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Multiple Sclerosis: Does the Apparent Diffusion Coefficient Have a Diagnostic Efficiency ın Active - Inactive Demyelinating Plaques?

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ABSTRACT

In multiple sclerosis (MS) patients, in the evaluation of active and inactive plaques, the contribution of Apparent Diffusion Coefficient (ADC) measurements to the diagnosis was investigated.
A total of 88 patients, 66 women and 22 men, were examined in this study. The patients' ages ranged from 19 to 53; the median age was 30.5 ±8.1. ADC measurements were taken of every plaque from active and inactive plaques using contrast enhancement (CE) Magnetic Resonance İmaging MRI. ADC measurements were considered active (92) or inactive (230) in accordance to their contrast enhancement, and specificity and sensitivity values were checked.
We examined and comparison the descriptive statistics results of MS plaques in relation to the active and inactive groups in terms of ADC measurement values. Accordingly, the averages for the active and inactive groups, respectively, were found to be 1.011 and 1.245, and the difference was statistically significant between these two averages ($p<0.01$). Accordingly, our study shows that ADC measurements are higher in the inactive group.
ADC measurements can be a useful imaging modality in the differentiation of MS plaques in diffusion-weighted imaging.

Keywords: Apparent coefficient diffussion, active-inactive plaque,Magnetic resonance imaging

Introduction

For young adults, multiple sclerosis (MS) is the most frequently seen chronic inflammatory demyelinating disease of the central nervous system (CNS). The pathology of the disease causes inflammation, demyelination, and axonal damage. As a result of this, the most common pathological finding of MS are cerebral or spinal plaques that have demyelination (1). Both the cortex and the deep gray matter of the brain are affected by MS. The main determinants of long-term disability in MS are irreversible white matter damage and severe demyelination which is caused by the loss of axon (2).

The definitive diagnosing of MS, despite having various imaging modalities, is still difficult. However, with the development of several new magnetic resonance imaging (MRI) techniques, the earlier and more precise diagnosis of MS has been revolutionized. The new imaging techniques available with MRI technology have also given us the chance to obtain more detailed imaging that can distinguish between active and inactive lesions in the diagnosis of MS (1). The main pathological features of MS plaques are axonal damage, gliosis, demyelination, and perivascular inflammation. Edema causes contrast enhancement (CE) on CE-MRI as well as different signal intensities in various MRI sequences. Traditionally, MS patients are diagnosed using various conventional MRI techniques, like gadolinium-enhanced T1-weighted imaging, T2-weighted, and non-contrast T1-weighted. Through the development of quantitative (non-traditional) MRI techniques, a new understanding of the histopathology of MS is now available to us. Due to the primary inflammatory changes exhibited in MS, which includes vasogenic edema following the cytotoxic type of edema, which causes changes in the apparent diffusion coefficient (ADC), which is an index that is used in diffusion-weighted imaging (DWI). In studies, DWI has shown changes in the white matter of patients suffering from acute MS (3, 4, 5). There are international studies that discuss DWI as a viable diagnostic imaging modality that has a reported capability comparable

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to a traditional CE-MRI (3,6). However, there are conflicting results in these studies.

In this study, we wanted to show that ADC measurements in DWI contributed to the diagnosis in the evaluation of MS plaque activity and could routinely be used in MS patients with suspected activity. This led to the evaluation of the consistency between ADC and CE-MRI imaging modalities in order to investigate the possible role that ADC has in the diagnosis of acute MS attacks.

Materials and Methods

Our study included a total of 88 cases, 66 female and 22 males, who were diagnosed with MS after undergoing a brain MRI at Van Yuzuncu Yil Medical School between 2015-2022. The age of the MS cases ranged between 19-53, the mean age was 30.5 ±8.1. MR scans were performed with a Siemens Magnetom Symphony 1.5T MRI System (Siemens, Erlangen, Germany). We first examined the contrast-enhanced brain MRIs of the plaques. We divided the plaques into two groups, active and inactive, according to the contrast uptake in the brain MRI. Then, for each plaque evaluated as acute and inactive, we performed DWI and ADC evaluations and measurements. In this study, we made ADC measurements in 92 active and 230 inactive plaques that we detected with CE-MRI (Figure 1,2).

The protocol we use in our clinic for echo-planar diffusion MRI is the 'trace-0-500-1000-ADC' protocol. The technical parameters were, TR 3600 msec, TE 107 msec, NEX 2, matrix size 128x128, FOV 240x260 mm, slice thickness 5 mm, and slice spacing 0.5 mm.

Contrast-enhanced images were evaluated with SE T1 weighed images (Figure 1). Images were taken 20 minutes after the intravenous administration of 0.1 mmol/kg gadolinium. Plaque images that showed contrast enhancement were considered active, while plaques without enhancement were considered inactive. Both homogeneous and annular contrast enhancing plaques were included in our study.

Regions of interest (ROI) were placed on the ADC map to calculate the ADC values of active and inactive plaque areas in the patients that were evaluated in our study (Figure 2). When placing an ROI in these areas, regions that were far from the ventricular system and gray matter areas were preferred. While examining the plaque areas, the area measurement method was used since most of the plaques' shapes were oval. The ROI area was taken as approximately 18 pixels/58 mm2, taking into account the size of the lesion, and the direct measurement taken from the pixel value was used. For example, if the ROI we obtained on an ADC map was 84.35 mm2, this was expressed as 0.84 and multiplied by '10-3 mm 2/sec'.

Statistical Analysis: In this study, the descriptive statistics for continuous variables were given as mean with a standard deviation, and categorical variables were given as numbers and percentages. The independent groups t-test was used to compare 2 (active and inactive) groups in terms of their ADC values. In addition, to determine the cutoff value when separating the active and inactive groups in terms of this value, a receiver operating characteristic (ROC) analysis was performed. A value of 5% in these calculations was considered to be a statistically significant level. To make these calculations, the IBM SPSS Statistics V21.0 program was used.

Results

The comparison and descriptive statistics results of MS plaques according to active and inactive groups in terms of ADC value are given on Table 1. Table 1 shows the average for the active and inactive groups, respectively was 1.011 and 1.245, and the difference between the two averages is statistically significant ($p<0.01$). Accordingly, it can be said that ADC measurements are higher in the inactive group than in the active group.

As a result of the ROC analysis to separate the inactive group from the active group for the ADC value; the area under the curve was found to be 0.826 ($p<0.01$). Accordingly, when the cut-off value for ADC was taken as 1.095, the sensitivity for this value was 74.8% and the specificity was 71.7% (Table 2).

Discussion

One of the first things that could occur in the development of a MS lesion, which is associated with a marked inflammatory process, may be the disruption of the blood-brain barrier (BBB). This transient disruption of the BBB is reflected on contrast enhancement on MR images through extravasation of contrast material into the brain parenchyma and represents a measure of lesion activity(1,3). As shown in serial MRI scans of patients with relapsing-remitting and secondary-progressive MS, it has been reported that in most

Table 1. Average ADC Values Obtained From Active and Inactive MS Plaques and Their Comparison

	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p
Active	92	1.01148	.138590	.014449	.680	1.310	0.001
Inactive	230	1.24474	.224238	.014786	.870	2.400	
Total	322	1.17809	.229031	.012763	.680	2.400	

Table 2: Sensitivity-Specfity and ROC Curve Analysis From Active and Inactive MS Plaques

Area Under the Curve				
Test Result Variable(s): ADC				
			Asymptotic 95% Confidence Interval	
Area	Std. Errora	p	Lower Bound	Upper Bound
0.826	0.025	0.001	.778	.874

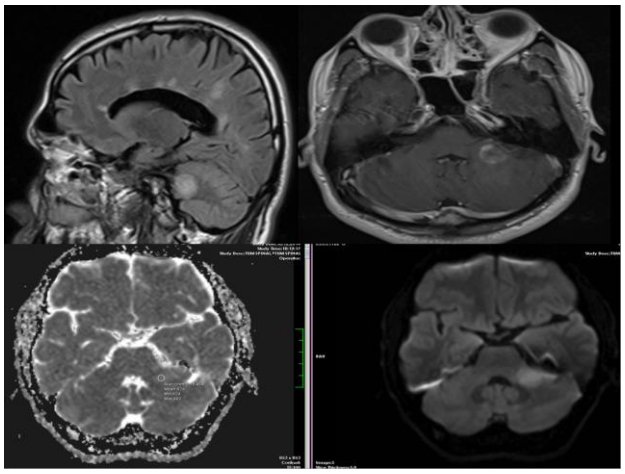

Fig. 1. Contrast Uptake and ADC Measurement Are Observed In The Active Plaque

cases healing occurs in almost all new lesions and takes approximately 4 to 6 weeks(7).

The evaluation of the random water motion at the molecular level is provided by diffusion-weighted MR imaging(5-7). The ADC is a rotationally constant measurement of the total amount of diffusion in a tissue(8). The structural features of the cellular parts of the tissue being studied are reflected by the ADC(7). The cell membranes that form a restrictive barrier against water diffusion are included in the in vivo cellular environment. Studies of model systems suggest that the axonal cell membrane in white matter is sufficient for the restriction of most water diffusion(8). Perpendicular to the axon axis, the diffusion rate is much more restricted, because of possible interactions with the myelin sheath(5). This restrictive property of tissue is reflected by the different directions of ADC in white matter. It

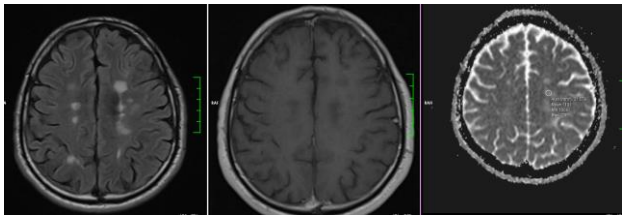

Fig. 2. ADC Measurement Is Observed In Inactive Plaque That Does Not Show Contrast Enhancement

is no surprise that any process disrupting the elimination of axons in white matter would also alter the diffusion properties of water in the tissue. There is increasing interest in the study of MS with diffusion-weighted MR imaging(8, 9, 10).

In other studies, ADC values were found to be higher in active plaques compared to inactive plaques(6, 11, 12). According to these hypotheses, as demyelination develops, the cellular environment of axons becomes less restrictive. These hypotheses are supported by the significant reduction in anisotropy seen in chronic and acute MS lesions (13).

However, Gass et al reported a decrease in the ADC at the border of acute plaques, which the study attributed to cytotoxic edema or hypercellularity. Their report includes the initial evidence that there may indeed be reductions in ADC associated with an MS lesion. Additionally, while contrast-enhancing lesions were hyperintense in diffusion-weighted images compared to white matter, chronic lesions were isointense (14).

We found similar values in our study.

The data from our study showed that ADC measurements in active plaques were lower than in inactive plaques.

The reduction of ADC measurements in active plaques may have caused changes in membrane permeability and shifts in intracellular water protons, or the presence of macromolecules associated with inflammatory cells may have resulted in the restriction of water diffusion and the reduction in ADC.

Our study has some important limitations. Solely patients with MS lesions were included in our study. The size of the ADC's ROIs were not the same, but efforts were made to ensure the measurements of the ROIs were very close to each other. This may have caused variability in the standard deviation of the measurements.

In conclusion, there is a relationship between the enhancement pattern and ADC in MS lesions. ADC measurements in diffusion-weighted MR imaging may offer a different perspective on the pattern of MS plaques.

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