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Microstructure of the Optic Disc Pit in Open-Angle Glaucoma

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Purpose: To investigate the structural and clinical characteristics of the optic disc pit (ODP) in primary open-angle glaucoma (POAG) via enhanced depth imaging (EDI) spectral-domain optical coherence tomography (SD-OCT).

Design: Prospective, observational case series.

Participants: Seventy POAG eyes clinically diagnosed with an ODP via stereo disc photography.

Methods: Optic discs were scanned using EDI SD-OCT. Serial horizontal and vertical B-scan images covering the optic discs were obtained from each eye. The structural characteristics of the ODP were investigated via 3-dimensional images constructed from the serial B-scans, focusing on the presence of alterations in the contour of the lamina cribrosa (LC) or prelaminar tissue (PLT), in conjunction with associated clinical characteristics.

Main Outcome Measures: The structural characteristics of the ODP and associated clinical characteristics.

Results: In the EDI SD-OCT images, the ODP was viewed as an isolated alteration of the LC (n = 14, 20.0%) or PLT (n = 16, 22.9%) or an alteration of both the LC and PLT (n = 40, 57.1%). Alterations of the LC were located at the mid-periphery near the LC insertion (n = 17) or far periphery adjacent to the LC insertion (n = 37), and the depth of alteration was deep (n = 23), involving nearly full-thickness LC, or shallow (n = 31), with partially visible LC at the base. Fifty-four eyes (77.1%) exhibited parafoveal visual field (VF) defect within 10 degrees of fixation, and in 98.1% of these eyes (53/54) it was spatially associated with the location of ODP. The parafoveal VF defect was more prevalent in eyes with LC alteration than those without (83.3% vs. 56.2%, $P = 0.023$) and in eyes with deep LC defect than those with shallow defect (95.7% vs. 74.2%, $P = 0.036$). Disc hemorrhage (32.4% vs. 0.0%, $P = 0.008$) and peripapillary retinoschisis (18.9 vs. 0.0%, $P = 0.055$) were more strongly associated with LC alterations located at the far periphery than at the mid-periphery.

Conclusions: Enhanced depth imaging SD-OCT facilitated visualization of the varied structure of the ODP, which presented as alteration of the LC or PLT or both. The clinical significance of differing characteristics of ODP microstructure remains to be determined. *Ophthalmology 2014;■:1–9 © 2014 by the American Academy of Ophthalmology.*

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The optic disc pit (ODP) has long been recognized as one of the numerous localized optic nerve changes associated with glaucoma.[1–5] On the basis of the higher prevalence of ODP in eyes with low intraocular pressure (IOP) than those with high IOP, it has been suggested that the ODP is associated with increased vulnerability of the focal optic nerve region to the damaging effects of IOP.[2,5] Consistent with this hypothesis, an ODP has frequently been observed in conjunction with optic disc hemorrhage (DH)[3,4] and paracentral visual field (VF) defect,[2,3,5,6] both of which are reportedly more frequent in low-tension glaucoma.[7–12]

The ODP is morphologically defined as a deep, focal excavation of the neuroretinal rim, with localized depression and loss of normal architecture of the lamina cribrosa (LC).[13,14] The affected area is generally pale, with little or no rim tissue remaining adjacent to the edge of the optic disc.[2,15] However, this definition is mainly based on ophthalmoscopic observations or fundus photography.[2–5] Thus, the precise microscopic structure of the ODP remains to be determined.

The use of high-resolution optical coherence tomography (OCT) techniques, such as enhanced depth imaging (EDI) spectral-domain (SD) OCT[16–22] or swept-source (SS) OCT,[22–25] has enabled evaluation of the detailed cross-sectional architecture of the deep optic nerve head (ONH), including the LC. With the use of EDI SD-OCT, a localized alteration of the LC, termed a "focal LC defect," has been demonstrated.[18–20] It has been shown that LC defects at the edge of the optic disc correspond to a clinically visible ODP.[20] However, another study using SS-OCT reported the absence of a relationship between an ODP and LC defects.[23]

Given that the ODP is associated with localized susceptibility of the optic nerve to glaucomatous damage,[2,3,5] precise evaluation of ODP structure may prove informative with regard to the mechanisms of optic nerve damage in individual glaucomatous eyes. The present study aimed to characterize the microscopic structure of the ODP using EDI SD-OCT and to determine its clinical characteristics depending on structure.

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Methods

This study was based on the Investigating Glaucoma Progression Study (IGPS), an ongoing prospective study being conducted since August 2011 by the Seoul National University Bundang Hospital Glaucoma Clinic. It was approved by the Seoul National University Bundang Hospital Institutional Review Board and conformed to the Declaration of Helsinki. Informed consent was obtained from all patients.

Study Subjects

The database of patients included in the IGPS between August 2011 and December 2013 was reviewed. The aim of the IGPS is to measure the rate of progression in open-angle glaucoma and to determine the factors associated with a rapid progression. Subjects who were enrolled in the IGPS underwent a complete ophthalmic examination, including visual acuity assessment, refraction, slit-lamp biomicroscopy, gonioscopy, Goldmann applanation tonometry, and dilated stereoscopic examination of the optic disc using a 90D lens. They also underwent central corneal thickness measurement (Orbscan II, Bausch & Lomb Surgical, Rochester, NY), axial length measurement (IOL Master ver. 5, Carl Zeiss Meditec, Dublin, CA), stereo disc photography, EDI SD-OCT scanning of the optic disc and retinal nerve fiber layer (RNFL) thickness measurement (Spectralis OCT, Heidelberg Engineering, Heidelberg, Germany), and standard automated perimetry (Humphrey Field Analyzer II 750; 24-2 Swedish interactive threshold algorithm; Carl Zeiss Meditec).

To be included in the IGPS, subjects were required to have primary open-angle glaucoma and to have a best-corrected visual acuity of at least 20/40, spherical refraction of −8.0 to +3.0 diopters, and cylinder correction of $<\pm 3.0$ diopters. Those with a history of ocular surgery other than cataract extraction and glaucoma surgery or with retinal diseases (e.g., diabetic retinopathy, retinal vessel occlusion, or macular disease) or neurologic diseases (e.g., pituitary tumor) that could cause VF loss were excluded. Primary open-angle glaucoma was defined as the presence of glaucomatous optic nerve damage and associated VF defect without ocular disease or conditions. A glaucomatous VF defect was defined as (1) values outside the normal limits in the glaucoma hemifield test or (2) 3 abnormal points, with a probability of being normal of $P < 5\%$, and 1 point with a pattern deviation of $P < 1\%$ or (3) a pattern standard deviation of $P < 5\%$. Those VF defects were confirmed on 2 consecutive reliable tests (fixation loss rate $\leq$20%, false-positive and false-negative error rates $\leq$25%).

To be included in the present study, eyes were required to have an isolated ODP visible on stereo disc photographs. An ODP was defined according to the criteria used by Javitt et al[2]: (1) a sharply localized depression of the LC with deep excavation and loss of laminar architecture, resembling a classic pit of the optic disc; (2) extreme pallor of the affected area, especially in contrast with other areas of the disc; (3) extension of the ODP to the outer edge of the disc so that little or no rim tissue remained adjacent to the pit; (4) no evidence of optic nerve coloboma or retinal detachment. The stereo disc photographs were carefully reviewed by 2 glaucoma specialists (Y.J.C. and E.J.L.) who were blinded to the clinical information relating to the participants to determine the presence/absence and the clock-hour location of the ODP. The ODPs that were not associated with glaucomatous optic neuropathy, such as neuroretinal rim thinning or notching, were excluded. The clock-hour location of the ODP was documented on the basis of the stereo disc photography (3 o'clock, nasal; 9 o'clock, temporal). Disagreements between observers were resolved by consensus.

Patients included in the IGPS were followed up with regular stereo disc photography and SD-OCT circumpapillary RNFL scanning at 4- to 6-month intervals. In the stereo disc photographs, the presence of DH was recorded with its location in relation to the ODP in each patient. In the SD-OCT circumpapillary RNFL scans, the presence of peripapillary retinoschisis that presented as splitting of retinal layers was recorded, together with its spatial relationship with the ODP.

Enhanced Depth Imaging Spectral-Domain Optical Coherence Tomography of the Optic Disc

The optic nerve was imaged using the EDI technique. The detail and advantages afforded by this technology when evaluating the LC have been described previously.[16,17] Approximately 65 to 70 horizontal and vertical B-scan images covering the optic disc, 30 to 34 μm apart (the scan-line distance being determined automatically by the instrument), were obtained from each eye. Each section had 42 OCT frames averaged, which provided the best trade-off between image quality and patient cooperation.[17]

With the use of Spectralis OCT, images are obtainable only when the quality score is higher than 15. When the quality score does not reach 15, the image acquisition process automatically stops and imaging of the respective section remains absent. Only eyes in which acceptable scans (i.e., quality score >15) were obtained at more than 60 sections and that allowed clear delineation of the anterior border of the entire LC were included.

Examination of the Optic Disc Pit Structure

The structure of the ODP was examined within the 3-dimensional OCT data set using image processing software (Amira 5.2.2; Visage Imaging, Berlin, Germany). The examination focused on the presence of any alteration in the smooth contour of the LC or prelaminar tissue (PLT).

Alteration of the LC was defined as described by Kiumehr et al.[18] The LC alteration was deemed to be present when focal LC defects violating the curvilinear U- or W-shaped contour of the anterior LC were observed.[18] The diameter of the defects at their opening needed to be >100 μm and the depth >30 μm, and the defects needed to be present in 2 neighboring B-scans to avoid false positives.[18]

The focal LC defects were classified as deep or shallow according to the depth of the defects, and mid-peripheral or far-peripheral defects according to the distance of the defects from the neural canal wall. A deep LC defect was defined as a defect connecting the intraocular space with the retrolaminar space without any high reflectivity within the hyporeflective defect space (Fig 1A, B). A shallow LC defect was defined as highly reflective LC tissue being partly present at the base, and thus there being no visible connection between the intraocular and the retrolaminar spaces (Fig 1C–E). A mid-peripheral LC defect was defined as the defect being located near the LC insertion, with the LC visible on either side of the defect (Fig 1B, D, E). A far-peripheral LC defect was defined as the defect being adjoined to the insertion, with the anterior LC visible on only the central side of the defect, and with the peripheral LC not visible because of being masked by the overlying scleral rim (Fig 1A, C). Alteration of the PLT was deemed to be present when abrupt discontinuation of the PLT surface at the location of the ODP was observed (Fig 1A–D, F). The presence of any alteration in the LC or PLT that was not associated with the ODP was also identified by reviewing all serial horizontal and vertical B-scan images.

Initial examinations were independently performed by 2 experienced ophthalmologists (Y.J.C. and E.J.L.) who were blind to subjects' clinical information. Each final decision was made by the