 6	True Negative 134

Sensitivity= Tp/(Tp+Fn)= 76/(76+6)*100=92.0%
Specificity= Tn/(Tn+Fp)= 134/(134+0)*100=100.0%
Positive Predictive Value= Tp/(Tp+Fp)*100= 76/(76+0)= 100.0%
Negative Predictive Value= Tn/(Tn+Fn)*100=134/(134+6)= 95.0%
Diagnostic Accuracy=(Tp+Tn)/All Patients*100 = (76+134)/58=97.0%

**CECT - Contrast-Enhanced Computed Tomography*
PET CT - Positron Emission Tomography/Computed Tomography

DISCUSSION

The study has determined that PET CT can detect metabolically active lesions without identifiable structural changes and can identify the disease process through extra-nodal involvement much earlier than CECT. The study has also proven F18FDG PET to be an effective method to stage the disease process. The new PET-CT systems help to get the CT and PET images both in a single setting. It becomes easy to characterize the lesion based on both findings, the CT image, which provides the anatomic details, and the PET images, which provide the details of metabolic status. Additionally, the study also concluded the fact highlighted in the studies conducted by Omur *et al.*, and Elshafey *et al.*, that lymphoma is more prevalent among males than females in the study population.[1,9]

This study also determined the common subtypes of both types of lymphoma. DLBCL proved to be the most common subtype of NHL, and mixed cellularity is most common among Hodgkin's lymphoma subtypes. Similar findings were described in a study by Das *et al.*, which stated that DLBCL proven to be the most common NHL subtype, and mixed cellularity was the 2nd most common after nodular sclerosis.[10]

Another parameter detected in this study was a total of 59 sites of extra nodal involvement and showed that PET CT has proven to be more sensitive and specific in detecting the disease process as compared to CECT. The sensitivity and specificity for 18-FDG PET-CT are calculated as 92.7% & 100%, which is comparable to the study conducted by Zaytoon *et al.*, who state that PET CT is 96.6% sensitive and 98.8% specific, as compared to CECT, which is 87.5% sensitive and 85.7% specific.[11]

In organ involvement in lymphoma, the study delineated that the spleen was the most common site of extra nodal involvement, with approximately 26.5% of the cases, which is in coherence with the study conducted by Othman *et al.*, whose results revealed spleen as the most common site of extra nodal involvement in 30% of the patients.[12] A study conducted in Egypt by Omar *et al.*, showed that the pancreas and parotid are the least involved sites. In the present study, no cases of pancreatic or parotid gland involvement were observed. Notably, the breast and heart were identified as sites of extra-nodal lymphomatous involvement, which are considered among the rarest locations for such manifestations.[13]

A study conducted by Sin KM *et al*., also reinforces the results of this study by stating that FDG PET is accurate in detecting extra-nodal lymphomatous spread in the staging of disease as well as in follow-up of patients after radiotherapy and chemotherapy.[14]

A study by Paone *et al*., highlighted a tailored approach to use these diagnostic tools in investigating other conditions, such as follicular lymphoma. PET/ldCT should be performed as a first-line imaging procedure, also in patients with prevalent abdominal and pelvic involvement, limiting the acquisition of CECT in selected cases. This tailored approach would contribute to avoid useless radiation exposure and preserve renal function of patients.[15]

Another study conducted by Panebianco *et al*., showed that PET CT is more sensitive in detecting sites of lymphomatous involvement as compared to CECT and helps in accurate staging of the disease process.[16]

Several studies have demonstrated that PET-CT is more sensitive and specific than conventional imaging modalities, such as CECT, in detecting sites of extra-nodal involvement across various lymphoma subtypes. PET-CT not only enhances diagnostic accuracy but also plays a pivotal role in staging, treatment planning, and monitoring therapeutic response. Consistent with these findings, our study also highlights the superior diagnostic utility of PET-CT in identifying extra-nodal disease, thereby contributing to more informed clinical decision-making and improved patient management.[17,18]

LIMITATIONS OF STUDY

This study had a few limitations. Being a single-center study, the findings may not be generalizable to the broader population. Additionally, the study duration was limited to six months; extending the study period could provide more robust data and help validate the results further.

CONCLUSION

PET CT is quite sensitive and specific in detecting extra-nodal lymphomatous spread by identifying all the possible sites, as compared to the CECT, which is only a structural assessment of the disease. PET CT can detect metabolically active lesions without identifiable structural changes and can identify the disease process earlier than CECT, thus improving the prognosis of the disease.

ACKNOWLEDGMENTS

We extend gratitude to all faculty and staff members for providing all the necessary guidance and assistance while conducting the study.

Conflict of Interest: None

Funding Source: None

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SAK & RB: Data acquisition, data analysis, critical review, approval of the final version to be published.

AURS & MS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SN & HS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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