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THE ROLE OF MRI IN DETECTING ACUTE LESIONS OF MULTIPLE SCLEROSIS USING DIFFUSION-WEIGHTED IMAGING AND CONTRAST-ENHANCED T1WI

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ABSTRACT

Introduction: Multiple Sclerosis (MS) or disseminated sclerosis is a chronic inflammatory demyelinating disease, expressed as a degenerative disease in the central nervous system (CNS). MS is a heterogeneous, multifactorial disease mediated by the immune system and caused by complex interactions between genes and the environment. The pathological hallmark of MS is the accumulation of demyelinating lesions primarily in the white matter and partially in the gray matter of the brain and spinal cord. There is no single diagnostic tool for MS, as the diagnosis relies on a combination of clinical history, laboratory tests, and medical imaging examinations. MRI is the most sensitive imaging method for detecting the spatial and temporal dispersion of asymptomatic white matter lesions, which underscores its importance in the early diagnosis of MS patients. Its sensitivity during the first year after an attack is about 94%, with a specificity of approximately 83%. MRI also helps in excluding alternative differential diagnoses such as spinal cord compressions and brain tumors. Early diagnosis is crucial as MS is the most frequent cause of neurological disability of non-traumatic origin, and early diagnosis plays a significant role in the immediate initiation of effective treatment. The contrast enhanced T1 Weighted Imaging (CE T1WI) has been used as the gold standard for distinguishing between active and inactive MS lesions[3]. However, there are some cases in which the use of gadolinium-based contrast agents (GBCAs) is contraindicated, or costly for patients, in addition to the extra time required for the examination with injection. Therefore, finding an alternative imaging technique with fewer contraindications, no additional cost, and reduced examination time while maintaining good diagnostic value is important. This highlights the significance of Diffusion-Weighted Imaging (DWI), which has emerged over the past decade as a new functional alternative for detecting brain lesions in MS patients. Moreover, distinguishing between active and chronic lesions is somewhat subjective due to several factors that can affect enhancement. Given the drawbacks of conventional MRI, finding an alternative imaging technique could be of significant value. **Study Objective:** This study aims to evaluate the sensitivity and specificity of Diffusion-Weighted Imaging (DWI) in detecting active lesions in MS patients, in addition to comparing the diagnostic value of DWI and CE-T1 in detecting active lesions. **Patients and Methods:** The study includes patients diagnosed with multiple sclerosis (MS) who are currently experiencing clinical symptoms indicative of active lesions. These patients underwent 1.5 Tesla MRI scans at Tishreen University Hospital between March 2022 and January 2024. **Results:** In this study, we followed 66 MS patients who were experiencing clinical symptoms indicative of active lesions. The ages of the patients in the sample ranged from 13 to 53 years, with a mean age of approximately 29.7 ±7.09 years. **Conclusion:** Our study showed that contrast-enhanced T1-weighted imaging (CE-T1) detected the highest number of MS lesions compared to Diffusion-Weighted Imaging (DWI). Despite the presence of false-positive lesions, the DWI/ADC map demonstrated a good ability to detect active lesions compared to CE-T1, with a sensitivity of 94%, specificity of 82%, positive predictive value (PPV) of 79%, negative predictive value (NPV) of 80%, and diagnostic accuracy of 83.4%. Therefore, DWI can be used during acute attacks alongside CE-T1 in cases where contrast injection is not feasible. Nevertheless, CE-T1 remains the gold standard for detecting active lesions in MS patients.

KEYWORDS: Multiple Sclerosis (MS), Contrast-Enhanced T1-Weighted Imaging (CE-T1WI), Diffusion-Weighted Imaging (DWI), Magnetic Resonance Imaging (MRI).

MEDICAL IMAGING METHODS

Plain Radiography

Plain radiographic studies do not have a positive predictive value in diagnosing multiple sclerosis (MS) and are primarily used to exclude other osseous lesions.

Computed Tomography (CT)

Findings from CT scans in MS patients are nonspecific and can sometimes be normal despite specific findings on MRI. MS plaques may appear as homogeneously hypodense areas that can enhance with contrast in the active phase of the disease. Brain atrophy may indicate chronic disease involvement.

Magnetic Resonance Imaging (MRI)

MRI has high sensitivity in detecting white matter changes, and the presence of just two lesions in the four specific locations (periventricular, juxtacortical, infratentorial, spinal cord) is sufficient to meet the McDonald criteria.

MS Lesions

An MS lesion is defined as a region with a high focal signal on T2-weighted imaging. Typical MS lesions are round to oval in shape, ranging from a few millimeters to over one or two centimeters in diameter. Generally, lesions should be at least 3 mm on the long axis to meet diagnostic criteria. Additionally, the lesion's location is crucial; for instance, a lesion less than 3 mm in the floor of the fourth ventricle should be considered abnormal, as flow-related artifacts are rare in this location. Lesions must be visible on at least two consecutive slices to rule out artifacts, although in thicker slices (e.g., ≥3 mm), smaller lesions might be visible on a single slice.

MS lesions typically occur in the hemispheres but often have an asymmetrical distribution in the early stages. White matter lesions caused by other pathologies can affect any white matter area, while MS lesions usually occur in specific regions such as periventricular white matter, juxtacortical white matter, corpus callosum, infratentorial regions (especially the pons and cerebellum), and the spinal cord (with a preference for the cervical segment).

1. Research Objective

- To evaluate the sensitivity and specificity of Diffusion-Weighted Imaging (DWI) in detecting acute lesions in patients with multiple sclerosis (MS).
- To compare the diagnostic value of DWI and contrast-enhanced T1-weighted imaging (CE-T1) in detecting acute lesions, both individually and in combination.

2.2 Research Justification

- Multiple sclerosis (MS) is the most frequent cause of non-traumatic neurological disability. It is crucial to monitor demyelinating diseases, detect new lesions, and determine their activity status.
- DWI is an advanced technique used to monitor patients with demyelinating diseases and detect new lesions before contrast administration.
- CE-T1 is considered the gold standard and is the best method for detecting active MS lesions in the brain.

2.3 Study Duration

- Between March 2022 and January 2023.

2.4 Study Location

- Department of Medical Imaging and Radiological Diagnosis at Tishreen University Hospital, Faculty of Medicine, Tishreen University.

2.5 Study Sample

- Patients diagnosed with MS, currently presenting with clinical symptoms indicative of active lesions, who meet the 2017 McDonald criteria, and are undergoing MRI with a 1.5 Tesla machine at Tishreen University Hospital in Latakia.

2.5.1 Inclusion Criteria

- Patients older than 13 years with a previous MS diagnosis and new indicative symptoms.

2.5.2 Exclusion Criteria

- Patients younger than 13 years.
- Patients with contraindications to MRI.
- Patients with brain trauma.
- Patients without an MS diagnosis.

2.6 Sample Size

- The sample included 66 patients who met the inclusion and exclusion criteria.

2.7 Research Methods

- After obtaining informed consent from the patients for participation in the study, a detailed clinical history was taken for each patient, followed by a thorough clinical and neurological examination to clinically confirm the presence of an acute MS attack.
- Patients underwent MRI with a 1.5 Tesla machine within three weeks of the onset of the acute attack. The imaging protocol at Tishreen University Hospital is as follows:

Before Contrast Administration

- Axial T1WI 5mm + sagittal T1WI 5mm
- Axial T2WI 5mm + sagittal T2WI 5mm
- Axial FLAIR 5mm + coronal FLAIR 5mm
- DWI/ADC (b1000)
- Axial T2WI hemo 4mm
- Sagittal FLAIR 1mm

After Contrast Administration (0.1 mmol/kg)

- Sagittal T1WI 1mm
- Axial T1WI 5mm

Lesions were examined in both DWI and CE-T1 sequences, and findings were recorded. Patients with white matter lesions due to MS were categorised based on MRI findings into four groups:

1. Patients with gadolinium-enhanced lesions (active).
2. Patients with non-enhanced lesions (chronic).
3. Patients with lesions showing restricted diffusion.
4. Patients with lesions not showing restricted diffusion.

- These findings were correlated, results recorded, and data analysed using SPSS Version 26.

2.8 Statistical Methods Used

- Observational Descriptive Study (Cross-sectional study).

RESULTS

The study initially included 82 patients who met the inclusion criteria. However, 11 patients were excluded because their MRI was performed more than three weeks after the diagnosis of an acute attack, 4 patients had contraindications to MRI, and one pregnant patient who underwent DWI refused contrast injection and was therefore excluded. This left a final sample of 66 patients.

- The patients' ages ranged from 13 to 53 years, with a mean age of approximately 29.7 ±7.09 years.
- Age distribution was categorised into the following ordinal groups: 13-22 years, 23-33 years, 34-43 years, and 44-53 years. The largest percentage of patients (69.7%) were in the 23-33 year age group, followed by 22.7% in the 34-43 year group, 4.5% in the 44-53 year group, and 3.03% in the 13-22 year group.

Table 5: Distribution of lesions based on contrast-enhanced T1.

Contrast-enhanced T1	Number of Patients	Percentage
With Enhancement	72 lesions	20%
Without Enhanced	304 lesions	80%

Table 6: Characteristics and location of lesions based on diffusion-weighted imaging (DWI)

DWI	Number of Patients	Percentage
Restricted	159 lesions	48.6%
Not Restricted	168 lesions	51.4%

Table 7: Comparison between contrast-enhanced T1 (CE-T1) and diffusion weighted imaging (DWI) contrast-enhanced T1.

Diffusion Weighted Imaging (DWI)	Contrast Material Enhancement	Not Enhanced
Restricted	68	91
Not Restricted	4	164

Table 8: Diagnostic performance characteristics of diffusion-weighted imaging.

Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Diagnostic Accuracy	Area Under the Curve (AUC)
94%	82%	79%	80%	83.4%	0.76

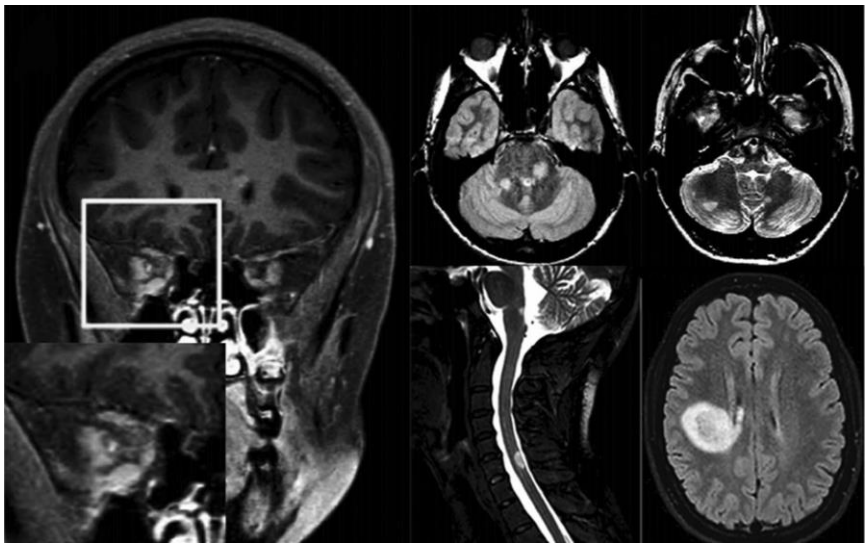

Figure 6: Locations of potential lesions observed in MS patients.

- a: Right optic nerve
- b: Left pons and right middle cerebellar peduncle
- c: Cerebellar hemispheres
- d: Cervical spinal cord
- e: Right cerebral hemisphere

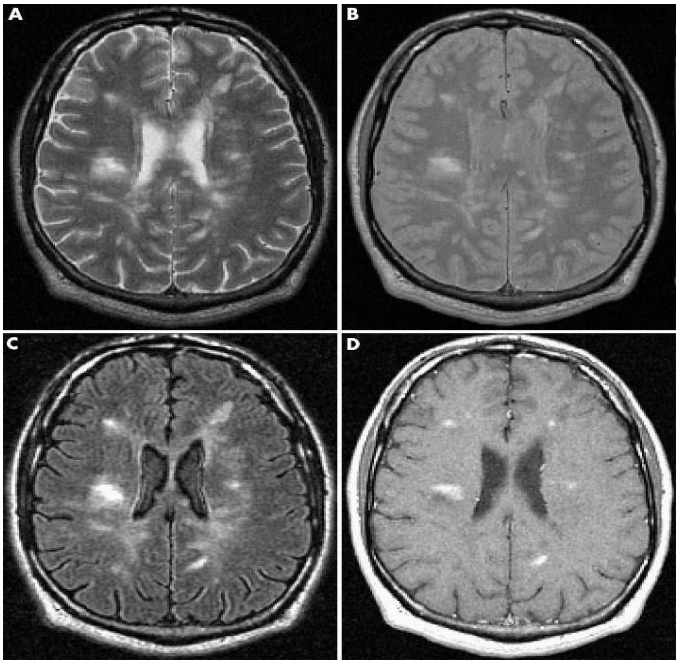

Figure 9: Transverse MRI section of a 30-year-old male with RRMS showing periventricular lesions.

- A: T2WI/ T1WI
- B: PDWI
- C: FLAIR
- D: CE

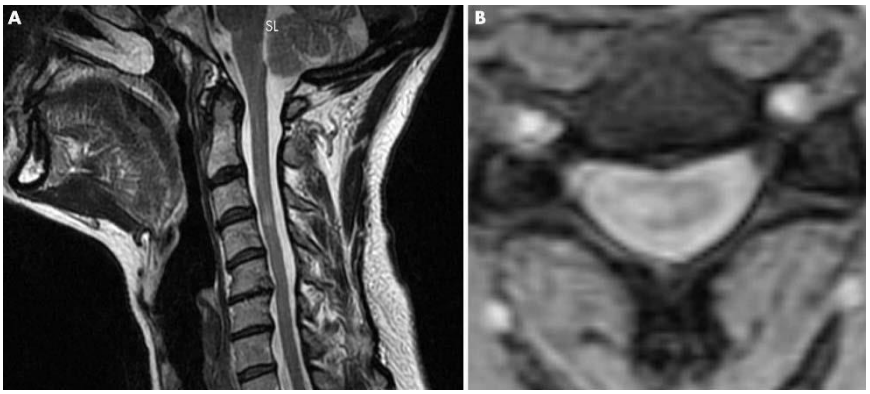

Figure 12: MRI of the cervical spinal cord of a 49-year-old female with CIS showing a lesion at cervical vertebrae C3/4.

- **(A): Coronal section**
- **(B): Transverse section showing the lesion on the right side of the spinal cord**

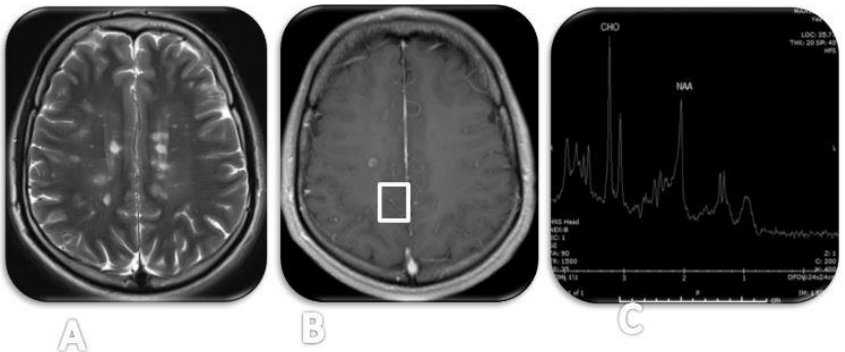

Figure 7: Transverse MRI sections T2WI, (A) T1CE, (B) showing bilateral MS plaques in the frontal and parietal white matter with enhancement in the right parietal region. (C) MRS showing a decrease in NAA levels and an increase in choline and lipids levels indicating areas of acute demyelination.

DISCUSSION

- The study included 66 patients who met the inclusion and exclusion criteria, with ages ranging from 13 to 53 years and a mean age of approximately 29.7 ±7.09 years. The majority of patients were in the younger age groups (23-33 years).
- Of the 66 patients, 25 (37.9%) were male and 41 (62.1%) were female.
- The most common symptom was optic neuritis (42 patients, 63.6%), followed by sensory symptoms (34 patients, 51.5%), pain in various body areas, and brainstem and cerebellar symptoms (32 patients, 31 patients, 48.4%, and 46.9% respectively).
- Lesions Detected: Using CE-T1, 376 lesions were observed, with an average of 5.7 ±2.5 lesions per patient. Of these, 72 lesions were contrast-enhancing, and 304 were not. Most lesions were oval (272 lesions, 72.3%), followed by round lesions (73 lesions, 19.4%), and irregularly shaped lesions (31 lesions, 8.3%).
- Using DWI, 327 lesions were observed, with an average of 4.8 ±1.9 lesions per patient. Among these, 159 lesions showed restricted diffusion, while 168 did not. The number of lesions detected with CE-T1 (376) was greater than those detected with DWI (327).
- There were 68 lesions that both enhanced with contrast and showed restricted diffusion, indicating 4 lesions that enhanced without restricted diffusion, typically seen in active MS lesions imaged within a short period (2-3 weeks) as in our study.
- There were 91 lesions with restricted diffusion that did not enhance with contrast.
- There were 164 lesions that neither enhanced with contrast nor showed restricted diffusion.

Statistical Analysis

- The area under the curve (AUC) for DWI was 0.76 (acceptable predictive ability), with a p-value of 0.43 (>0.05) from the two-tailed Student's T-test, indicating a non-significant statistical result. Thus, the null hypothesis was accepted, suggesting no significant difference between the groups regarding the AUC.

Diagnostic Accuracy

- DWI showed a sensitivity of 94%, specificity of 82%, positive predictive value (PPV) of 79%, negative predictive value (NPV) of 80%, and diagnostic accuracy of 83.4%.

CONCLUSION

CE-T1 had the best capability for detecting true active lesions due to its higher PPV compared to DWI, which had an acceptable but insufficient PPV. Additionally, CE-T1 had a much better diagnostic accuracy than DWI. Therefore, CE-T1 remains the preferred method for identifying active MS lesions, although DWI can still be a valuable supplementary tool in certain scenarios.

Comparison with Global Studies

Comparison with the Study by Lo:

- Agreement:
- Sensitivity outperformed specificity in DWI.
- Used a 1.5-T MRI machine.
- Higher negative predictive value (NPV) compared to positive predictive value (PPV).
- Difference:
- Differences in percentages are due to the difference in the number of patients between the samples.

Comparison with the Study by Yousefi

- Difference
- Found that the specificity of DWI was higher than sensitivity.
- Did not mention the imaging protocol used, raising questions about the causes of differences.
- High false positive rate for DWI and the impossibility of replacing CE-T1 with DWI, which aligns with our study results.

Comparison with the Studies by Unal and Ismail

- Unal
- Used a 3-T MRI machine.
- DWI/ADC maps detected active MS lesions within the first few days of the attack.
- Ismail
- Used a 1.5-T MRI machine.
- Found agreement between CE-T1 and DWI in detecting active MS lesions.
- Our study agrees that CE-T1 cannot be replaced by DWI due to lower specificity and higher false positive rates.

Comparison with the Study by Jahromi

- Used a 1.5-T MRI machine.
- Active MS lesions enhancing with contrast showed diffusion restriction on DWI.
- Preferred using 12D DWI over 3D DWI for higher accuracy.
- Concluded that CE-T1 cannot be replaced by DWI due to high false positive rates.

Comparison with the Study by Foroughi

- Did not mention the imaging protocol used.
- Specificity outperformed sensitivity.
- Agreed that CE-T1 remains the gold standard for detecting active MS lesions, and DWI can be used when contrast injection is not possible.

CONCLUSION

- The diagnostic significance of MRI in diagnosing and monitoring MS patients has increased.
- CE-T1 showed the greatest ability to detect the highest number of MS lesions, making it preferable for routine monitoring of MS patients and identifying active lesions.

- Despite the presence of false positive lesions, DWI/ADC map demonstrated a good ability to detect active lesions compared to CE-T1, with sensitivity at 94%, specificity at 82%, PPV at 79%, NPV at 80%, and diagnostic accuracy at 83.4%. Thus, it can be used during acute attacks when CE-T1 cannot be performed.
- CE-T1 remains the gold standard for detecting active MS lesions.
- Our study showed a higher incidence in females compared to males, with a higher incidence in the younger age group.
- No significant difference was observed using a higher magnetic field device (3-T MRI), and our results agreed with studies using such devices.

Recommendations

1. Emphasize the importance and role of MRI in detecting and monitoring patients with demyelinating diseases, including MS.
2. Use CE-T1 as the gold standard for detecting active MS lesions.
3. Rely on DWI as a sensitive method for detecting active MS lesions when CE-T1 cannot be performed.
4. Emphasize the importance of combining clinical history, laboratory tests, and MRI in diagnosing MS.
5. Preferably conduct MRI within three weeks of the onset of clinical symptoms after ensuring accurate clinical information from the patient by coordinating well with the referring physician to achieve the best results and detect the highest number of active lesions through the combination of CE-T1 and DWI.
6. Highlight the importance of future studies with a larger number of patients and the potential use of more advanced techniques, including higher magnetic field strength and advanced DWI techniques.
7. Combining CE-T1 and DWI can identify MS lesions at different stages, whether active or chronic.

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