Current Research in MRI

Original Article

Effectiveness of Diffusion-Weighted Magnetic Resonance Imaging in Differentiating Mediastinal Lymphadenopathy

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Cite this article as: Çetin T, Memiş F. Effectiveness of diffusion-weighted magnetic resonance imaging in differentiating mediastinal lymphadenopathy. *Current Research in MRI*, 2024;3(3):77-82.

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Received: November 7, 2024 **Revision Requested:** November 17, 2024 **Last Revision Received:** December 2, 2024 **Accepted:** December 3, 2024 **Publication Date:** April 24, 2025

DOI:10.5152/CurrResMRI.2024.24110

Abstract

Objective: Several methods are used to diagnose mediastinal lymphadenopathy, which may result from many benign and malignant etiologies. Various radiodiagnostic imaging methods, bronchoscopy, mediastinoscopy, and thoracoscopy are used for diagnosis and management. This study attempted to enhance the diagnostic reliability of diffusion-weighted magnetic resonance imaging (MRI) for characterizing mediastinal lymph nodes and to identify conventional MRI sequences that could be beneficial.

Methods: A retrospective investigation was conducted on 40 patients exhibiting mediastinal lymphadenopathy as shown on chest MRI, including 27 with malignant and 13 with benign origins. The patients underwent echoplanar diffusion-weighted MRI, and apparent diffusion coefficient (ADC) maps were generated. The ADC values for lymph nodes located in the mediastinal region were computed. Additionally, statistical analysis was carried out, and the ADC values were connected to the findings of the histopathological examinations.

Results: The average assessment of the lymph nodes' ADC value that were malignant was found to be considerably lower ($P < .001$) compared to the value for lymph nodes that were benign. With a cut-off point of 1.50×10^{-3} mm^2/s, the ADC variable is now being utilized. In the process of differentiating benign lymph nodes from malignant nodes, we were able to acquire a sensitivity rate of 85% and a specificity rate of 77%. The sensitivity and specificity values of short axis diameter measurements in this differentiation are 61% and 85%, respectively.

Conclusion: Apparent diffusion coefficient levels are essential in differentiating between benign and malignant mediastinal lymphadenopathies.

Keywords: ADC value, chest MRI, diffusion-weighted imaging, lymph node

INTRODUCTION

Mediastinal lymphadenopathy can result from diverse infectious (tuberculosis), inflammatory (sarcoidosis), and neoplastic (lung cancer, lymphoma, and extrathoracic cancer) diseases. The assessment of mediastinal lymphadenopathy is critical for efficient treatment and precise prognosis. Metastasis of lung cancer to mediastinal lymph nodes serves as a significant prognostic factor in staging.[1] Accurate diagnosis necessitates the integration of clinical, radiological, and pathological findings for effective management.[2]

The most effective approach in the staging of lymphadenopathy and differentiating between malignant and benign conditions in the mediastinum remains contentious. Diagnostic radiological imaging techniques, including computed tomography (CT) and magnetic resonance imaging (MRI), as well as invasive interventional procedures such as bronchoscopy, mediastinoscopy, and thoracoscopy, together with nuclear medicine imaging methods like positron emission tomography (PET), are employed in diagnosis.[1,3]

Computed tomography remains the primary imaging method for assessing thoracic abnormalities. The morphological characteristics, including the location, size, and distribution of lymph nodes, can be assessed via CT imaging. The evaluation of mediastinal lymph nodes via CT has historically relied on anatomical characteristics, particularly the measurement of the short diameter. Nonetheless, the sensitivity and specificity of this method have demonstrated low levels (nearly 60%).[4,5] F-18-deoxyglucose (FDG) uptake in lymph nodes during PET examinations is an alternative method for assessing lymphadenopathy that does not definitively confirm malignancy. Infectious or inflammatory lymphadenopathies show FDG uptake similar to malignant lymph nodes.[3-5] Surgical procedures like mediastinoscopy or thoracotomy are effective yet invasive and carry possible risks.[5]

Magnetic resonance imaging is another method employed to ascertain the existence and dimensions of lymph nodes. Standard MRI sequences are unable to differentiate between malignant and benign lymph nodes. Nonetheless, this distinction can be achieved through particular techniques, including diffusion-weighted imaging (DWI) and magnetization transfer imaging.[3-5] Besides differentiating between benign and malignant lymphadenopathy, MRI offers advantages over CT and PET, including superior soft tissue visualization and the absence of ionizing radiation.[6]

Diffusion-weighted imaging evaluates diffusion restrictions by detecting the microscopic Brownian movements of water within biological tissues, thereby reflecting the characteristics of those tissues. Measurement of the apparent diffusion coefficient (ADC) values allows for the achievement of a quantitative evaluation of the water molecule diffusion that occurs in these nodes.[7] Lymphadenopathies that are malignant have much lower ADC values as compared to lymph nodes that are benign.[8] This is the most effective non-invasive technique for distinguishing between benign and malignant mediastinal lymphadenopathy. It also provides the opportunity to initiate early treatment while awaiting the pathological diagnosis from invasive procedures.[8,9] Previously, numerous studies have shown the efficacy of DWI in the characterization of mediastinal lymphadenopathy.[1,3,4,8] Recently, Ramamoorthy et al[9] established that the ADC value is the paramount criterion for differentiating both benign and malignant mediastinal lymphadenopathies.

The purpose of this research was to enhance the diagnostic reliability of DWI for the characterization of mediastinal lymph nodes and to identify conventional MRI sequences that could be beneficial.

MATERIAL AND METHODS

This retrospective investigation obtained approval from the Erzincan University Ethics Committee (Number: 412235 2024-17/15 Date: December 16, 2024). All patients participating in the trial provided signed informed consent.

All imaging reports of contrast-enhanced chest MRI examinations conducted at our hospital's radiology clinic from January 2021 to November 2024 will be scanned utilizing the search term "mediastinal lymphadenopathy". Patients presenting with mediastinal lymphadenopathy will be evaluated by one of the authors, and those having diagnostic MR images, DWI sequences, and histopathological sampling of lymph nodes performed within a maximum of 1 month after MRI scanning and whose results are received from our hospital will be included in the study. Patients demonstrating motion artifacts in MR images, those for whom DWI images could not be obtained due to inadequate MR examinations stemming from factors such as claustrophobia, and individuals from whom histopathological sampling results were unachievable were excluded from the study.

The MRI scans were performed utilizing a 1.5 Tesla MRI device using a body phased-array coil (Siemens, Aera, Germany). During the entirety of the examination, patients were positioned in the supine posture. In order to acquire DW images, a single-shot echo-planar imaging sequence was utilized. These images were taken along the axial plane.

MAIN POINTS

- Computed tomography, magnetic resonance imaging (MRI), bronchoscopy, mediastinoscopy, thoracoscopy, and positron emission tomography are used for the evaluation and management of mediastinal lymphadenopathy.
- Magnetic resonance imaging, including diffusion-weighted sequences, serves as a non-invasive technique to ascertain the etiology of mediastinal lymphadenopathy.
- In addition to apparent diffusion coefficient measurement in mediastinal lymph nodes, evaluation of short-axis diameters and T2 heterogeneity increases diagnostic accuracy in characterization.

The DW MRI series encompassed the following parameters: on a scan that was triggered by respiration, every slice had a thickness of 6 millimeters. In the process of obtaining the DWI sequence, images with 2 different *b* values were obtained. These values were determined to be $b = 0b$ and $=400$ s/mm^2, respectively. Measurements and findings on DWI were performed on images with a *b* factor of 400 s/mm^2. The field of view was 360-400 mm, TR = 3800 ms, TE = 70 ms, and the matrix dimensions were 128 × 128. Images of ADC maps were generated automatically from each DW image, and quantitative measurements were carried out at workstations with the assistance of the Syngo® MR software system (Siemens, Germany).

A radiologist with 20 years of experience in thoracic radiology will then conduct a retrospective examination of the images without knowledge of the histopathological diagnosis or additional case details. The largest mediastinal lymph node will be identified in each patient. The localization, dimensions (particularly the short diameter), and appearance on standard MR sequences will be documented, and ADC values will be evaluated. The ADC values of these lymphadenopathies will be computed using the region-of-interest (ROI) placed. The width of the ROI circle will vary from 1 to 2 cm^2. The mean of 3 distinct ADC value measurements from the largest lymph node identified in each patient will be documented. The diameters of the short axis of the lymph nodes were also incorporated into the assessment. Furthermore, associated parenchymal lung pathologies depicted in the images will also be recorded. The contribution of ADC values and other MRI sequences to the diagnosis of benign or malignant lymphadenopathy will be evaluated by comparing the measured values with histopathological results.

Utilizing SPSS for Windows, version 24.0 (IBM SPSS Corp.; Armonk, NY, USA), the data were analyzed. The numerical parameters demonstrating a normal distribution that is normal were reported as mean ± standard deviation. The parameters that deviated from normal distribution of normality were reported as maximum and minimum values. The categorical parameters were presented as either numbers or percentages. The mean ADC values of the numeric variables across the diseased categories were analyzed using an ANOVA test with a 1-way design. The diagnostic performance of the testing method was assessed by receiver operating characteristic (ROC) curve analysis, shown by positive and negative predictive values, sensitivity, and specificity. In lymph nodes with a heterogeneous structure due to necrotic components, ROI placement was performed away from the necrotic area. The statistical significance of the results was determined by a *P*-value lower than .05.

RESULTS

Chest MRI scans of 52 patients with mediastinal lymphadenopathy reported within the specified time frame were analyzed. We excluded Four patients whose chest MR images were not sufficient for our evaluation and 8 patients who did not have histopathological sampling results of lymph nodes within 1 month after MRI at the hospital were excluded. Consequently, 40 patients who met the criteria were incorporated in the study. Twenty-six (65%) patients were male and the overall mean age was 55.4 ± 15.3 years.

Histopathological findings showed granulomatous diseases (tuberculosis and sarcoidosis) in 10 patients, metastatic bronchogenic carcinoma in 8 patients, non-Hodgkin lymphoma in 7 patients, Hodgkin lymphoma in 6 patients, metastatic lymph nodes from distant regions in 6 patients, and reactive lymphoid hyperplasia in 3 patients. The mean ADC values measured according to these pathologies are shown in Table 1.

Table 1. Mean ADC Values of Mediastinal Lymphadenopathy

Histopathological Diagnosis	n	Mean ± SD ($\times 10^{-3}$ mm²/s)
Granulomatous diseases		
Tuberculosis	4	1.94 ± 0.44
Sarcoidosis	6	1.78 ± 0.35
Metastatic bronchogenic carcinoma		
SCLC	3	1.19 ± 0.27
NSCLC	5	1.35 ± 0.15
Non-Hodgkin lymphoma	7	0.89 ± 0.23
Hodgkin lymphoma	6	0.95 ± 0.13
Metastatic lymph nodes from distant		
Breast cancer	3	0.99 ± 0.28
Thyroid carcinoma	1	1.08
Esophageal cancer	1	0.95
Renal cell carcinoma	1	1.11
Reactive lymphoid hyperplasia	3	2.10 ± 0.46

There were 13 patients presented with benign conditions, yielding a mean ADC value, as determined by the largest lymph nodes that are the largest at $1.90 \pm 0.45 \times 10^{-3}$ mm²/s. Conversely, the average ADC value of lymphadenopathies in 27 individuals with malignancy was $1.05 \pm 0.25 \times 10^{-3}$ mm²/s. Comparative analysis of these data revealed that the assessed ADC levels effectively distinguished between benign and malignant lymphadenopathies ($P < .001$). Our attempts to differentiate between malignant lymph nodes based on their etiology, such as lymphoma or metastasis, using ADC measurements yielded no significant results.

Non-Hodgkin's lymphoma exhibited the lowest mean ADC values, whereas granulomatous lymphadenopathy resulting from tuberculosis demonstrated the highest mean ADC values.

In the ROC analysis, utilizing a threshold of 1.50×10^{-3} mm²/s for the ADC variable, we observed a sensitivity of 85%, a specificity of 77%, a positive predictive value of 78.7%, and a negative predictive value of 83.7% in differentiating benign from malignant lymph nodes.

The mean short-axis diameter of lymph nodes was 2.86 ± 1.02 cm (range: 0.7-7.5 cm). All of the subcentimetric ones belonged to reactive lymph nodes. The mean short-axis diameter of the lymph nodes in the benign group was 1.71 ± 0.55 cm. In the malignant group, the average short-axis diameter was 3.41 ± 0.98 cm. Benign and malignant lesions could be differentiated based on short-axis diameter ($P = .03$). The evaluation

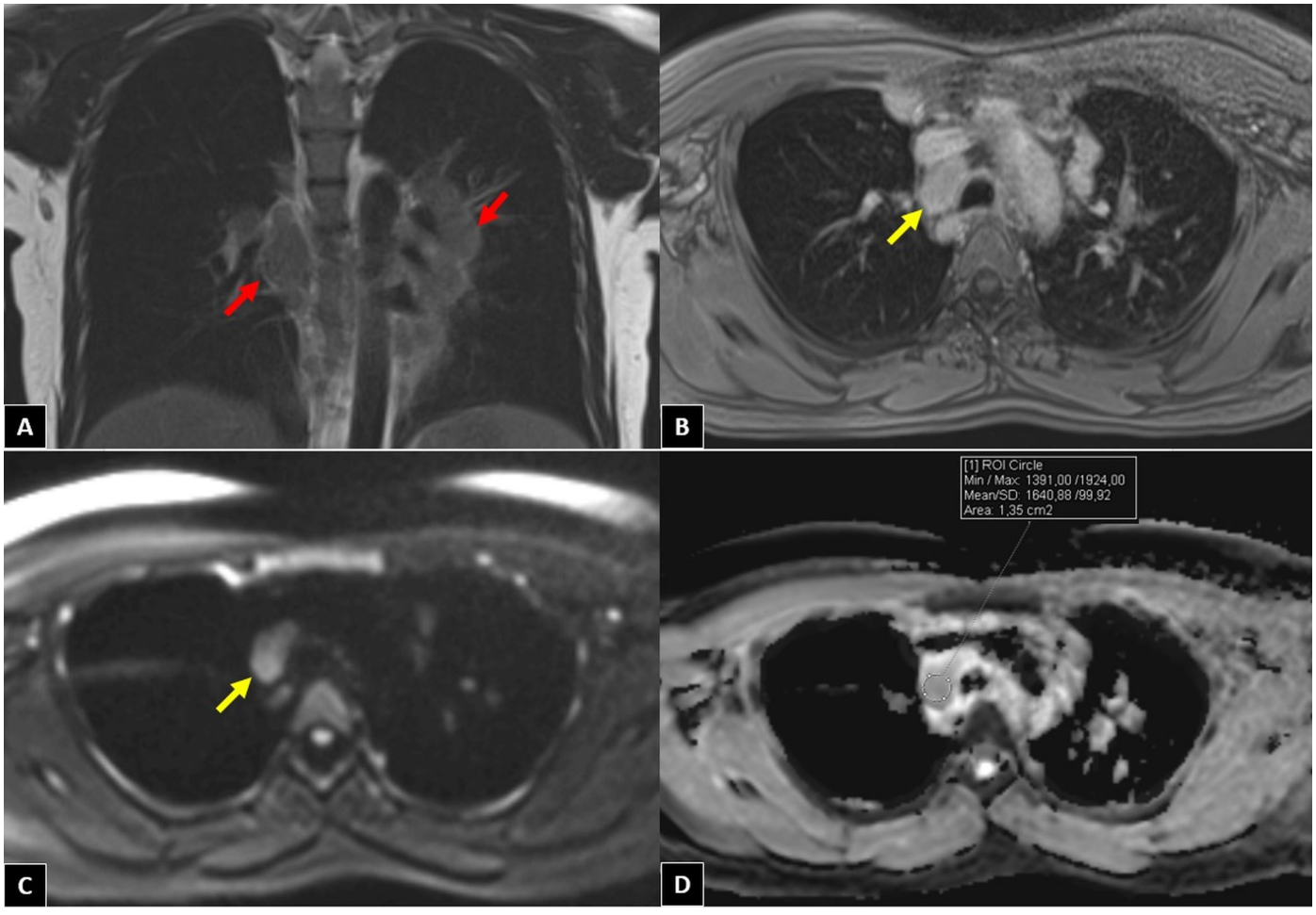

Figure 1. A 38-year-old patient with sarcoidosis. (A) Coronal T2W magnetic resonance (MR) image shows multiple bilateral hilar lymphadenopathy (red arrows); (B) axial post-contrast T1W MR image shows hyper-enhancing right upper paratracheal lymph node (yellow arrow); (C) b = 800 s/mm² diffusion-weighted MR image shows hyperintense right upper paratracheal lymph node (yellow arrow); (D) in the ADC map image, the mean ADC value of this lymph node was measured as 1.64×10^{-3} mm²/s.

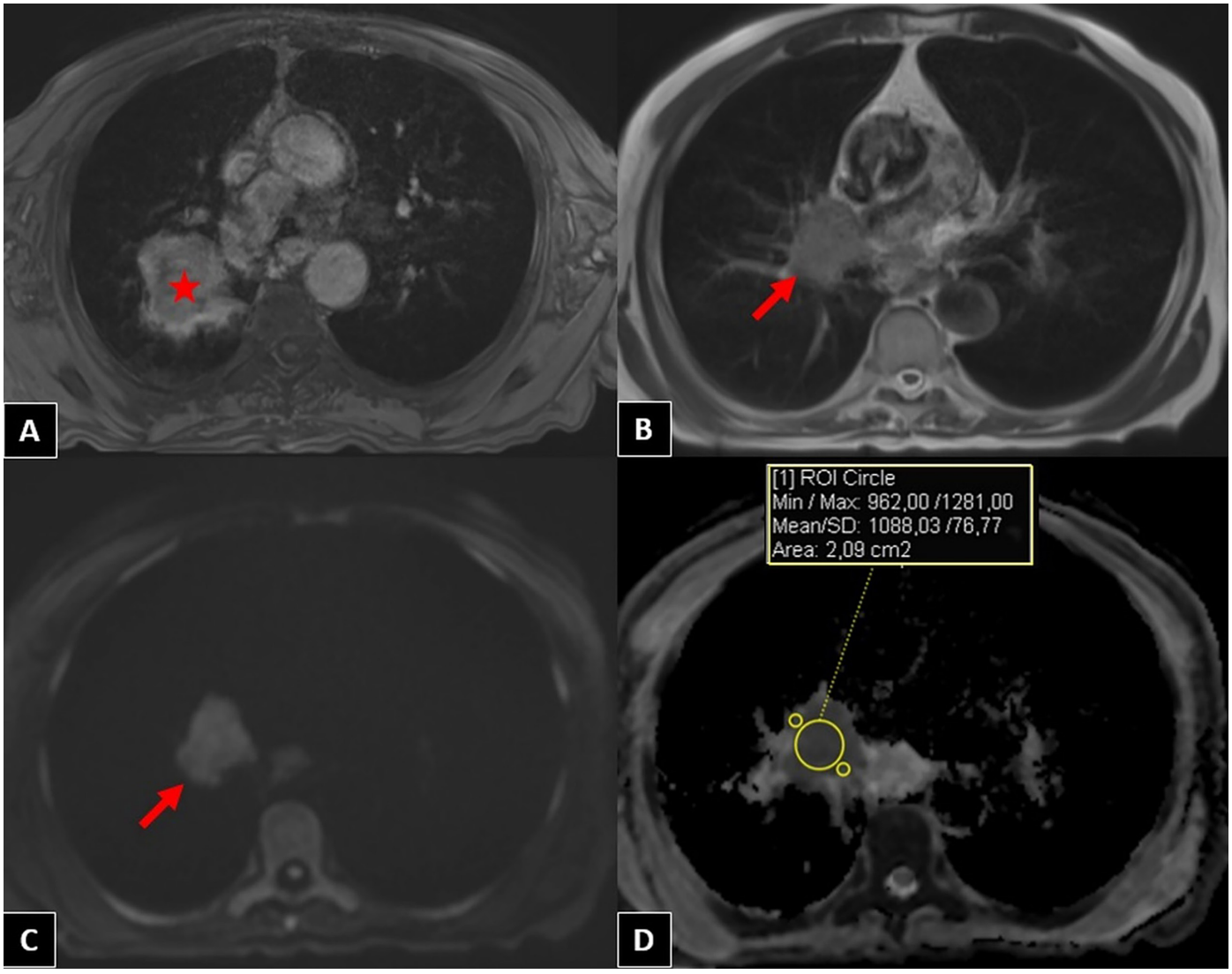

Figure 2. A 65-year-old patient with non-small cell lung cancer. (A) An axial post-contrast T1W magnetic resonance (MR) image shows a hyper-enhancing right upper lobe lung mass (red asterisk); (B) an axial T2W MR image shows right hilar lymphadenopathy (red arrow); (C) A b = 800 s/mm^2 diffusion-weighted MR image shows hyperintense right hilar lymphadenopathy (red arrow); (D) in the ADC map image, the mean ADC value of this lymph node was measured as 1.08× 10^{-3} mm^2/s.

of lymphadenopathies based on short-axis diameters for the purpose of distinguishing between benign and malignant lymphadenopathies showed a sensitivity of 61% and a specificity of 85%, respectively.

The signal intensities of lymph nodes assessed in T1 and T2-weighted conventional MR sequences exhibited no significant difference between benign and malignant groups.

Figures 1 and 2 show chest MRI images of patients with sarcoidosis and non-small cell lung cancer (NSCLC), respectively.

DISCUSSION

Different methods are employed in diagnosing mediastinal lymphadenopathy, which may arise from numerous benign and malignant etiologies. Computed tomography is primarily utilized for the identification of mediastinal lymphadenopathy, with only morphological characteristics being recognized. The gold standard for definitive diagnosis is histopathological sampling via mediastinoscopy, an invasive procedure. Recent studies utilizing ADC measurements in MRI have produced encouraging outcomes in lesion characterization.[3-6]

In the present study, the mean ADC measurement for malignant lymph nodes was substantially reduced ($P < .001$) compared to the values for benign lymph nodes. The primary cause is believed to be the hypercellularity of malignant lesions. Hypercellularity reduces the diffusion area of extracellular water molecules, resulting in lower ADC values in malignant lesions.[10]

Compared to histopathology results, the measurement of ADC values has 85% sensitivity and 77% specificity for the characterization of mediastinal lymphadenopathy (benign and malignant). Wu et al[11] conducted a meta-analysis in which they compared the lymphadenopathies of patients with NSCLC with the lymph nodes of healthy persons. They found that the pooled sensitivity for DWI parameters was assessed to be 72%, while the specificity was around 95%. In comparison to our investigation, the specificity in this meta-analysis was greater;

nevertheless, our approach has shown higher sensitivity. Increased sensitivity is a significant parameter in cancer diagnosis.

In our investigation, we determined 1.50×10^{-3} mm^2/s as the ideal cutoff ADC threshold for distinguishing benign from malignant lymph nodes according to the ROC curve. Different results have been obtained using different threshold values in the literature. Diverse results have been produced with varying threshold ADC values in the literature. Sigovan et al[1] found sensitivity 68.2% and specificity of 84.6% for benign and malignant lymph node differentiation with a cutoff ADC value of 1.28×10^{-3} mm^2/s. In another study, Abdel Razek et al[4] reported sensitivity and specificity rates of 96.4% and 71.4%, respectively, for differentiating between benign and malignant lymph nodes, using a cutoff ADC value of 1.85×10^{-3} mm^2/s. These results show that an increase in the ADC value used as a threshold for mediastinal lymph node characterization enhances sensitivity while diminishing specificity. This factor must be considered while establishing the threshold value.

The ADC value of metastatic lymphadenopathies was higher than that of lymphoma in our analysis; however, this difference was not statistically significant. Moreover, this present research observed no substantial variation in ADC values for lymphadenopathy between Hodgkin and non-Hodgkin lymphoma, although Sabri et al[12] found notable differences in ADC values for both lymphoma types in a prior study. Research findings utilizing diffusion MRI and ADC measures for textural analysis of mediastinal lymphadenopathy indicate that ADC values are the most significant parameter for identifying lymph nodes affected by lymphoma.[13] These studies highlighted that lymphoma exhibited the lowest mean ADC value among malignant pathologies. The primary benefit of this circumstance in clinical practice is significant at this juncture. Lymphoma involvement can be identified if a specific threshold value is established by assessing tiny lymph nodes, which are challenging to diagnose, by ADC measurement.

Despite the lack of significant findings in our study, existing literature demonstrates that the heterogeneity shown in T2-weighted MRI images is much more prevalent in malignant lymph nodes.[9,14] Ramamoorthy et al[9] reported that T2 heterogeneity has a sensitivity of 72.2% and a specificity of 84% in distinguishing malignancies from benign lymph nodes in the mediastinum. According to these results, T2 heterogeneity provides lymph node characterization with a precision close to ADC measurement.

It has been shown in the research, along with several studies in the literature, that short-axis diameter assessment may effectively distinguish between benign and malignant lymphadenopathies. Although it is not as high as ADC measurement, its sensitivity and specificity are promising.[2,4,9] Based on these findings, we may enhance diagnostic sensitivity and specificity by combining T2 heterogeneity and short-axis diameter measurements with ADC data.

The diffusion MRI images acquired from all patients in the investigation were obtained prior to the administration of various therapies. Recent literature indicates that the monitoring of ADC values has been effective in assessing treatment response, particularly in malignant lymph nodes. Besides alterations in lymphadenopathy size, diffusion MRI and ADC values can provide insights into the cellular composition of the lymph node. Usuda et al[15] demonstrated that diffusion MRI outperformed CT in assessing the treatment response of malignant lymph nodes. The absence of post-treatment imaging data constitutes an important constraint in our research.

This research has a few limitations to consider. First of all, since a retrospective single-center study was conducted, the generalizability of the results is weak. The sample size is fairly limited, and the incidence of patients with lymphadenopathy due to benign causes is notably low. This may impact the efficacy and reliability of statistical analyses. Further study involving larger cohorts is essential for strengthening the statistical significance of these results. When it comes to the differential diagnosis of mediastinal lymphadenopathies, the combination of ADC values with biological markers that have the potential to affect the accuracy of diagnosis has not been carried out.

Apparent diffusion coefficient levels are useful in distinguishing benign and malignant mediastinal lymphadenopathies. Consequently, unnecessary utilization of mediastinoscopy, an invasive diagnostic procedure, may be spared.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by Ethics Committee of Erzincan University (Number: 412235 2024-17/15, Date: December 16, 2024).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – T.C., F.M.; Design – F.M.; Supervision – T.C., F.M.; Resources – T.C.; Materials – T.C.; Data Collection and/or Processing – T.C., F.M.; Analysis and/or Interpretation – T.C., F.M.; Literature Search – F.M.; Writing Manuscript – F.M.; Critical Review – T.C., F.M.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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