

IJMA



INTERNATIONAL JOURNAL OF MEDICAL ARTS

Volume 7, Issue 7 (July 2025)



<http://ijma.journals.ekb.eg/>

P-ISSN: 2636-4174

E-ISSN: 2682-3780



Available online at Journal Website
<https://ijma.journals.ekb.eg/>
 Main Subject [Radiology]



Original Article

Whole-Body Diffusion-Weighted MRI VERSUS ¹⁸F-FDGPET/CT in Assessment of Lymphoma

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Abstract

Article information

Received: 14-04-2025

Professionally accepted: 28-05-2025

DOI: [10.21608/ijma.2025.375443.2165](https://doi.org/10.21608/ijma.2025.375443.2165)

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Citation: Gomaa MI, Zidan HS, Korayem EM, Tawfeek EA, Abokoura S. Whole-Body Diffusion-Weighted MRI VERSUS ¹⁸F-FDGPET/CT in Assessment of Lymphoma. IJMA 2025 July; 7[7]: 5917-5922. doi: [10.21608/ijma.2025.375443.2165](https://doi.org/10.21608/ijma.2025.375443.2165)

Background: Lymphomas comprise 5-6% of all cancers. While positron emission tomography [PET] scans, using the [¹⁸F]- Fluorodeoxyglucose tracer [¹⁸F-FDG PET/CT] remain standard for staging/follow-up, radiation concerns have increased interest in whole-body diffusion-weighted MRI [WB-DW MRI], which provides both anatomical and functional data through apparent diffusion coefficient values. This study aimed to compare the diagnostic accuracy of DW WB-MRI with that of ¹⁸F-FDG PET/CT for assessment of malignant activity in lymphoma patients during follow-up period .

Patients and methods: This prospective study included 35 pathologically proven lymphoma patients at National Liver Institute [June 2024-February 2025]. All underwent both ¹⁸F-FDG PET/CT and WB-DW MRI imaging modalities approximately 2.5 days apart. Nine lymph node groups and extra-nodal organs were evaluated per patient, with PET/CT as the gold standard.

Results: WB-DW MRI showed high performance for nodal disease [sensitivity 94.44%, specificity 94.12%, accuracy 94.29%] and excellent sensitivity [100%] for extra-nodal assessment with good accuracy [91.43%]. A significant negative correlation existed between apparent diffusion coefficient [ADC] values and Maximum standardized uptake value [SUVmax] [p=0.001]. A staging agreement occurred in 65% of patients. In discordant cases, WB-DW MRI upstaged 27.3% of stage II patients and downstaged 75% of stage III patients [p<0.001].

Conclusion: Health literacy significantly influences medication adherence among elderly patients with WB-DW MRI offers a radiation-free alternative to ¹⁸F-FDG PET/CT for lymphoma restaging, with comparable accuracy in nodal assessment and superior sensitivity for diffuse BM involvement. However, its limitations in spleen evaluation and lack of standardized protocols temper its routine adoption.

Keywords: Whole-Body diffusion; MRI; ¹⁸F FDGPET; Computed Tomography; Lymphoma.



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INTRODUCTION

Lymphomas are prevalent malignant tumours that affect individuals across all age groups, including children, young adults, and the elderly, constituting 5-6% of all cancers. Specifically, Hodgkin lymphoma [HL] and non-Hodgkin lymphoma [NHL] rank as the third most common malignancy in children, with HL also being one of the most frequently diagnosed cancers during pregnancy^[1].

While many lymphomas can be cured, their prognosis depends on factors such as stage and histological classification^[2].

Diagnostic positron emission tomography [PET] scans, using the [18F]- Fluorodeoxyglucose tracer [18F-FDG], are the cornerstone of imaging in lymphoma and play a crucial role in staging. It facilitated the functional evaluation of disease behaviour such as tumor grade, metabolic response to therapy, and earlier detection of disease recurrence, providing the advantage of combining functional and anatomical information with good attenuation correction^[3].

Concerns have been raised about radiation exposure from multiple imaging scans used for staging and follow-up in cancer patients. Studies have shown a link between radiation and an increased risk of secondary cancers in lymphoma patients^[4].

This has led to a growing interest in using whole-body magnetic resonance imaging [whole-body MRI] as a radiation-free alternative to traditional imaging techniques for evaluating lymphoma patients^[5].

Whole-body magnetic resonance imaging [WB-MRI] with Diffusion Weighted Imaging [DWI] proved to be a promising, radiation-free technique for staging and monitoring lymphoma and other cancers. It provides both anatomical and functional information. Specifically, DWI-derived apparent diffusion coefficient [ADC] values measure the extent of water molecule movement within tissues, which correlates with the density of tumour cells^[6].

Studies have shown that lymphomas have significantly lower ADC values compared to normal lymph nodes and carcinoma nodal sites. Furthermore, ADC values tend to increase in patients who respond to treatment^[7].

However, WB-MRI is not yet routinely used in lymphoma patients due to the lack of standardized parameters for assessing disease burden and treatment response, in contrast to 18F-FDG PET/CT^[7]. So, the added value of our research lies in demonstrating that DW WB-MRI offers a radiation-free, functionally comparable alternative to 18F-FDG PET/CT for assessing malignant activity in lymphoma patients during follow-up, supporting its potential integration into routine clinical practice.

THE AIM OF THE WORK

This study aimed to compare the diagnostic accuracy of DW WB-MRI with that of 18F-FDG PET/CT to assess malignant activity in lymphoma patients during follow-up period.

PATIENTS AND METHODS

This is a prospective diagnostic test accuracy study. We studied 35 patients who were pathologically proven to have lymphoma and attended the National Liver Institute, Menoufia University, from June 2024 to February 2025 for follow-up and restaging of lymphoma by radiological imaging using the available 18F-FDG PET/CT scans. The study was approved by the Research Ethics Committee of National Liver Institute, Menoufia University. 18F-FDG PET/CT scans were obtained on a helical CT scanner [Siemens AG, 128 slice, high-speed advantage scanner] used for the standard PET protocol. First, a low-dose CT scan [120 kV, 100 mAs, 0.9 pitch, and 5 mm slice thickness] was obtained from the skull base down to mid-thighs for attenuation correction. This was immediately followed by PET imaging at the same scanning range in three-dimensional mode with 3 min/bed; PET axial field of view 11.4 cm/ bed position.

Data were filtered [FWHM 4.0 mm] and corrected for scatter using resolution recovery software at reconstruction. After completion of the PET scan, Non-contrast CT was done at the same scanning range [188 mAs, 120 kV, 5 mm slice thickness, 0.9 pitch and 2.5 mm incremental reconstruction] with a limited breath-hold technique to avoid motion-induced artefacts' DWI MRI protocol: Diffusion study, Axial diffusion-weighted imaging with background body signal suppression [b values = 0 and 800 s/mm²; repetition time, 8696 ms; echo time, 67 ms; slice thickness, 6 mm; gap, 0 mm; craniocaudal coverage, scan time is about 3.5 min/ station, average station numbers about 5/6 stations according patient's length]. Adjustment of b value is very important as higher b values [≥ 500 sec/mm²] give diffusion information that helps lesion characterization, so in our technique, we used b values of 0 and 800.

To the best of our knowledge, our study is the 1st one to use DWI sequence with no additional sequences to evaluate its standalone efficacy in comparison to PET CT. For each patient, the attenuation-corrected FDG-PET images, CT low-dose images were automatically fused on True D Siemens software or transferred to Philips Intelli space portal or OSIRIX fusion workstation via the hospital network, where FDG-PET and CT data sets were automatically fused. About 315 lymph node groups were examined, 9 lymph node groups for each patient involving both sides of [cervical, supraclavicular, axillary, Iliac, inguinal groups], mediastinal, Porta hepatis, Para-aortic, and mesenteric groups. Extra-nodal organs were screened for lesions, mainly the spleen & bone marrow in both DW WB-MRI and PET/CT images. PET/CT images were evaluated in axial, coronal and sagittal reconstructed planes.

The diagnostic criteria of lymphoma by PET/CT depended on the detection of any hyper-metabolic foci [being on top of underlying lesion or not] with FDG uptake exceeding that of the mediastinal reference background. Lymph nodes [LN] were considered involved in the case of FDG uptake above the background or the mediastinal blood pool.

The sign of diffuse spleen involvement in HL and NHL and diffuse BM involvement was diffuse FDG uptake above the liver. Two quantitative criteria of diffuse BM involvement in NHL were additionally studied: the BM SUV of more than 100% or 150% of the liver SUV. Soft tissues were considered involved if there was any abnormal morphology with increased metabolic activity above the background. Estimation of their FDG uptake by SUV max and its correlation with the mediastinal reference background.

According to PET/CT findings, the number and distribution of the affected sites were detected and then staged according to the Deauville classification of lymphoma. Regarding WB DW - MRI, the same lymph node groups and extra nodal organs were examined as detailed before. The diagnostic criteria of lymphoma by DW MRI depended on the detection of any diffusion restriction [being on top of the underlying lesion or not] on DWI b800 images. Organ involvement was established in the presence of foci or areas of pathological signal intensity of non-liquid or non-vascular nature in the liver, spleen, other organs and soft tissues, as well as in the presence of foci or infiltrates of restricted diffusion. Bone destruction, pathological soft tissue component, focal, or diffusely reduced signal intensity, and the foci with signal intensity above the surrounding BM were signs of focal BM involvement, while the symptom of a diffuse increase in spine signal intensity above the kidney parenchyma was the sign of diffuse BM involvement. The ADC value of each focal lesion detected is measured by drawing a region of interest over the lesion. Data was statistically analysed for lesion counts and percentages, with sensitivity, specificity, and accuracy calculated for comparison.

PET CT served as the gold standard for result interpretation, with follow-up conducted for select patients, incorporating their findings.

Statistical analysis was performed using SPSS version 22, with graphics generated through Excel and SPSS. The analysis included descriptive statistics where normally distributed continuous variables were expressed as mean \pm standard deviation, while non-normally distributed continuous variables were expressed as median with interquartile range or range. Categorical variables were presented as frequency and percentage. For analytical statistics, comparison tests including Chi-square, Fisher Exact, and Kruskal-Wallis were employed. Normality was assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Diagnostic metrics, including sensitivity, specificity, positive/negative predictive values, and accuracy, were calculated. Statistical significance was defined as $p < 0.05$.

RESULTS

Our study population included pathologically proven non-Hodgkin lymphoma [NHL] patients, representing about 60% of the cases, compared to 40% with Hodgkin lymphoma [HL]. In NHL, female affection [52.4%] was higher than male affection [47.6%], while in HL male affection [64.3%] was higher than female affection [35.7%]. The most affected age group by NHL [47.5%] was >60 years, while the most affected age group by HL [35.7%] was both 40- <50 and 50- <60 years, as shown in **Figure [1]**.

The time interval between PET CT scan and DW WB-MRI ranged from 0 to 8 days with a Mean \pm SD [2.46 \pm 2.23]. All patients examined were interim [during the follow-up period] having received cycles of chemotherapy or immunotherapy.

The last cycle was received in months ranging from 0.46 to 60 with a mean \pm SD of 9.16 \pm 17.08.

Diagnostic efficiency of DW WB MRI to detect lymphoma involvement was as follows: For nodal involvement, It showed overall nodal positive predictive value [PPV] 94.44%, NPV 94.12%, sensitivity 94.44%, specificity 94.12% & accuracy 94.29% with a significant p-value [$P < 0.001$], while it was lower PPV for splenic involvement detection It showed PPV 47%, specificity 67% & accuracy 74% with a significant p-value [$P < 0.001$] as shown in **Table [1]**.

For all lesions that showed diffusion restriction, ADC value was obtained in the form of ADC maximum, mean, and minimum. ADC mean of positive nodes ranged from [0.59 – 1.61] with Mean \pm SD [0.92 \pm 0.31x 10⁻³mm²/s]. ADC max of positive nodes ranged from [0.74 – 1.9] with Mean \pm SD [1.1 \pm 0.42x 10⁻³mm²/s]. ADC min of positive nodes ranged from [0.1 – 0.95] with Mean \pm SD [0.67 \pm 0.18x 10⁻³mm²/s].

To undergo lymphoma staging, the SUVmax value of mediastinal blood pool and liver background were obtained. SUVmax Value for mediastinum ranged from [0.8 - 2.8] with Mean \pm SD [1.6 \pm 0.6]. SUVmax Value for liver background ranged from [1.8 – 3.6] with Mean \pm SD [2.55 \pm 0.55]. SUVmax Value for metabolically active lesions ranged from [2.9 - 28] with Mean \pm SD [11.35 \pm 7.91].

A negative correlation was found between ADC mean and SUVmax. [$p = 0.001$]. Symmetrical disease staging using both modalities was observed in 65% of patients at stages I, IV, and V. Discordant staging by DW MRI and PET/CT was found in 35% of the patients. Lymphoma was upstaged by DW MRI in 27.3% of stage II patients from stages II to stage III and was down staged in 75% of the patients of stage III from stage III to stage II, with a significant p value < 0.001 .

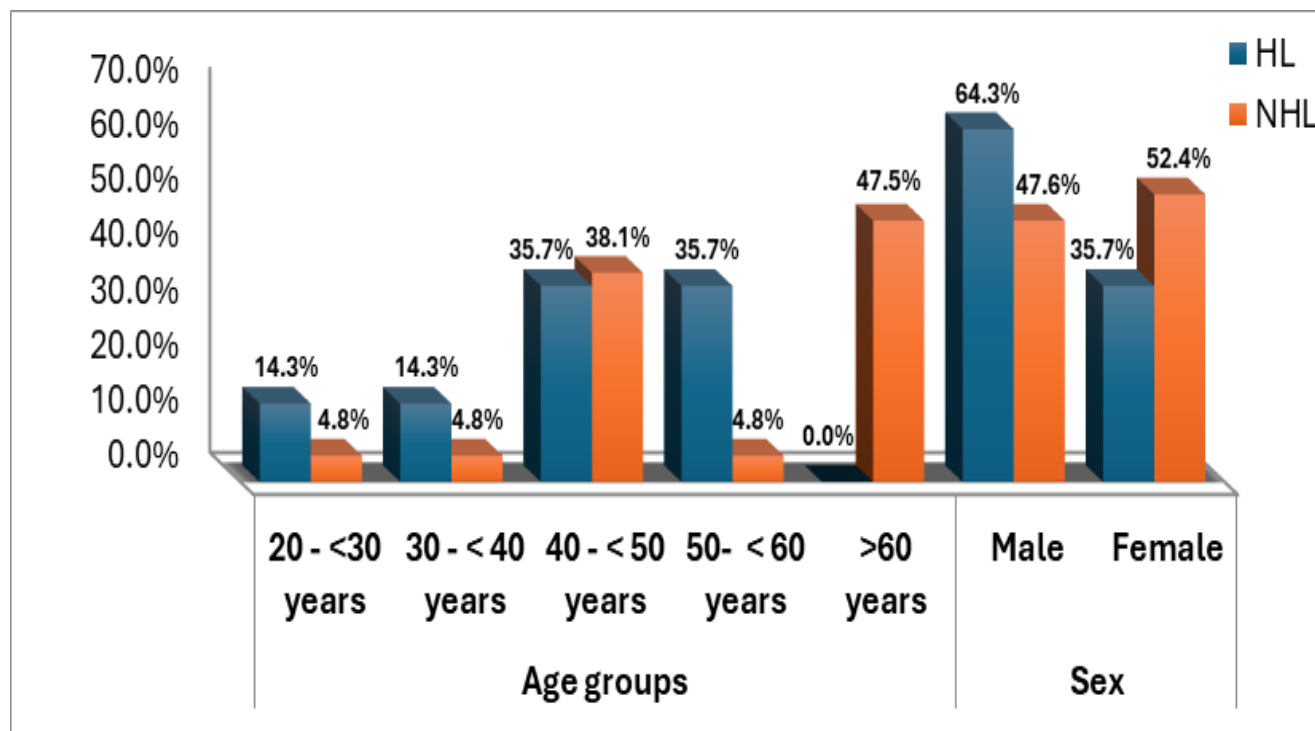


Figure [1]: Patient characteristics.

Table [1]: DWI MRI diagnostic performance

	MRI	PPV [%]	NPV [%]	Sensitivity [%]	Specificity [%]	Accuracy [%]	Kappa coefficient	P value
Nodal	Cervical	100	93	71	100	94	0.8	<0.001
	supraclavicular	100	100	100	100	100	1	<0.001
	Axillary	100	93	71	100	94	0.8	<0.001
	Mediastinal	100	85	67	100	89	0.724	<0.001
	Porta hepatis	80	88	73	92	86	0.66	<0.001
	Para-aortic	100	100	100	100	100	1	<0.001
	Mesenteric	100	100	100	100	100	1	<0.001
	Iliac	100	100	100	100	100	1	<0.001
	Inguinal	100	100	100	100	100	1	<0.001
	Others	-	91	-	100	91	-	-
	All nodes combined	94.44	94.12	94.44	94.12	94.29	0.886	0.001
Extra-nodal	Spleen	47	100	100	67	74	0.478	0.001
	Lung	-	100	-	100	100	-	-
	Bone marrow	85	100	100	83	91	0.829	<0.001
	Others	50	100	100	97	97	0.653	<0.001
	All organs combined	86.96	100	100	80	91.43	0.821	<0.001

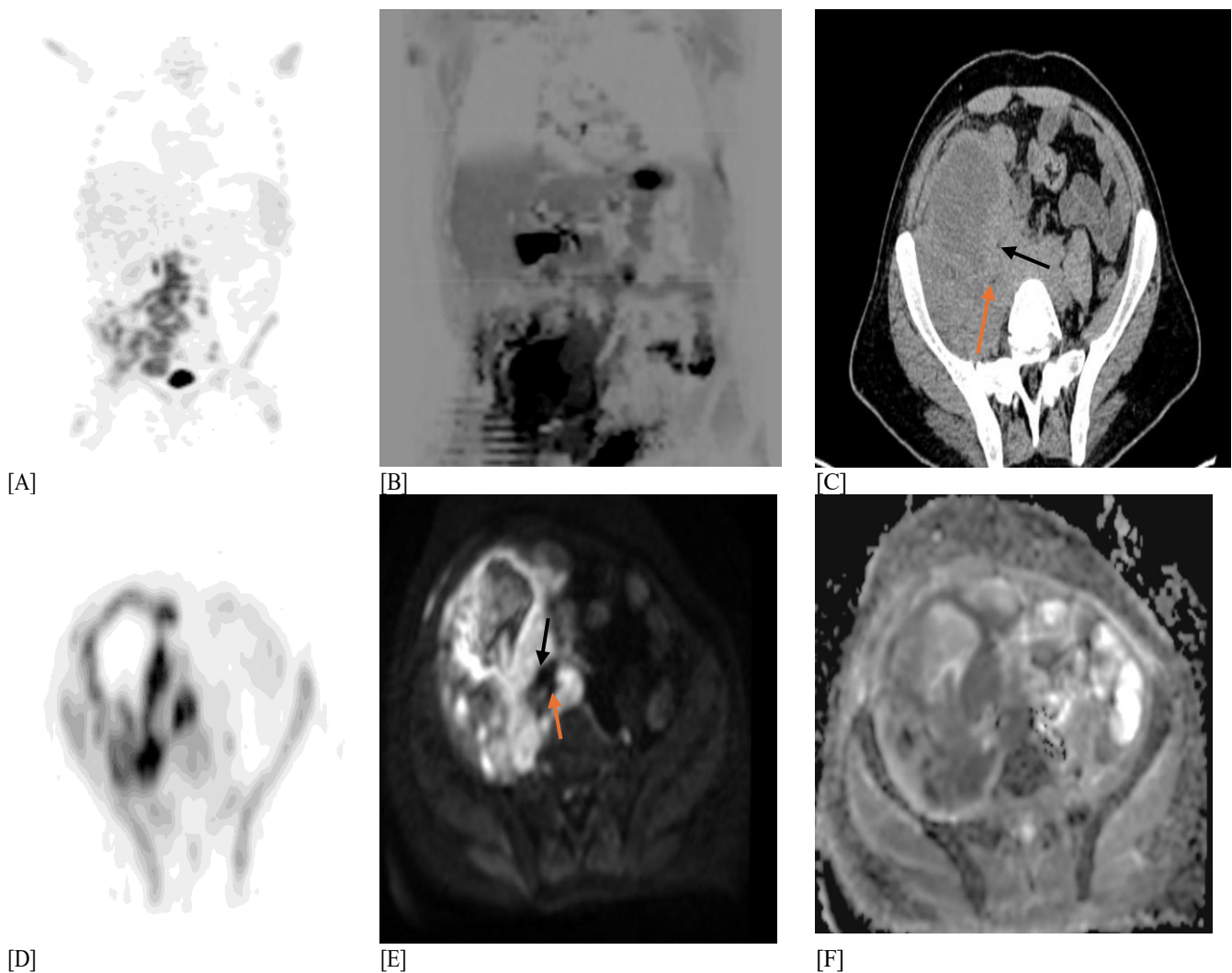


Figure [2]: Stage V HL male patient showing intense FDG uptake and restricted diffusion corresponding to a sizable right lower abdominal heterogeneous mass lesion is seen inseparable from the right psoas and iliocostalis muscles. Metabolic activity [and diffusion restriction] of multiple abdomino-pelvic lymphadenopathy. [A] Coronal PET CT image. [B] Coronal MPR DWI b800 image in the inverted grey scale. [C] Axial non-contrast CT image shows the previously described mass lesion encasing the external iliac artery [black arrow] with indistinct borders; the internal iliac artery is not completely identified [orange arrow]. [D] The peripheral portion of the right iliac fossa mass lesion shows peripheral increased metabolic activity, with an SUVmax of about 25, with central FDG-starving areas of necrosis. [E] Axial b800 DWI MRI image shows the previously described mass lesion complete encasement of both external and internal iliac arteries with no gross invasion [arrows], which appeared as signal void, so it was better than NC PET CT images in vascular relation assessment and characterization without the need for contrast injection. [F] ADC axial image, the peripheral portion of the lesion is low signal on ADC, value of ADC max 0.99, min 0.67, mean 0.81 $\times 10^{-3}$ mm²/s.

DISCUSSION

Our study demonstrates an excellent agreement between 18F-FDG-PET/CT and WB-MRI with DWI in the staging of patients with lymphoma even with using diffusion weighted sequences only, which reduces the time used for WB DWI MRI examination. That agreement was particularly notable during the assessment of nodal and extra-nodal disease, with the main limitations noted in spleen evaluation making WB DWI MRI an excellent option for incorporation into follow-up imaging protocols for lymphoma patients, particularly those requiring frequent monitoring [e.g., paediatric or pregnant patients]. This could reduce cumulative radiation exposure while maintaining diagnostic accuracy. The highest discrepancies between the two modalities were found in the mediastinal lymph node groups, these results aligned with those reported by **Maccioni et al.** who reported that there was significant agreement in staging of lymphoma by both modalities with the highest discrepancies was found in the pulmonary hilar region [8].

The differences observed between the two modalities in the mediastinal or pulmonary hilar regions can be attributed to the proximity to the lungs and heart, where artifacts from cardiac and respiratory motion may impact the MRI evaluation of nodal involvement. After all, the discrepancies in identifying nodal and extra-nodal regions did not influence the final disease staging. Symmetrical staging at both modalities was found in 65% of patients at stages I, IV & V, Discordant staging by DWI MRI and PET/CT was found in 35% of the patients, mainly either upstaging or downstaging from stages II to stage III. This is considered clinically insignificant as both stages denote complete metabolic response and require follow-up, not further treatment plans [9].

Our findings suggest that MRI-DWI is not sufficiently efficient for true interpretation of spleen involvement with a specificity of 67% & accuracy 74%, possibly due to the physiological limitations of MR diffusion in the spleen. The criterion for diffuse spleen involvement established by

international guidelines [a vertical size increase of more than 13 cm] demonstrated low sensitivity ^[10]. Additionally, the quantitative ADC assessment did not enhance diagnostic efficiency. On the other side, the spleen-to-liver attenuation ratio on contrast-enhanced CT has proven effective in diagnosing diffuse spleen involvement in lymphoma ^[11]. However, it is important to note that this is not the sole factor in our study, as we relied on non-contrast PET-CT imaging for evaluation. When comparing PET/CT and MRI-DWI for diagnosing bone marrow [BM] involvement, some studies fail to specify clear involvement criteria.

According to **Adams et al.** the sensitivity of MRI-DWI for detecting BM involvement was reported at 45.5%, with only 23.5% sensitivity for indolent non-Hodgkin lymphoma ^[12].

This relatively low sensitivity may be attributed to the focus on focal BM involvement, whereas diffuse BM involvement is more prevalent in indolent lymphomas. In response, we were stuck to the diagnostic criterion for diffuse BM involvement reported by **Kharuzhyk, S, et al.** that considered a diffuse increase in spine signal intensity on high b-value DWI images above the kidney parenchyma. This approach yielded a diagnostic sensitivity of 100%, a specificity 83% & accuracy 91% with a significant p-value [$P < 0.001$] compared to a sensitivity of 87.1 reported by **Kharuzhyk, S, et al.** ^[13]. Additionally, the efficacy of MRI-DWI in diagnosing bone marrow involvement has been demonstrated in other malignancies, such as prostate cancer and multiple myeloma ^[14].

Study Limitations: The major limitation of this study was related to the fact that we depended on the apparent morphological restriction of lesions and lymph nodes then ADC values were measured. The ADC cutoff varies depending on the anatomical LN group, which makes it questionable to use a single cutoff. Besides, the ADC quantitative assessment in non-enlarged LN may be inaccurate due to the different attributable factors ^[15].

Another limitation is the relatively small sample size of patients included in the study. When interpreting the results, individual observations were noted that require a larger cohort to achieve statistical significance when comparing diffusion-weighted imaging to non-contrast positron emission tomography-computed tomography [NC PET/CT].

Financial and non-financial activities and relationships of interest: None

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IJMA



INTERNATIONAL JOURNAL OF MEDICAL ARTS

Volume 7, Issue 7 (July 2025)



<http://ijma.journals.ekb.eg/>

P-ISSN: 2636-4174

E-ISSN: 2682-3780