Ischemic Injury of the Papillomacular Bundle Is a Predictive Marker of Poor Vision in Eyes With Branch Retinal Artery Occlusion

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• PURPOSE: To propose a novel prognostic feature of spectral-domain optical coherence tomography (SDOCT) in macula-involving branch retinal artery occlusion (BRAO).

• DESIGN: Retrospective comparative case study.

• METHODS: We analyzed 66 eyes diagnosed with acute BRAO involving the macula from our hospital RAO registry. At presentation, a detailed ophthalmic and medical history was obtained from all patients, and all underwent a comprehensive ophthalmic evaluation, which included visual acuity examination, fundus photography, fluorescein angiography, and SDOCT. This evaluation was performed at each follow-up visit.

• RESULTS: The 66 eyes diagnosed with acute BRAO involving the macula were divided into 2 groups according to initial vision: Good Vision (≥20/40, 29 eyes, 44%) and Poor Vision (<20/40, 37 eyes, 56%). The Poor Vision group was further divided into Improvement (18 eyes, 27%) and Nonimprovement (19 eyes, 28%) groups, according to visual recovery at the final examination. Among multiple OCT parameters, the involvement of papillomacular bundle, but not that of the central fovea, was consistently observed in the Poor Vision group ($P < .001$) and more significantly in the Nonimprovement group ($P < .001$). Papillomacular bundle involvement features included signs of inner retinal ischemia, including inner retinal thickening, inner retinal hyperreflectivity, and loss of layer-by-layer integrity. Loss of layer-by-layer integrity was seen consistently in the Nonimprovement group. Quantitative analysis of inner retinal thickness also supported this association.

• CONCLUSION: In eyes with macula-involving BRAO, ischemic injury of the papillomacular bundle at the acute stage, as seen on OCT, correlates closely with poor vision and can explain the poor visual prognosis. (Am J Ophthalmol 2016;162:107–120. © 2016 by Elsevier Inc. All rights reserved.)

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RETINAL ARTERY OCCLUSION (RAO) IS A RELATIVELY common, visually disabling, ocular vascular occlusive disorder. Branch retinal artery occlusion (BRAO) is estimated to account for about 38% of all acute RAO cases and typically occurs at vessel bifurcation and involves the temporal vessel in 98% of cases.[1] The cause of vascular occlusion disease is typically thought to be emboli, blood clots, or lipid plaques, and similar mechanisms apply to RAO; thus, a vascular etiology, with stroke and embolism from carotid artery plaques, is the most common pathogenic mechanism.[2,3]

In previous studies, Hayreh and Podhajsky[4] (44 eyes), Yuzurihara and Iijima[5] (30 eyes), Mason and associates[6] (52 eyes), and Hayreh and Podhajsky[7] (212 eyes) presented information about the natural history and visual outcomes of BRAO. Mason and associates[6] suggested that the visual prognosis after BRAO seems to be correlated with the initial presenting visual acuity, while Hayreh and Podhajsky[7] classified BRAO into permanent, transient, and cilioretinal artery occlusion, and showed a relatively favorable visual outcome even when BRAO was permanent. Although BRAO is recognized as a disease with a relatively favorable outcome, in the clinical situation we often see patients who present with severe visual loss or deteriorated central vision. This can sometimes not be explained with a classic diagnostic approach, which involves slit-lamp biomicroscopy, fundus photography (FP), or fluorescein angiography (FA), without spectral-domain optical coherence tomography (SDOCT), and unfortunately this would not be recovered until the final visit. Furthermore, some BRAO patients who show FP and FA features similar to those in patients with poor vision are found to experience relatively good visual restoration upon follow-up.

Upon examination of the retinal vascular circulation state in RAO using FP and FA, the condition can easily be categorized into central retinal artery occlusion (CRAO) or BRAO, and the ischemic retinal area involved can be delineated.[8] However, determination of the ischemic retinal area using retinal opacification on FP or the nonperfused area on FA is rather subjective and

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inaccurate. Most importantly, it is difficult to evaluate the perfusion status of the fovea using FA, because the foveal-avascular zone masks the ischemic involvement of the fovea. Therefore, to evaluate the ischemic involvement of the fovea in BRAO, it is necessary to investigate the retinal microstructure of the fovea and macula directly. Recently, our group[9] demonstrated the importance of SDOCT in predicting prognosis in CRAO and showed that different OCT features are seen in different stages of the condition. Chu and associates[10] described a prominent middle limiting membrane sign as a characteristic of acute retinal ischemic damage seen with OCT. More recently, Yu and associates[11] described the spectrum of superficial and deep retinal capillary ischemia features seen on SDOCT in RAO. Although these studies have revealed retinal structural changes in RAO, studies on the retinal changes and visual outcome in BRAO using OCT are limited.

Therefore, we hypothesized that SDOCT might be a helpful diagnostic tool for evaluating ischemic injury of the retina involving the macula and for predicting visual prognosis in BRAO. In the present study, using SDOCT, we investigated the retinal structural changes in eyes with macula-involving BRAO and searched for anatomic factors that could predict the visual prognosis.

METHODS

THE INSTITUTIONAL REVIEW BOARD OF THE SEOUL National University Bundang Hospital approved the study, which was conducted in accordance with the Declaration of Helsinki.

• **PATIENT SELECTION:** The Seoul National University Bundang Hospital RAO registry included records of a total of 304 eyes of patients who had visited Seoul National University Bundang Hospital between 1 January 2009 and 31 October 2014 for vision loss or a defect of the visual field occurring within 14 days of the initial visit. In addition to cases of CRAO (n = 169), ophthalmic artery occlusion (n = 22), cilioretinal artery occlusion (n = 6), and iatrogenic cosmetic filler-induced RAO (n = 32), there were 75 eyes with BRAO; our retrospective comparative case study focused on the latter group of eyes. All BRAO patients had undergone FA and SDOCT (Spectralis OCT; Heidelberg Engineering Inc, Heidelberg, Germany) evaluation at the initial visit, except in 2 cases of patient refusal owing to financial constraints. Patients with a history of ocular trauma, ocular surgery other than cataract surgery, any retinal disease of the contralateral eye, severe nonproliferative or proliferative diabetic retinopathy, nonmacular BRAO (n = 2, 1 that was nasal to the optic disc and another that was outside of the vascular arcade), retinal vascular disease other than BRAO (n = 3; combined retinal vein occlusion), follow-up of less than 2 months (n = 2), unavailable OCT data, or refusal of the OCT test (n = 2) were excluded. Finally, a total of 66 eyes from 66 patients with acute BRAO were included for analysis. BRAO patients were divided into Good Vision and Poor Vision groups according to their initial best-corrected visual acuity (BCVA) of 20/40. Additionally, the Poor Vision group was further divided into Improvement and Nonimprovement groups according to their visual improvement since the initial examination at their final examination. Visual improvement was defined as both final BCVA ≥20/60 and 20/100 degree improvement from initial visit (Figure 1).

• **MAIN OUTCOME MEASURE:** The main outcome measures are retinal microstructural factors predicting (1) initial poor vision and (2) visual recovery.

• **OPHTHALMIC EXAMINATION:** All patients were followed up for at least in excess of 3 months from the initial visit and underwent a complete ophthalmic examination at the initial visit; at 1 month, 3 months, and 6 months; and every year thereafter. The examination included a measurement of the BCVA, Goldmann visual field (GVF) assessment, slit-lamp biomicroscopy, indirect ophthalmoscopy, FP (VX-10; Kowa OptiMed, Tokyo, Japan), FA, and SDOCT imaging. Initial OCT images were compared with those obtained at the final visit, which was at least 3 months after the initial visit, to assess the quantitative and qualitative changes in the inner retina over time. If the patient showed abrupt changes in visual acuity at the follow-up visit, GVF was reevaluated to determine whether central scotoma or central visual field defect had changed as compared to that at the initial or previous GVF, in order to rule out the possibility of extramacular fixation. If there were no significant changes to the GVF, BCVA was remeasured carefully, emphasizing central gaze fixation.

• **QUALITATIVE ANALYSIS OF INNER RETINAL LAYER CHANGE:** SDOCT scans were performed at a scan rate of 40 000 A-scans/second over a 4.5 × 6.0 mm area. The eye-tracking system (ART Module; Heidelberg Engineering Inc) of the Spectralis SDOCT was used to minimize motion artifacts and to enhance image comparability over time. Follow-up scans were performed automatically in the same location at each visit, and the scan position was confirmed before comparing serial images. We defined the "papillomacular bundle area" as an inner retinal area that included the papillomacular bundle, a collection of retinal nerve fibers that carry the information from the macula (the central retina) to the optic nerve. Nasal retinal scan images were used to analyze the retina in the papillomacular bundle area. For qualitative analysis of inner retinal structure, images of the papillomacular bundle area (nasal macula) and the temporal macula in the horizontal scan of the foveal center point, and involving the