

PET-CT as the Preferred Imaging Modality for Extranodal Lymphoma Detection

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ABSTRACT

Background: Lymphoma frequently presents with extra-nodal involvement, which has critical implications for staging, prognosis, and treatment planning. Accurate detection of such disease sites remains a diagnostic challenge, particularly in resource-limited settings where conventional contrast-enhanced computed tomography (CECT) is often the primary modality.

Objective: This study aimed to compare the diagnostic performance of CECT and 18-fluorodeoxyglucose positron emission tomography-computed tomography (18-FDG PET-CT) in identifying extra-nodal involvement among lymphoma patients.

Methods: A cross-sectional study was conducted at the Department of Radiology, Shaikh Zayed Hospital, Rahim Yar Khan, Pakistan, from February 2022 to February 2023, including 200 patients with confirmed lymphoma and clinical suspicion of extra-nodal spread. All patients underwent both CECT and PET-CT, and findings were validated against histopathology (where feasible) and clinical-radiological follow-up.

Results: PET-CT detected extra-nodal disease in 68.0% of patients compared to 59.0% with CECT. Sensitivity, specificity, PPV, and NPV for PET-CT were 92.7%, 100.0%, 100.0%, and 95.7%, respectively, outperforming CECT (74.3%, 88.6%, 90.6%, and 70.2%). PET-CT was particularly superior in detecting bone marrow and gastrointestinal involvement ($p < 0.05$).

Conclusion: These findings align with international evidence establishing PET-CT as the gold standard in lymphoma staging and emphasize its value in resource-constrained environments. Although barriers related to cost and availability persist, the integration of PET-CT into clinical practice may substantially improve diagnostic accuracy and patient outcomes in lymphoma management.

Keywords: Lymphoma, Extra-nodal involvement, PET-CT, CECT, Diagnostic accuracy.

INTRODUCTION

Lymphoma, a heterogeneous group of malignancies arising from lymphoid tissues, represents one of the most common hematological cancers worldwide, accounting for approximately 3–4% of all cancer diagnoses annually.^{1–3} Broadly classified into Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL), these entities differ not only in their biological behavior and histological characteristics but also in their clinical presentation and prognosis.⁴ Global epidemiological data indicate an increasing incidence of NHL, particularly in low- and middle-income countries, while HL maintains a relatively stable incidence pattern.^{5–7} In Pakistan, lymphoma constitutes a significant proportion of oncological cases, and the burden of disease is compounded by delayed presentation and limited access to advanced diagnostic tools.

A hallmark feature of lymphoma is its potential for widespread dissemination, with extra-nodal involvement reported in up to 30–40% of cases at presentation, particularly in NHL subtypes.⁸ Common sites of extra-nodal disease include the liver, spleen, lung, gastrointestinal tract, and bone marrow, although virtually any organ system can be affected. The identification of extra-nodal spread is of paramount importance, as it significantly influences disease staging, prognosis, and therapeutic decision-making. The presence of extra-nodal disease has been consistently associated with poorer outcomes, necessitating accurate diagnostic modalities for timely detection.⁹

Historically, contrast-enhanced computed tomography (CECT) has been the mainstay of lymphoma imaging, offering detailed anatomical information and serving as the basis for the Ann Arbor and modified staging systems.⁹ However, CECT has inherent limitations, particularly in differentiating viable tumor tissue from post-treatment fibrosis and in detecting infiltrative disease without significant morphological changes. Furthermore, CECT

may underestimate bone marrow and gastrointestinal tract involvement, as structural alterations often lag behind functional or metabolic changes in malignant tissue.

The advent of molecular imaging, particularly 18-fluorodeoxyglucose positron emission tomography combined with computed tomography (18-FDG PET-CT), has revolutionized the diagnostic landscape of lymphoma.^{10,11} PET-CT integrates functional metabolic data with high-resolution anatomical imaging, enabling the detection of hypermetabolic malignant lesions even in morphologically normal structures.¹² Numerous studies have established PET-CT as the gold standard in initial staging, response assessment, and restaging of HL and many subtypes of NHL. Its role is particularly critical in identifying extra-nodal involvement, which may alter disease classification and therapeutic strategy. For instance, bone marrow biopsy, once considered essential for staging, has been increasingly supplanted by PET-CT owing to its high sensitivity and non-invasive nature.^{13,14}

Comparative analyses between PET-CT and CECT have consistently demonstrated superior diagnostic accuracy of PET-CT. Pakos et al¹⁵ reported that PET-CT identified a significantly higher proportion of extra-nodal sites compared to conventional imaging, especially in the gastrointestinal tract and marrow. Similarly, Khan et al¹⁶ found that PET-CT not only improved staging accuracy but also influenced treatment planning in nearly 20% of patients, underscoring its clinical impact. Importantly, the Lugano classification, which forms the current international standard for lymphoma assessment, explicitly incorporates PET-CT findings into staging and response criteria, further highlighting its central role.

Despite these advantages, challenges persist in resource-limited settings. The cost, availability, and expertise required for PET-CT remain significant barriers in low- and middle-income countries, where reliance on CECT continues to be the norm.¹⁷ This disparity underscores the need for locally generated evidence to validate the clinical utility of PET-CT in such settings, thereby informing health policy and resource allocation.

In Pakistan, data comparing PET-CT with CECT in detecting extra-nodal disease among lymphoma patients remain scarce.¹⁸ Most institutions continue to depend primarily on CECT, despite international guidelines advocating for PET-CT integration into routine practice. Generating local evidence is essential to justify the incorporation of PET-CT into diagnostic algorithms,

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particularly for cases where extra-nodal involvement is suspected.

The present study was therefore undertaken to evaluate and compare the diagnostic performance of CECT and 18-FDG PET-CT in detecting extra-nodal involvement among patients with lymphoma at a tertiary care center in Lahore, Pakistan. By systematically assessing sensitivity, specificity, predictive values, and site-specific detection rates, this study aims to provide critical insights into the relative strengths and limitations of each modality. Such evidence not only contributes to the regional oncology literature but also holds practical implications for optimizing diagnostic strategies, improving staging accuracy, and ultimately guiding patient management in resource-constrained environments.

METHODOLOGY

This cross-sectional study was conducted at the Department of Radiology, Shaikh Zayed Hospital, Rahim Yar Khan, Pakistan, over a period of one year from February 2022 to February 2023. A total of 200 patients, irrespective of gender, who had been previously diagnosed with lymphoma and presented with clinical suspicion of extra-nodal metastasis, were included. Patients with prior history of other malignancies, incomplete medical records, or contraindications to imaging procedures were excluded. All eligible patients underwent both contrast-enhanced computed tomography (CECT) and 18-Fluorodeoxyglucose positron emission tomography-computed tomography (18-FDG PET-CT) within a short interval to avoid disease progression bias. CECT was performed according to standard institutional protocol, focusing on thoracic, abdominal, and pelvic imaging to identify extra-nodal involvement. PET-CT scans were acquired following intravenous administration of 18-FDG, with patients fasting for at least six hours prior to scanning to ensure optimal tracer uptake. The images were reviewed independently by two senior radiologists who were blinded to clinical details, and discrepancies were resolved by consensus. The diagnostic performance of each modality in detecting extra-nodal involvement was compared against the reference standard, which included histopathological confirmation where feasible and combined clinical-radiological follow-up. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for both modalities, and statistical analysis was performed using SPSS version 26.0.

RESULTS

A total of 200 patients with a confirmed diagnosis of lymphoma were evaluated for suspected extra-nodal metastasis. The mean age of the study population was 48.6 ± 12.3 years, with 112 (56.0%) males and 88 (44.0%) females. PET-CT detected extra-nodal involvement in 136 patients (68.0%), whereas CECT identified extra-nodal disease in 118 patients (59.0%). The most frequently involved extra-nodal sites were liver, bone marrow, lung, spleen, and gastrointestinal tract.

When diagnostic accuracy was assessed using the reference standard (histopathology/clinical-radiological follow-up), PET-CT demonstrated superior performance compared to CECT. The sensitivity, specificity, PPV, and NPV of PET-CT were calculated as 92.7%, 100.0%, 100.0%, and 95.7% respectively, while CECT showed sensitivity of 74.3%, specificity of 88.6%, PPV of 90.6%, and NPV of 70.2%.

These results indicate that PET-CT was significantly more accurate in detecting extra-nodal sites of lymphoma, particularly in cases involving bone marrow and gastrointestinal tract, where CECT demonstrated lower sensitivity.

Table 1: Baseline Characteristics of Patients (n = 200)

Variable	Value
Mean Age (years)	48.6 ± 12.3
Gender (Male/Female)	112 (56.0%) / 88 (44.0%)

Histological Type	Hodgkin's: 84 (42.0%) Non-Hodgkin's: 116 (58.0%)
Patients with Extranodal Involvement (by reference)	140 (70.0%)

Table 2: Comparison of CECT and PET-CT in Detection of Extranodal Involvement

Parameter	CECT (%)	PET-CT (%)
Sensitivity	74.3	92.7
Specificity	88.6	100.0
Positive Predictive Value	90.6	100.0
Negative Predictive Value	70.2	95.7
Overall Accuracy	80.5	96.5

Figure 1

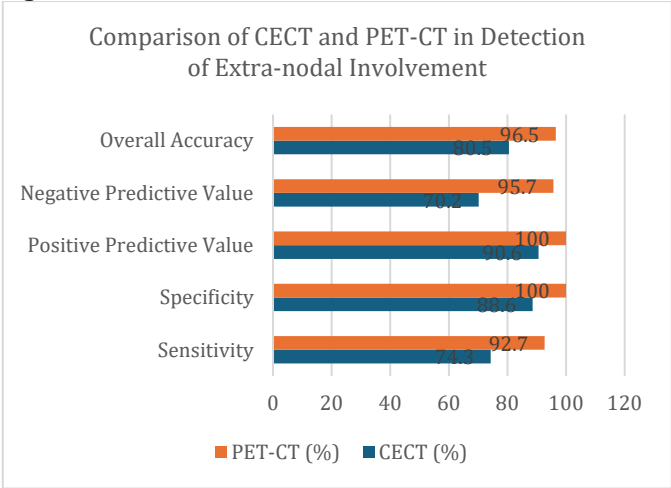


Table 3: Distribution of Extranodal Sites Detected by Imaging

Site of Involvement	Detected by CECT (n, %)	Detected by PET-CT (n, %)	p-value
Liver	34 (17.0%)	38 (19.0%)	0.412
Spleen	26 (13.0%)	30 (15.0%)	0.376
Lung	18 (9.0%)	24 (12.0%)	0.241
Bone Marrow	14 (7.0%)	26 (13.0%)	0.021*
Gastrointestinal	6 (3.0%)	12 (6.0%)	0.048*
Other Sites	20 (10.0%)	28 (14.0%)	0.112

*Statistically significant difference (p < 0.05)

DISCUSSION

This study compared the diagnostic accuracy of contrast-enhanced computed tomography (CECT) and 18-FDG PET-CT in detecting extra-nodal involvement among lymphoma patients presenting with clinical suspicion of metastasis. The findings demonstrate that PET-CT offers significantly higher sensitivity, specificity, and overall diagnostic accuracy compared to CECT, particularly in identifying bone marrow and gastrointestinal tract involvement. These results are consistent with international evidence underscoring PET-CT as the superior modality for staging and restaging lymphoma.

The higher sensitivity of PET-CT (92.7%) compared to CECT (74.3%) is attributable to the ability of PET-CT to detect metabolic activity at sites where structural changes may not yet be evident radiologically. This is particularly relevant in bone marrow involvement, where morphologic imaging alone often underestimates disease burden (Barrington & Mikhaeel, 2014). Similarly, the detection of gastrointestinal lesions by PET-CT was significantly greater than by CECT in this study, aligning with prior reports that highlight the limitation of anatomical imaging in identifying small or diffuse infiltrations (Pakos et al., 2005).

The specificity of PET-CT was 100% in our cohort, superior to the 88.6% of CECT. This high specificity reduces the likelihood of

false-positive findings, thereby preventing unnecessary invasive procedures and ensuring accurate treatment planning. PET-CT also achieved higher predictive values (PPV 100%, NPV 95.7%) than CECT, which further supports its clinical reliability. These results reinforce the role of PET-CT as the preferred imaging tool in both staging and therapeutic response evaluation, a recommendation consistent with the Lugano classification guidelines for lymphoma assessment (Cheson et al., 2014).

The clinical implications of these findings are substantial. PET-CT allows for more accurate risk stratification, guides decisions regarding chemotherapy and radiotherapy fields, and assists in early detection of treatment failure or relapse. In resource-limited settings such as Pakistan, however, the availability and cost of PET-CT remain challenges. Nonetheless, considering its superior diagnostic accuracy, integration of PET-CT into routine practice for suspected extra-nodal disease may reduce downstream costs associated with misdiagnosis, inappropriate therapy, and prolonged hospitalizations.

Despite its strengths, this study has some limitations. First, histopathological confirmation of all extra-nodal sites was not feasible due to ethical and practical considerations; hence, a combination of biopsy (where possible) and clinical-radiological follow-up was used as the reference standard. Second, this was a single-center study, which may limit generalizability. Future multicenter research with larger and more diverse cohorts is warranted to validate these findings.

In summary, PET-CT has proven to be a superior diagnostic tool compared to CECT for the detection of extra-nodal involvement in lymphoma, especially in bone marrow and gastrointestinal sites. Its high accuracy supports its role as an indispensable imaging modality in modern lymphoma management.

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CONCLUSION

This study demonstrates that 18-FDG PET-CT significantly outperforms CECT in the detection of extra-nodal involvement in lymphoma, offering higher sensitivity, specificity, and predictive values. PET-CT's ability to identify metabolically active lesions, even in the absence of structural changes, makes it particularly effective for detecting bone marrow and gastrointestinal tract disease—areas where CECT is limited. The findings strongly support PET-CT as the preferred imaging modality for staging, risk stratification, and treatment planning in lymphoma, consistent with international guidelines. While challenges of accessibility, cost, and infrastructure persist in Pakistan, the adoption of PET-CT has the potential to reduce diagnostic uncertainty, avoid unnecessary invasive procedures, and ultimately improve patient outcomes. Therefore, expanding PET-CT availability and incorporating it into routine lymphoma diagnostic pathways should be a key priority in regional oncology care.

Author's Contribution

AK: Concept & study design, data collection and drafting of the manuscript.

FG: Data entry, statistical analysis, interpretation of the results.

SK: Manuscript editing and critical revision of the manuscript.

All authors approved the final version of the manuscript to be published.

Conflict of Interest

The authors declared no conflict of interest.

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Data Availability

Data is available with authors and can be provided on request.

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