

Neuroradiology || ORIGINAL ARTICLE

Diffusion-Structure Coupling in Optic Neuritis: Correlating Optic Nerve Diameter with ADC Metrics on MRI

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ABSTRACT

Purpose: This study aimed to evaluate the association between DWI-derived apparent diffusion coefficient (ADC) values and optic nerve diameter in patients with optic neuritis.

Material and methods: This retrospective observational study included 43 adult patients with optic neuritis. MRI examinations were analysed to assess optic nerve diameter across different segments and corresponding ADC values. Correlation between optic nerve diameter and ADC values was evaluated using Pearson correlation analysis.

Results: A significant correlation was observed between optic nerve diameter and ADC values, with strong

statistical significance in the intraorbital and intracranial segments ($p < 0.001$) and a weaker but significant correlation in the intracanalicular segment ($p = 0.046$). These findings suggest a relationship between structural changes and diffusion alterations in optic neuritis.

Conclusion: Optic nerve diameter is significantly associated with ADC values in optic neuritis, indicating a potential link between structural and diffusion-based imaging parameters.

These findings support the role of DWI as a complementary tool for assessing optic neuritis, although it should be interpreted in conjunction with clinical and laboratory evaluation.



KEY WORDS

Magnetic Resonance Imaging, Optic Neuritis, Diffusion Weighted Imaging, Apparent Diffusion Coefficient



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Introduction

Optic neuritis is a disease condition characterized by progressive loss of vision which is usually accompanied by pain in eye movements and abnormal pupillary reflexes. The causes of optic neuritis vary widely from idiopathic, inflammatory factors, infections to autoimmune. This optic neuritis can also be at risk of recurrence but can be prevented from complications of blindness if detection can be done more quickly and accurately [1].

The incidence rate of optic neuritis cases (per 100,000 population per year) is estimated at 1 to 6 new cases per 100,000. Magnetic resonance imaging (MRI) is routinely used to evaluate optic neuritis because it can depict structural changes, location of abnormalities, blood-brain barrier disruption and diffusion changes, and identify foci of demyelination. Diffusion-weighted imaging (DWI) is a highly sensitive MRI technique for assessing molecular movement. The Apparent Diffusion Coefficient (ADC) value, which indicates the quantity of diffusion in a specific area, can be calculated using the DWI technique [1-3].

DWI is important for diagnosing optic neuritis, especially in terms of the progression and prognosis of optic neuritis, but the relationship between DWI and the pathophysiology of optic neuritis has not been widely studied. Preliminary research conducted by Fatima et al. (2013) showed a correlation between optic nerve diameter and ADC values in cases of acute and chronic neuritis. This research supports previous research conducted by Hickman et al. (2005) and Iwasawa T. (1997) which demonstrated the role of ADC values in cases of optic neuritis [1,4,5].

The aim of this study was to assess the relationship between DWI images and optic nerve diameter in cases of optic neuritis. This research is expected to help predict the cause and prognosis of optic neuritis and also provide new protocols, particularly the addition of DWI sequences to MRI examinations in optic neuritis cases. This will allow for a precise diagnosis of optic neuritis and enable the public to receive prompt treatment to prevent complications that can lead to permanent blindness.

Material and Methods

This research is a type of observational analytical research with a retrospective research design. The sample size for this study is 43 adults with both eyeballs

collected and analysed. Sampling using consecutive sampling method, patient who meets the inclusion criteria is included in the study. Potential selection bias was minimised by including consecutive eligible patients during the study period. MRI image reading is done by one Professor Specialist Radiology Consultant Neuro Head Neck who evaluates MRI. The observed images are T1, T2, T1 post contrast. DWI, Optic nerve diameter and analyzes the relationship to the assessment system.

Inclusion Criteria are Asian race patients, complete raw data, patients who have undergone MRI examination, patients with unilateral and/or bilateral optic neuritis, patients with acute, subacute or chronic optic neuritis. Exclusion Criteria are incomplete patient raw data, non-Asian patients, stroke patients, patients with Space Occupying Lesion (SOL), patients with infections. The MRI used is a 1.5 Tesla machine. This study was conducted at the Radiology Department of Universitas Airlangga Hospital, Surabaya using patients with optic neuritis cases from July 2021 to December 2023.

The clinical diagnosis of optic neuritis includes symptoms of unilateral and/or bilateral vision loss. The stages can be acute, subacute, or chronic. Acute phase was defined as symptom onset within 2 weeks, subacute phase between 2-6 weeks, and chronic phase beyond 6 weeks.

MRI images show hyperintensity on post-contrast T1WI Fat Sat and T2FSE. Diffusion Weighted Imaging (DWI) is an advanced MRI technique based on the movement of water molecules. The DWI technique in this study used a b value of 1000. In acute cases, intracellular edema occurs and an increase in proinflammatory molecules that disrupt the movement of water molecules and give a restricted diffusion image that appears hyperintense on DWI. In subacute cases, edema will begin to decrease, giving a facilitated diffusion image that appears isointense on DWI. In the chronic phase, hypocellularity occurs, giving an unrestricted diffusion image that appears hypointense on DWI. The optic nerve is segmented into intraocular segment, intraorbital segment, intracanalicular segment, intracranial segment.

This study was conducted at the diagnostic radiology installation of Airlangga University Hospital, Surabaya, using patients with optic neuritis cases at Airlangga University Hospital, Surabaya, from July 2021 to

December 2023. The research data were arranged in a table and then processed using Statistical Programme for Social Sciences (S.P.S.S) software version 30. Correlation test between optic nerve diameter and ADC value using Pearson correlation test. Statistical analysis data comparison between groups using Oneway ANOVA.

The study was conducted after obtaining approval from the UNAIR/Airlangga University Hospital Medical Research Ethics Commission, which was submitted prior to the study's implementation. The study prioritized the interests of the subjects, and each respondent was not charged additional fees for data collection related to the study.

Results

This study is a retrospective cross-sectional analysis. Researchers assessed DWI images in cases of optic neuritis. The assessment included orbital involvement, brain lesions, and nerve segments. Orbital involvement included unilateral or bilateral involvement. Brain lesions associated with optic neuritis included white matter lesions, such as those in Multiple Sclerosis. The affected nerve segments included the intra-orbital, intra-canal, and intra-cranial segments. Researchers also assessed ADC based on the results of the DWI images. The diameter of the optic nerve in each segment was also measured by researchers and then categorized as long or short segments involved in cases of optic neuritis.

The research data were drawn from raw MRI data of optic neuritis patients and medical records of patients who met the inclusion and exclusion criteria. Statistical analysis was performed using IBM SPSS for MacOS version 30 (IBM Corp., Armonk, NY, USA). The study data, from July 2021 to December 2023, included a total of 91 optic neuritis patients at Airlangga University Hospital, with an ICD-10 diagnosis. Forty-three patients met the inclusion and exclusion criteria.

Based on (Table 1), it can be seen that the distribution of the most affected age groups for optic neuritis is in the age range of 41-60 years, amounting to almost 41.9% of the total sample, and the second most affected age group is 20-40 years, amounting to 30.2%. For gender, the largest percentage for this study sample is female, amounting to 25 (58.1%) and male, amounting to 18 (41.9%). The optic nerve segments most affected are long segments, amounting to 33 (76.7%) and short seg-

Table 1: Distribution of Research Samples

No	Variable	Sample
1	Age	
	0 - 19 years old	6 (14 %)
	20 - 40 years old	13 (30.2 %)
	41 - 60 years old	18 (41.9 %)
	61 - 80 years old	6 (14 %)
2	Sex	
	Male	18 (41.9 %)
	Female	25 (58.1 %)
3	Segment Category	
	Long Segment	33 (76.7 %)
	Short Segment	10 (23.3%)
4	Orbital Involvement	
	Unilateral	12 (27.9 %)
	Bilateral	31 (72.1 %)
5	Brain Lesion	
	Yes	4 (9.3 %)
	No	39 (90.7%)
6	Onset	
	Acute	33 (38.4 %)
	Subacute	22 (25.6 %)
	Chronic	18 (20.9 %)

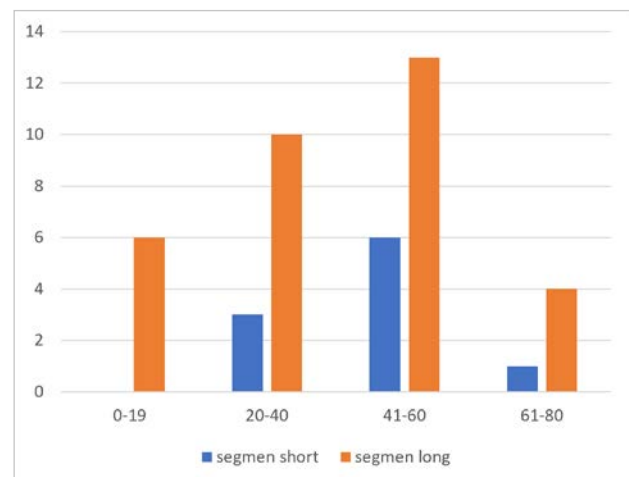


Fig.1: Distribution of segment category by age

ments, amounting to 10 (23.3%). The most affected orbital involvement is on the bilateral side, amounting to 31 (72.1%) compared to the unilateral side, amounting to 12 (27.9%). Most of the samples do not have lesions in the brain, amounting to 39 (90.7%), and those with lesions in the brain are only 4 (9.3%). The affected onset based on clinical and imaging findings was divided into acute phase 33 (38.4%), subacute phase 22 (25.6%) and chronic phase 18 (20.9%).

The characteristics of the research sample based on the age range with optic nerve segment involvement can be seen in the bar chart in (Fig.1). The sample totaled 43 patients with the distribution of the largest number of ages in the age range of 41-60 years as many as 18 (41.9%). Meanwhile, based on the cross tabulation in (Fig.1), it was found that in the age range of 41-60 years, the most optic nerve segment involvement was in the long segment (13 samples out of a total of 18 samples in that age range). In the age range of 20-40 years, the involvement of the optic nerve segment was also most in the long segment (10 samples out of a total of 13 samples in that age range).

The correlation between optic nerve diameter and ADC values was performed using the Pearson correlation test, provided the data were normally distributed. The Kolmogorov-Smirnov test was used to determine the normality of data distribution, with a significance level of 0.2 ($p > 0.05$), indicating that the data met the requirements for normal distribution for the next test, the Pearson correlation test. The correlation test results between optic nerve diameter and ADC values showed a significance level of <0.001 for intraorbital and intracranial diameters, and a significance level of 0.046 for intracanal diameters. Therefore, optic nerve diameter has a significant relationship with ADC values in optic neuritis cases, as the p value was <0.05 .

Comparison between the optic nerve diameter and DWI images using the ANOVA (Analysis of Variance) test with the condition that the data is normally distributed. The normality test for data distribution used the Kolmogorov Smirnov test with a significance result of 0.2 ($p > 0.05$) so that the data meets the requirements for normal distribution to be carried out the next test, namely the ANOVA (Analysis of Variance) test. The results of the difference test between the optic nerve diameter and DWI images showed a significance value

<0.001 . This indicates that there is a significant difference between the DWI image and the optic nerve diameter in each segment.

Discussion

This study aims to assess the relationship between optic nerve diameter and DWI images in optic neuritis cases. This study also assesses the ADC value as an objective value in determining diffusion criteria in contrast-enhanced MRI of the head. Optic nerve diameters were studied in the intra-orbital, intra-canal, and intracranial segments, while the optic neuritis cases studied ranged from the acute, subacute, and chronic phases. All research variable data were correlated with the obtained ADC values and tested differently with DWI image criteria obtained in optic neuritis patients. This study also examined the optic nerve diameter value on the normal orbital side so that it can be used as a reference for normal values in the Indonesian population and also the range of optic nerve diameter values in each intra-orbital, intra-canal, and intracranial segment in optic neuritis cases in Indonesia.

The demographic distribution and optic nerve segments involved provide important information regarding the epidemiology of optic neuritis cases, particularly in Indonesia. At (Fig.2), the 43 patients who met the inclusion criteria, the majority were in the 41-60 years age range (41.9%), with the 20-40 years age range (30.2%) as the second largest group. Based on gender, women were more dominant (58.1%) compared to men (41.9%). This is in accordance with (Sembiring et al., 2015) that optic neuritis is more common in women with a ratio of 3:1 compared to men [6].

In this study, long segment involvement was defined as the involvement of more than one anatomical segment of the optic nerve, including intraorbital, intracanalicular, and intracranial segments, while short segment involvement was limited to a single segment. This distinction is clinically relevant, as longitudinally extensive involvement is more commonly associated with NMOSD and MOGAD, whereas shorter segment involvement is more typical in multiple sclerosis-related optic neuritis [7,8,9].

Orbital involvement and the affected optic nerve segment are key factors in differentiating the type and type of optic neuritis. In multiple sclerosis (MS), optic

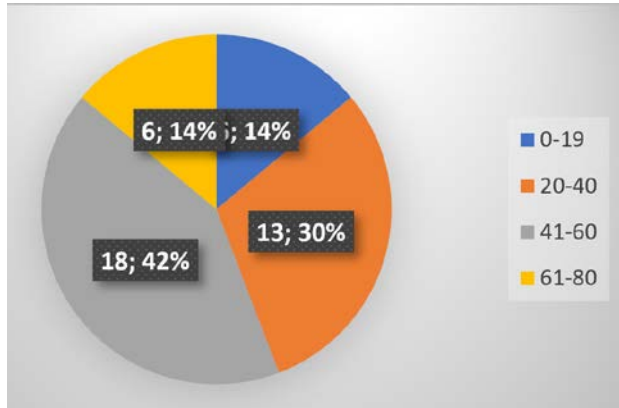


Fig.2: Age Distribution Percentage Diagram

neuritis lesions tend to be unilateral and located on the anterior side of the optic nerve, specifically in the intraorbital and intracanal segments. In Neuromyelitis Optica Spectrum Disorder (NMOSD) cases with AQP4-IgG positivity, optic neuritis lesions are often bilateral and involve multiple segments. 75% of NMOSD cases involve at least two segments and 57% involve more than three segments. Meanwhile, in anti-MOG Antibody-Associated Disease (MOGAD) cases, optic neuritis lesions are often bilateral and more likely to occur in the intraorbital segment, a more anterior location compared to NMOSD [7,10].

In this study, the majority of cases occurred in the long segment (76%), while the short segment only occurred in 23.3% of the total 43 samples. The intraorbital segment is the segment most frequently affected in optic neuritis cases, covering 42% compared to the intracanal segment (30.4%) and the intracranial segment (27.5%).

White matter lesions are a definite finding in multiple sclerosis optic neuritis, involving both the cortex and deep gray matter. The central vein sign is a key feature in differentiating optic neuritis in multiple sclerosis from NMOSD and MOGAD. In NMOSD, brain lesions are also common, but are fewer and do not involve the cortex. In MOGAD, brain lesions are rare and do not involve the cerebral cortex, but MOGAD is often accompanied by ADEM-like brain lesions, especially in children. In this study, only 9.3% of the total sample had brain lesions, and all were clinically diagnosed as multiple sclerosis [7,8].

Diffusion-weighted imaging in optic neuritis should be interpreted cautiously, as diffusion alterations in inflammatory conditions differ fundamentally from cy-

totoxic edema seen in acute ischemia. In optic neuritis, the observed diffusion changes are more likely related to vasogenic edema, inflammatory cell infiltration, and microstructural disorganization rather than true restricted diffusion [11-13].

The stage of optic neuritis plays a crucial role in interpreting imaging findings. In the acute phase, inflammatory edema leads to increased optic nerve diameter and altered diffusion characteristics. In the subacute phase, partial resolution of edema and ongoing demyelination result in normalization trends in both diameter and ADC values. In the chronic phase, axonal loss and gliosis contribute to optic nerve atrophy and increased diffusivity. These dynamic changes highlight the importance of considering disease timing when interpreting MRI findings [12-16].

There is a significant correlation between optic nerve diameter and ADC values, with a significance value of <0.001 . This is consistent with the diffusion theory in cases of edema, which states that the acute phase involves edema and an increase in macrophages. This process results in thickening of the optic nerve diameter and impaired intracellular diffusion. This impaired diffusion is characterized by restricted diffusion on DWI sequences and decreased ADC values. In this study, the acute phase showed thickening of the optic nerve compared to the normal average. The average diameter of the intraorbital segment is 0.48 ± 0.12 cm, the intracanal segment is 0.39 ± 0.09 cm, the intracranial segment is 0.36 ± 0.08 cm, when compared to the diameter in normal cases, the intraorbital segment is 0.41 ± 0.13 cm, the intracanal segment is 0.35 ± 0.11 cm and the intracranial segment is 0.32 ± 0.10 cm [17-18].

The correlation between optic nerve diameter and ADC values observed in this study should be interpreted as a reflection of microstructural changes rather than a direct diagnostic marker. Enlargement of the optic nerve may correspond to inflammatory edema, while ADC variations reflect changes in water mobility influenced by inflammatory and demyelinating processes. These findings support the concept of imaging biomarkers but should be considered exploratory and hypothesis-generating [12,13,19].

In subacute cases, NK cells and microglia accumulate and demyelination begins, with a reduction in intracellular edema. This transition results in a near-normal optic nerve diameter, but signs of inflammation remain

visible on imaging with hyperintense T2 images and contrast enhancement. This reduction in edema results in facilitated DWI images and ADC values approaching normal. In this study, the subacute phase showed a mean diameter nearly equal to normal. The average diameter of the intraorbital segment is 0.43 ± 0.11 cm, the intracanal segment is 0.35 ± 0.10 cm, the intracranial segment is 0.32 ± 0.009 cm, when compared to the diameter in normal cases in the intraorbital segment is 0.41 ± 0.13 cm, the intracanal segment is 0.35 ± 0.11 cm and the intracranial segment is 0.32 ± 0.10 cm [17,18].

The chronic phase is characterized by the loss of axon cells and results in atrophy of the optic nerve. This mechanism occurs through the process of gliosis and results in a shrinking of the optic nerve diameter. DWI then shows an unrestricted diffusion area. In this study, the chronic phase showed a smaller average diameter compared to normal values. The average diameter in the intraorbital segment was 0.33 ± 0.15 cm, the intracanal segment 0.29 ± 0.11 cm, and the intracranial segment 0.27 ± 0.10 cm, compared to the diameter in normal cases in the intraorbital segment of 0.41 ± 0.13 cm, the intracanal segment 0.35 ± 0.11 cm, and the intracranial segment 0.32 ± 0.10 cm [17,18].

Previous studies have demonstrated similar trends in diffusion changes in optic neuritis, although findings remain heterogeneous due to differences in imaging protocols and disease stages. Some studies report decreased ADC values in acute inflammation, while others suggest variable or even increased ADC depending on

the balance between intracellular and extracellular water components. This variability underscores the need for standardized imaging protocols [11,13,15].

DWI images are divided into restricted, facilitated, and unrestricted diffusion areas based on the level of diffusivity. This value is quantified by the ADC value. Parametric tests demonstrated a strong correlation between optic nerve diameter and ADC values ($p < 0.001$). Similar results were also found in the comparative analysis of optic nerve diameter and DWI images, characterized by a significant difference between DWI images and optic nerve diameter in each segment ($p < 0.001$). The results showed consistent values between optic nerve diameter, ADC values, and DWI images. A thickened optic nerve diameter is accompanied by a decrease in ADC values, with a restricted diffusion area image (Fig.4). Meanwhile, in chronic cases, the optic nerve diameter atrophies, accompanied by an increase in ADC values, with an unrestricted diffusion area image (Fig.3).

The application of DWI in orbital imaging presents several technical challenges, including susceptibility artifacts from adjacent bone structures, motion artifacts, and limited spatial resolution. These challenges are particularly pronounced in the intracanalicular segment, where small anatomical size and surrounding osseous structures may reduce image quality. Therefore, the reproducibility of DWI measurements in optic neuritis may vary across imaging centres depending on MRI hardware and expertise [9,13,19].

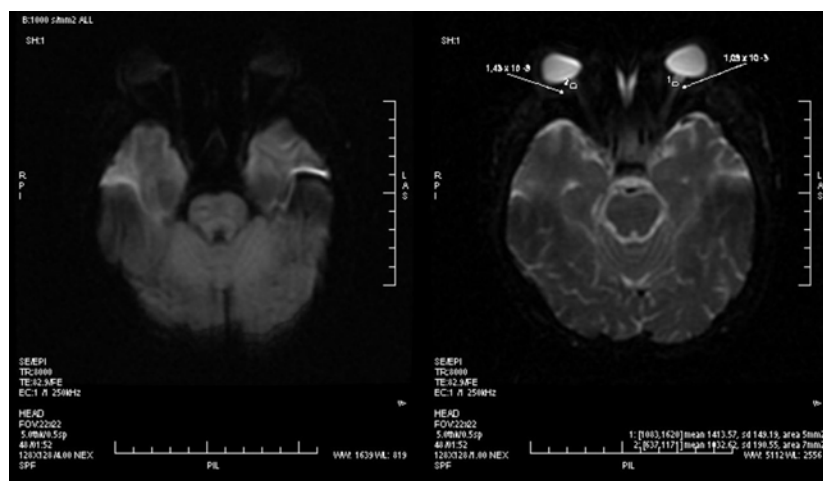


Fig.3: DWI image of chronic optic neuritis shows an unrestricted diffusion area in the long segment with an ADC value of $1.43 \times 10^{-3} \text{ mm}^2/\text{s}$ in right eye and $1.03 \times 10^{-3} \text{ mm}^2/\text{s}$ in left eye

Given these technical limitations, the implementation of orbital DWI requires optimized acquisition protocols, including the use of high-field MRI, dedicated orbital coils, and motion reduction strategies. Consequently, this technique may not yet be universally applicable in all clinical settings, particularly in resource-limited environments. This limitation should be acknowledged when considering its role in routine clinical practice [9,14,19].

This study demonstrated a significant correlation between optic nerve diameter and ADC values. This correlation was also supported by a significant difference between optic nerve diameter and DWI images. These imaging findings were then clinically correlated based on the onset of optic neuritis: acute, subacute, and chronic. There was a significant difference in the

diameter of the optic nerve in the intraorbital segment between groups with different onsets. This is because most of the segments involved in this study occurred in the intraorbital segment.

The present study contributes to the growing body of literature by integrating structural and diffusion parameters, emphasizing the concept of diffusion-structure coupling. Unlike prior studies that focused solely on ADC values, this study highlights the relationship between morphometric changes and microstructural alterations, offering a more comprehensive imaging perspective. This approach may enhance the understanding of optic neuritis pathophysiology [12,16].

Despite the potential of MRI-based parameters, imaging findings should not be considered a replacement for serological biomarkers such as AQP4-IgG and MOG-IgG.

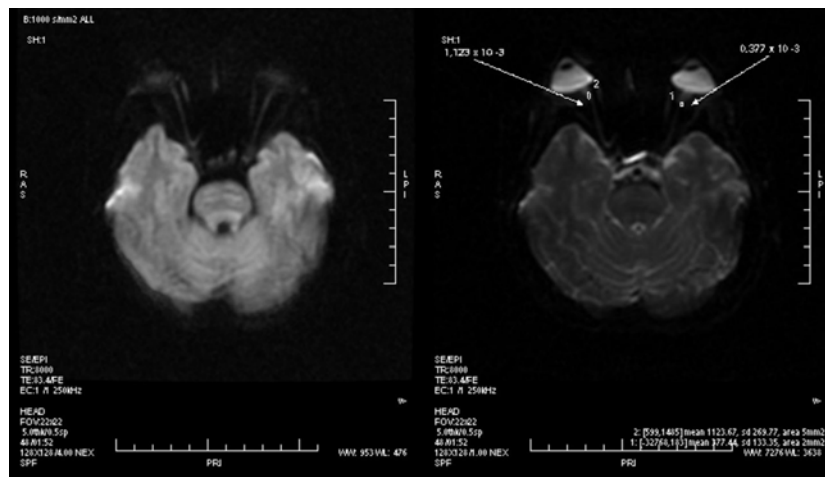


Fig.4: DWI image of subacute optic neuritis at right eye and acute optic neuritis at left eye shows a facilitated diffusion area in the short intra-orbital segment with an ADC value of $1,123 \times 10^{-3} \text{ mm}^2/\text{s}$ at right eye and $0,377 \times 10^{-3} \text{ mm}^2/\text{s}$ at left eye

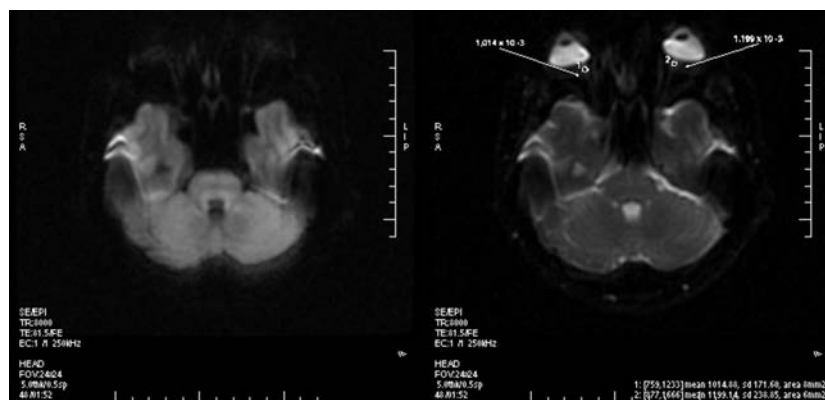


Fig.5: DWI image of subacute optic neuritis shows a restricted diffusion area in the short intra-orbital segment with an ADC value of $1.014 \times 10^{-3} \text{ mm}^2/\text{s}$ at right eye and $1.199 \times 10^{-3} \text{ mm}^2/\text{s}$ at left eye

Instead, MRI should be viewed as a complementary tool that provides structural and functional insights, aiding in diagnosis and disease characterization, particularly in settings where serological testing is unavailable or inconclusive [7,8,20].

Future research should focus on multicentre studies with standardized imaging protocols, as well as the integration of advanced MRI techniques such as diffusion tensor imaging, tractography, and artificial intelligence-based analysis. These approaches may improve the diagnostic accuracy and prognostic value of imaging in optic neuritis, ultimately facilitating personalized patient management [15,16,20,21].

Conclusion

Diffusion-weighted imaging provides valuable insight into microstructural changes in optic neuritis, particularly through its association with optic nerve diameter. This study demonstrates a significant correlation between optic nerve diameter and ADC values, suggesting a relationship between structural and diffusion alterations across different disease stages. However, these diffusion changes should be interpreted cautiously, as they likely reflect inflammatory and microstructural alterations rather than classical restricted diffusion seen in cy-

totoxic edema. Given the technical challenges of orbital DWI and variability across imaging settings, the clinical application of this technique may be limited to centres with adequate expertise and optimized protocols.

Importantly, MRI findings should be regarded as complementary to clinical and laboratory evaluation. While imaging may provide supportive diagnostic and pathophysiological information, it cannot replace biomolecular testing such as AQP4-IgG and MOG-IgG. Future studies with larger cohorts and standardized imaging protocols are needed to further validate the role of diffusion-based MRI parameters as potential imaging biomarkers in optic neuritis. **R**

Conflict of Interest

The authors declare no conflict of interest.

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This project did not receive any specific funding.

Ethical Approval

This retrospective study was approved by the Ethics Committee of Universitas Airlangga Hospital (Number : 045/KEP/2025). Requirement for informed consent was waived.

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