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Changes of normal appearing optic nerve head on diffusion-weighted imaging in patients with diabetic retinopathy

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ABSTRACT

Purpose: To investigate whether there is any change by measuring ADC values particularly of the optic nerve head (ONH) in patients with diabetic retinopathy (DR).
Material and methods: ADC values at the ONHs was measured in 56 patients and 68 controls.
Results: ADC values of ONHs were significantly higher in patients with DR compared to controls ($p = 0.011$). ADC values in patients with macular edema were higher than those without macular edema ($p = 0.017$).
Conclusion: DWI of ONHs can be useful in cases where it is difficult to assess macular edema during fundus examination, especially in diabetic patients with cataract.

1. Introduction

The optic nerve or cranial nerve II is not a true cranial nerve but a fiber tract of the brain formed by axons of the retinal ganglion cells, which become myelinated by oligodendrocytes as they leave the optic nerve head. A wide variety of benign and malignant conditions may affect the optic nerve.

Diabetes mellitus (DM) is a multisystemic disease which causes damage in many organs and systems. Although the pathogenesis of diabetes has not yet been completely elucidated, the optic nerve is one of the target tissues of diabetic organ damage [1,2]. It is thought that several factors such as decreased blood flow, oxidative stress, metabolic disorders, irregular changes in blood glucose levels secondary to the use of exogenous insulin, and vascular disorders may cause functional and structural changes in the nervous system [3–5]. Diabetic retinopathy is a serious sight-threatening complication of diabetes [6].

Diabetic retinopathy (DR) is characterized by microvascular abnormalities, proliferation of retinal vessels and increased retinal vascular permeability, leading to the development of nonproliferative DR (NPDR), preproliferative DR (PPDR), proliferative DR (PDR), and diabetic macular edema (DME), respectively [7]. The main reasons for loss of vision in patients with diabetes mellitus are diabetic macular edema and proliferative diabetic retinopathy. New blood vessels of PDR and contraction of the accompanying fibrous tissue can distort the retina and lead to tractional retinal detachment, producing severe and often irreversible vision loss [8]. Given that proper management of patients with DR can prevent more than 90% of cases of visual loss, it is extremely important to categorize, classify and stage the severity of DR in order to establish adequate therapy [9]. In particular, in diseases like DM where a multidisciplinary approach is needed, communication among colleagues of different medical specialties is crucial.

Like optical coherence tomography (OCT) in ophthalmology, magnetic resonance imaging (MRI) is one of the computationally intense sensing modalities. Diffusion-weighted imaging (DWI) is an MR imaging technique that provides image contrast related to the random microscopic motion of water protons. DWI refers to any conventional MR imaging technique that has been made sensitive to the properties of molecular motion. Diffusion of water molecules depends on tissue microstructure and microdynamics [10,11]. DWI therefore has the potential to increase understanding of the pathogenetic mechanisms behind CNS disorders, going beyond T1 and T2 characteristics. Diffusion of water molecules in vivo is affected by the structure of the tissue, and can be measured by diffusion-weighted imaging. The apparent-diffusion-coefficient (ADC) is a quantitative parameter calculated from DWI. The ADC of different tissues can be calculated by drawing the region of interest (ROI) on the map.

Although DWI is currently used routinely in brain imaging, their application in the optic nerve has been recently described. DWI findings related to changes in the brain are limited in the patients with DM. Moreover there are a few studies evaluating the optic nerve with DWI [12–18]. DWI may be able to detect changes in the optic nerve head in diabetic patients with retinopathy. To the best of our knowledge, changes at the ON or ONH has not been previously evaluated with DWI in these patients. In this study, our aim was to detect whether there is

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any change by measuring ADC values particularly of the optic nerve head in patients with different stages of DR by using DWI.

2. Materials and methods

2.1. Patients and controls

This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and was approved by our Institutional Ethics Committee. Patients who applied to our Retina Unit of Ophthalmology Department were enrolled in the study. The study included 56 patients (27men, 29 women; median age, 52.5 ± 7.1 years) with DR. Grading levels were as follows: non proliferative retinopathy (background retinopathy) (0), preproliferative retinopathy (1), proliferative retinopathy (2), and maculopathy. The medical history of each patient was recorded. Patients were excluded from the study if their history included any of the following: uncontrolled hypertension, vitreoretinal pathology, uveitis, corneal and/or lenticular disease and glaucoma.

The control group included 68 controls (33 men, 35 women; median age, 52.3 ± 8.1 years) without DM, who had a normal ophthalmologic examination and did not have any other sign except for presbyopia. Additional exclusion criteria for the patients and control group included intracranial mass identified on MR imaging; optic neuropathy from ischemic or other causes; a history of visual loss; a mass compressing the optic nerve/chiasm/tracts; and a history of orbital surgery, diplopia, or isolated cranial nerve palsy.

Based on clinical features, 56 patients were divided into three groups according to results of the ophthalmologic examination. Thirty two patients with non-proliferative diabetic retinopathy with finding such as retinal hemorrhages, microaneurysms, hard exudates and venous bleeding were classified as group 0, sixteen patients with preproliferative diabetic retinopathy such as venous beading, intraretinal microvascular abnormality, and multiple deep, round blot retinal hemorrhage were classified as group 1, while eight patients with proliferative diabetic retinopathy who had findings such as neovascularization, preretinal hemorrhage and vitreous hemorrhage in the fundus examination were classified as group 2. The duration of disease was recorded in the groups. The control group was numbered as group 3. Measurements of the macular thickness and the presence of macular edema in patients using spectral domain optical coherence tomography (SD OCT) (Nidek RS-3000 OCT Advance; Nidek Co. Ltd., Gamagori, Japan) were recorded. Patients were also divided into two groups according to those as with or without macular edema.

2.2. Diffusion weighted magnetic resonance imaging (DWI) and evaluation

DWI was performed on 1.5 T (Achieva; Philips Medical Systems, Best, The Netherlands) scanner. The maximum gradient amplitude and a maximum gradient slew rate of the imager are 33 mT/m and 80 mT/m/s respectively. All experiments were performed using an inner diameter of 24 cm of a head coil in conduction.

DWI was performed using a single-shot echo-planar imaging (EPI) sequence from the orbital level, to be aligned parallel to the optic nerve and its head. The images were obtained using the parallel imaging technique. The selected b-values of 0 and 1000 s/mm^2 were used for the calculation of ADC in this study. DWI was performed with the following parameters: TR/TE, 3908/123 ms; flip angle, 90°; field of view (FOV), 150 × 150 × 66 mm; number of acquisitions, 4; matrix,100 × 149; and slice orientation, axial planes. 15 axial sections were obtained, with a slice thickness of 2.5 mm, an intersection gap of 0.3 mm. The ADC maps were reconstructed with the commercially available software. Magnitude images were transferred from the MR imaging system to an independent workstation for the calculation trace images and ADC values. The two attending radiologists (S.Y., V.B.) evaluated the quality of DWIs and selected, by consensus, images for further analysis which had a minimum of distortion from susceptibility artifacts and ghosting. ADC values were obtained from the right optic nerve head in each patient and controls (Fig. 1). Regions of interest (ROIs) drawn manually on the regions were identified and ADC values were automatically calculated from the ADC map. The areas of ROIs were 1.3–1.4 mm^2 in ONH (Fig. 1). We minimized the partial volume effects by inspecting the slices above and below the region to avoid averaging with cerebrospinal fluid. Two radiologists, with more than 10 years of experience, blindly evaluated together the DWI of these patients and the control group without clinical information. The mean values were used for statistical comparisons.

2.3. Statistical analysis

All statistical analyses were performed using a commercially available SPSS release 17.0 software package. Continuous variables were described as mean and standard deviation (SD). The Student's *t*-test was used for comparison of the two different groups. Variance analysis was used for comparing more than two groups. The relationship between numeric variables was determined by the Pearson's correlation analysis. The relationship between categorical variables was analyzed by the Spearman's correlation analysis. p value <0.05 was considered to be statistically significant.

3. Results

Age, gender, duration of disease of all groups, macular edema, foveal thickness and the mean ADC values are shown in Table 1. No statistically significant difference was found in age and gender between the patients and control group ($p > 0.05$). A statistically significant difference was found in the ADC values between the patient and control groups. ADC values of ONH significantly increased in the patients compared to the control group ($p = 0.011$).

The relationship between variables revealed that there was a significantly inverse proportional correlation between the ADC values and the foveal thickness ($p = 0.002$) ($r = -0.397$), and between the ADC values and macular edema ($p = 0.017$) ($r = -0.316$), respectively. There was no correlation between the duration and groups of disease ($p > 0.05$).

We next assessed comparison of the ADC values according to the DR groups and the presence of macular edema in the diabetic group. There was significant change in terms of the presence of macular edema; however, there were not significant changes in terms of the groups of DR. The ADC values in patients with macular edema in the diabetic group was found to be higher compared to patients without macular edema ($p = 0.017$). Values are shown in Table 2.

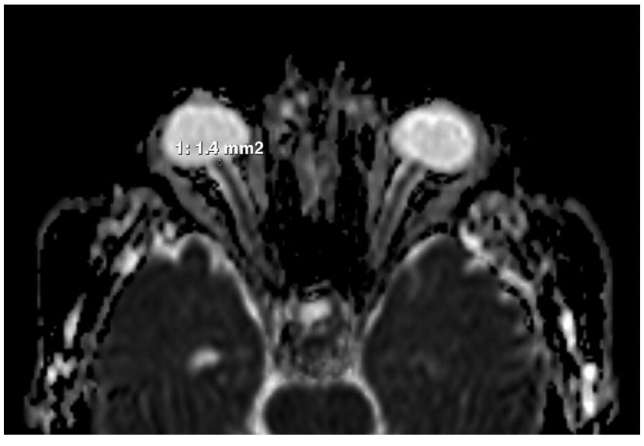

Fig. 1. Axial ADC map image at the level of the optic nerve heads. ROI placement at the ONHs onto the image.