ORIGINAL ARTICLE

Magnetic Resonance Imaging as a Potential Optic Nerve Area Measurement in Optic Nerve Atrophy Diagnosis

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Objective: To report a threshold optic nerve area on magnetic resonance imaging (MRI) that predicts the clinical diagnosis of optic nerve atrophy in the population made by ophthalmologist. Those values could further clinically apply.

Materials and Methods: The authors evaluated 23 clinical consistent patients with optic nerve atrophy. Among 46 patients' eyes, 33 "affected" eyes were clinically diagnosed with optic nerve atrophy and 13 "unaffected" eyes were used for analyses. Twenty-three controls were also included, and their 46 eyes were used for analyses. Images from the coronal sequence on MRI, excluding the optic nerve sheath, at an image slice along the intraorbital portion of the optic nerve were used to measure optic nerve area. A freeform ROI measurement tool on the PACS was used to outline and measure the cross-sectional optic nerve areas.

Results: There was a statistically significant difference in optic nerve area among patients' eyes with optic nerve area (mean 1.35±0.41 mm^2), patients' unaffected eyes (mean 2.55±0.48 mm^2, $p<0.001$), and control eyes (mean 4.21±1.08 mm^2, $p<0.001$). In addition, a statistically significant difference in optic nerve area was observed between patients' unaffected eyes and control eyes ($p<0.001$). Selecting a threshold MRI-measured optic nerve area was 2.7 mm^2 yielded a sensitivity of 100% and a specificity of 97.8% in predicting the presence of optic nerve atrophy by clinical diagnosis.

Conclusion: The present study data suggests that MRI-measured optic nerve area of 2.7 mm^2 or less has both high sensitivity and high specificity for predicting the presence of optic nerve atrophy, making it a potential diagnostic tool for radiologists.

Keywords: Optic nerve measurement; Optic nerve atrophy

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Optic nerve is a small white matter fiber bundle that exits the globe and courses posteriorly to optic chiasm, and responsible for communicating all visual stimuli to the optic tracts. It is immediately surrounded by cerebrospinal fluid (CSF) and sits inside the fatty tissue of the orbit.

Optic nerve atrophy occurs when there is an injury to the retinal ganglion cells or their axons and is primarily diagnosed on a clinical basis[1,2]. Careful assessment, considering the clinical context of the patient including visual acuity, color vision, pupils, and the fundus, combined with specific ancillary testing such as computerized visual fields, is necessary to establish the diagnosis and etiology. The classic clinical presentation of optic nerve atrophy includes decreased visual acuity, visual fields, and color vision[3].

Previous study discussed the normal size of optic nerve using magnetic resonance imaging (MRI) in Thai population[4], however, there is no research discussing the optic nerve atrophy in Thai population compared with the normal optic nerve population.

MRI of the orbits represents a viable diagnostic tool for optic neuritis. In the acute phase, optic neuritis may present as an active lesion of optic nerve on T1-weighted (T1w) post-contrast sequences. This may leave a hyperintense lesion on T2-weighted (T2w) MRI upon the resolution of the inflammatory event. Signal alterations on T2-weighted MRI may not be visible even in the presence of a clear acute clinical event or chronic symptoms sequelae of tissue injury. Capturing axonal loss that results in optic nerve atrophy is virtually impossible. Measuring volume of the optic nerve is challenged by lack of contrast within the optic nerve and resolution

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sufficiently high to discriminate between the optic nerve and surrounding CSF.

The present study aimed to report a threshold optic nerve area on MRI that predicted the clinical diagnosis of optic nerve atrophy in the population made by ophthalmologist which values could be clinically applied.

Materials and Methods

The present study was approved by the Ethic Committee, COA 151/65, and informed consent was waived. Retrospective analyses of patients and controls in Vajira Hospital between May 2018 and April 2022. The gender and age were evaluated. From the outpatient department (OPD), patients who were clinically consistent with optic nerve atrophy from an optical coherence tomography (OCT) examination and orbital MRI by the ophthalmologists' staff in the hospital were recruited. The controls were collected from patients who underwent imaging for seizure, headache or other conditions suspected orbital abnormalities but had no findings suggestive of optic nerve atrophy on neuro-ophthalmologic examination.

MRI data acquisition

MRI examinations were performed on 3.0 tesla MR system (Ingenia, Philips Medical System, Best, the Netherlands) with 20-channel head coil. MRI parameters for patients and controls were the following: MRI T2w/fat suppressed (FS) parameters: repetition time (TR) 900 ms, echo time (TE) 20 ms, inversion time (TI) 200 ms, slice thickness 3 mm, gap 0.3 mm, field of view (FOV) 150. Pulse sequence for orbit protocol: conventional MRI T1w/FS, T2w/FS, T1w/Gd/FS in axial and coronal planes. For both patients and controls, the routine MRI orbit was performed and the images from a coronal T2w/FS sequence were used to measure optic nerve area, excluding the optic nerve sheath, at an image slice along the intraorbital portion of the optic nerve. The image was chosen on the basis of where the optic nerves appeared most round and most perpendicular to the coronal plane based on visual inspection, approximately halfway between the optic nerve-globe junction and the orbital apex. Measurements were obtained from the same image slice by two of the coauthors, who are neuroradiologist with more than five years of experience, independently and blinded to whether the study belonged to a patient or a control. Then, the mean value of the two coauthors were collected in the study data.

A freeform region of interest (ROI) measurement tool on the picture archiving and communication system (PACS) was used to outline and measure the cross-sectional optic nerve areas (Figure 1). The optic nerve area measurement process involved zooming in on each nerve separately to facilitate precise and accurate outlining of the nerve contours.

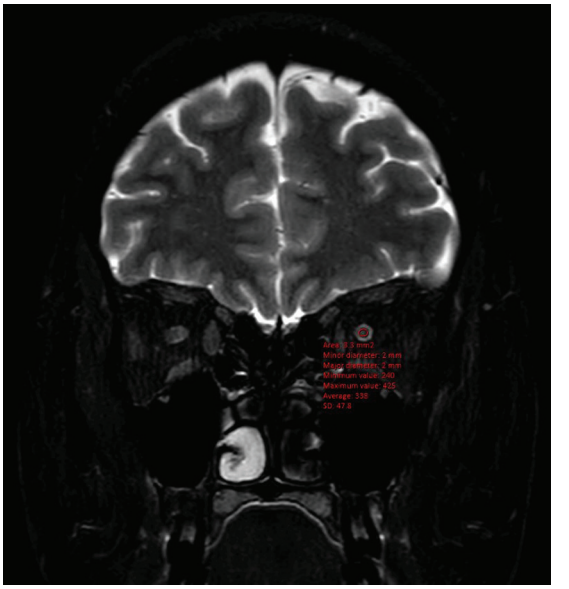

Figure 1. Example of MRI measurement of the optic nerve area. Coronal image through the orbits approximately midway between the orbital apex and globes. The measurement of the crosssectionalarea of the left optic nerve (excluding the optic nerve sheath) is shown using a freeform ROI measurement tool.

Statistical analysis

Demographic continuous data were presented by mean ± standard deviation (SD). Categorical data were presented as number and percentage. Independent t-test was used to compare continuous data, and chi-square test was used to compare categorical data. The difference in mean optic nerve area between groups were tested by analysis of variance (ANOVA) with a Bonferroni post hoc test. Receiver operating characteristic (ROC) curve was used to evaluate the optimal cut-off point for predictive abnormal group. A p-value of less than 0.05 was considered statistically significant. All data were analyzed using PASW Statistics, version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

The characteristics of subjects and controls are presented in Table 1. Twenty-three patients that included 18 males and 5 females were included. Their age ranged between 13 and 86 years, with a mean of

Table 1. Demographic data

	Control (n=23)	Patients (n=23)	p-value
Age (years); mean±SD	60.65±15.19	60.47±15.09	0.973
Sex; n (%)			0.016
Male	10 (43.5)	18 (78.3)	
Female	13 (56.5)	5 (21.7)	

SD=standard deviation

60.47±15.09 years. Twenty-three controls, including 10 males and 13 females were also included. They were aged between 13 and 85 years, with a mean of 60.65±15.19 years). There was no statistically significant difference in age (p=0.973) between the patient and control groups.

Among the 46 patients' eyes, 33 "affected" eyes with clinical diagnosis of optic nerve atrophy and 13 "unaffected" eyes were used for analyses. Among the 23 control eyes, 46 eyes were used for analyses, as shown in Table 2. There was a statistically significant difference in optic nerve area among patients' eyes with optic nerve area with a mean of 1.35±0.41 mm^2, patients' unaffected eyes with a mean of 2.55±0.48 mm^2 (p<0.001), and control eyes with a mean of 4.21±1.08 mm^2 (p<0.001). In addition, a statistically significant difference in optic nerve area was observed between patients' unaffected eyes and control eyes (p<0.001).

An ROC curve was created to test the ability of optic nerve area to predict the diagnosis of optic nerve atrophy, namely its ability to separate 33 affected eyes from 46 healthy eyes (Figure 2). The area under the curve was 1.00 (95% CI 95.4 to 1.00). Selecting a threshold MRI-measured optic nerve area was 2.7 mm^2 yielded a sensitivity of 100% and a specificity of 97.8% (Table 3) in predicting the presence of optic nerve atrophy by clinical diagnosis.

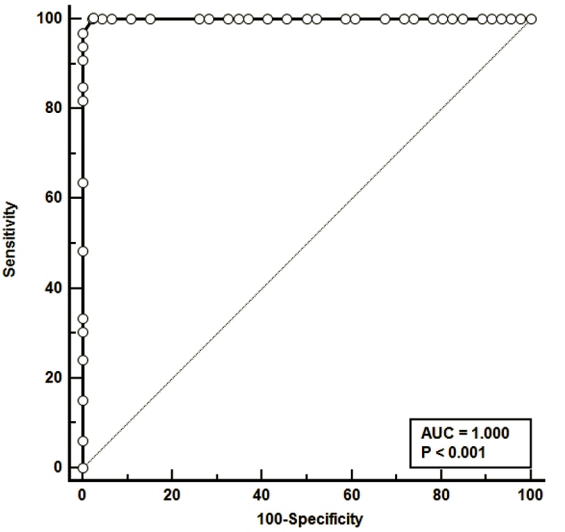

Figure 2. ROC curve analysis (n=33, n=46) of optic nerve area measurement in patients with optic nerve atrophy compared with control subjects.

Discussion

The present study investigation has excluded very young subjects with an age below 13 years because a prior study from Al-Haddad et al.[5] shows that most optic nerve growth occurred in the first two

Table 2. Comparison of optic nerve area between groups

	Control (n=46) mean±SD	Patients; mean±SD		p-value		
		Normal (n=13)	Abnormal (n=33)	Control vs. normal	Control vs. abnormal	Normal vs. abnormal
Optic nerve area (mm^2)	4.21±1.08	2.55±0.48	1.35±0.41	<0.001	<0.001	<0.001

SD=standard deviation

Table 3. Criterion values and coordinates of the ROC curve with sensitivity and specificity

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	–LR	95% CI
<0.6	0.00%	0.0 to 10.6	100%	92.3 to 100.0			1.00	1.0 to 1.0
≤2.1	96.97%	84.2 to 99.9	100%	92.3 to 100.0			0.030	0.004 to 0.2
≤2.7	100%	89.4 to 100.0	97.83%	88.5 to 99.9	46.00	6.6 to 319.6	0.00	
≤6.9	100%	89.4 to 100.0	0.00%	0.0 to 7.7	1.00	1.0 to 1.0		
Youden index J	0.9783							
Associated criterion	≤2.7							
Sensitivity	100%							
Specificity	97.83%							

CI=confidence interval; +LR=positive likelihood ratio; –LR=negative likelihood ratio

years of life. In fact, the optic nerve increases in size in utero to reach normal neonate size at 36 weeks of gestation[6], then it continues to grow up to two years of age and less rapidly thereafter according to histologic studies[7,8].

The present study of optic nerve area measured by MRI in optic nerve atrophy patients with mean age 60.47±15.09 years in affected eyes and unaffected eyes compare them to each other and to age-matched control with mean age 60.65±15.19 years. The present study showed statistically significant difference in mean optic nerve area between patients affected eyes 1.35±0.41 mm², patients' unaffected eyes 2.55±0.48 mm², and control healthy eyes 4.21±1.08 mm², corresponding with prior study. For example, in the previous study, Zhao et al.[9] reported mean optic nerve area in patients affected eyes 3.09±1.09 mm², patients' unaffected eyes 5.27±1.39 mm², and control eyes 6.27±2.64 mm². The present study shows statistically significant difference in optic nerve area between patients' unaffected eyes and control eyes ($p<0.001$) differed from the previous study of Zhao et al.[9] reported no significant difference in optic nerve area between patients' unaffected eyes and control eyes ($p=0.21$). Patients' unaffected eyes from the present study investigation may have underlying disease to further progression to optic nerve atrophy in the future.

When ganglion cells or their axons are injured, optic nerve atrophy ensues. Optic neuritis, which is commonly associated with multiple sclerosis, and other optic neuropathies, such as ischemic as hypertension, diabetes, and giant cell arteritis, compressive as orbital or intracranial mass, and inflammatory, toxic, traumatic, or hereditary as mitochondrial disease, can all cause this process[1,3]. Optic nerve atrophy is still mostly a clinical diagnosis. The findings of the present study suggested that measuring optic nerve area on orbital MRI can help detect and diagnose optic nerve atrophy.

The variation in optic nerve area measurement is caused by manual technique, which may cause interobserver variability. The authors evaluated optic nerve area at the same intraorbital site to reduce variation, which was approximately half-way between optic nerve-globe junction and the orbital apex, in both patients and controls.

There are limitations to the present study including the small sample size and single time study. This will be a subject for future investigation with large sample size, longitudinal and multicenter studies.

Conclusion

The present study data suggests that MRI-measured optic nerve area of 2.7 mm² or less has both high sensitivity and high specificity for predicting the presence of optic nerve atrophy, making it a potential diagnosis tool for radiologists.

What is already known on this topic?

Optic nerve atrophy is diagnosed by clinical but there is no threshold optic nerve area on MRI.

What does this study add?

This study shows the threshold optic nerve area on MRI for predicting the presence of optic nerve atrophy.

Acknowledgement

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Data availability

The authors confirm that the data supporting the findings of this study are available within the article. Raw data that support the findings of this study are available from the corresponding author, upon reasonable request.

Conflicts of interest?

The authors declare no conflict of interest.

References

1. Biousse V, Newman NJ. Diagnosis and clinical features of common optic neuropathies. Lancet Neurol 2016;15:1355-67.
2. Trip SA, Schlottmann PG, Jones SJ, Li WY, Garway-Heath DF, Thompson AJ, et al. Optic nerve atrophy and retinal nerve fibre layer thinning following optic neuritis: evidence that axonal loss is a substrate of MRI-detected atrophy. Neuroimage 2006;31:286-93.
3. Behbehani R. Clinical approach to optic neuropathies. Clin Ophthalmol 2007;1:233-46.
4. Watcharakorn A, Witayapiboon S, Mingkwansook V. Measurement of normal diameter of optic nerve and optic nerve sheath using MRI. Sci Technol Asia 2021;26:167-73.
5. Al-Haddad CE, Sebaaly MG, Tutunji RN, Mehanna CJ, Saaybi SR, Khamis AM, et al. Optic nerve measurement on MRI in the pediatric population: Normative values and correlations. AJNR Am J Neuroradiol 2018;39:369-74.
6. Haratz K, Viñals F, Lev D, Feit H, Ben-Sira L, Lerman-Sagie T, et al. Fetal optic nerve sheath measurement as a non-invasive tool for assessment of increased intracranial pressure. Ultrasound Obstet Gynecol

2011;38:646-51.
7. Dolman CL, McCormick AQ, Drance SM. Aging of the optic nerve. Arch Ophthalmol 1980;98:2053-8.
8. Magoon EH, Robb RM. Development of myelin in human optic nerve and tract. A light and electron microscopic study. Arch Ophthalmol 1981;99:655-9.
9. Zhao B, Torun N, Elsayed M, Cheng AD, Brook A, Chang YM, et al. Diagnostic utility of optic nerve measurements with MRI in patients with optic nerve atrophy. AJNR Am J Neuroradiol 2019;40:558-61.