AMERICAN ACADEMY™
OF OPHTHALMOLOGY

Optic Nerve Head Drusen Prevalence and Associated Factors in Clinically Normal Subjects Measured Using Optical Coherence Tomography

Mark P. Ghassibi, MD,[1] *Jason L. Chien, BS,*[1,2] *Ramiz K. Abumasmah, MD,*[1] *Jeffrey M. Liebmann, MD,*[3] *Robert Ritch, MD,*[1] *Sung Chul Park, MD*[4,5]

Objective: To investigate the prevalence of optic nerve head drusen (ONHD) in clinically normal subjects using enhanced depth imaging (EDI) optical coherence tomography (OCT) and to evaluate associated factors.

Design: Prospective, cross-sectional, observational study.

Participants: Total of 130 clinically normal subjects.

Methods: Serial horizontal and vertical EDI OCT B-scans (interval between scans, ~30 μm) of the optic nerve head (ONH) were obtained in both eyes of clinically normal subjects. Signs of ONHD were defined as horizontal hyperreflective bands perpendicular to the OCT beam with or without a signal-poor core. The minimum length of isolated hyperreflective bands was determined based on analysis of 34 eyes with clinically definite ONHD. Age, gender, ONH diameter, and axial length were obtained from participants.

Main Outcome Measures: Prevalence of ONHD in clinically normal subjects and its association with age, gender, ONH diameter, and axial length.

Results: Based on the measurements of 94 isolated hyperreflective bands in the 34 eyes with clinically definite ONHD, the minimum length of isolated hyperreflective ONHD bands in clinically normal subjects was set as 45 μm (mean minus 2 standard deviations). Among 260 clinically normal eyes (130 subjects; 68 women; mean age, 40±17 years), EDI OCT was positive for horizontal hyperreflective ONHD bands in 28 eyes (10.8%) of 19 subjects (14.6%). Of these 28 eyes, 25 eyes (9.6% of total 260 eyes) of 16 subjects (12.3% of total 130 subjects) showed isolated hyperreflective bands with no signal-poor core, and 3 eyes (1.2% of total 260 eyes) of 3 subjects (2.3% of total 130 subjects) showed a signal-poor core surrounded by hyperreflective bands. No significant differences were found in mean age (44 vs. 39 years; $P = 0.121$) or gender distribution (56% vs. 52% female; $P = 0.766$) between clinically normal subjects with hyperreflective ONHD bands and those without. Logistic regression analysis showed that a decrease in ONH diameter by 100 μm and axial length by 1 mm increased the odds of ONHD presence by 1.5-fold (odds ratio [OR] = 1.56 [confidence interval (CI), 1.22–2.00]; $P < 0.001$) and 2-fold (OR = 2.00 [CI, 1.15–3.49]; $P = 0.015$), respectively.

Conclusions: Subclinical ONHD may be more prevalent than previously believed. Significant associations of subclinical ONHD with smaller ONH and shorter axial length were found. *Ophthalmology 2016;■:1–6 © 2016 by the American Academy of Ophthalmology*

Optic nerve head drusen (ONHD) are acellular, calcified, hyaline deposits in the optic nerve head[1–3] and can lead to progressive visual field loss of varying severity.[4–7] Ultrasound B-scan was formerly the preferred method for diagnosis of ONHD, as it is more reliable than ophthalmoscopy, autofluorescence photography, and orbital computed tomography.[8–10] Optical coherence tomography (OCT) can also detect ONHD effectively.[11–14]

Among OCT technologies, enhanced depth imaging (EDI) OCT, which better images deeper posterior segment structures,[15] provides better assessment of the entire ONHD shape and structure and has a significantly higher ONHD detection rate than ophthalmoscopy, ultrasound B-scan, and non-EDI spectral-domain OCT.[16] In a previous study, EDI OCT–detected ONHD appeared as signal-poor regions surrounded by short, hyperreflective bands perpendicular to the OCT beam or isolated/clustered hyperreflective bands without a signal-poor core; none of the ONHD diagnosed by ophthalmoscopy, ultrasound B-scan, or non-EDI spectral-domain OCT were missed by EDI OCT.[16] EDI OCT also detected ONHD in clinically normal fellow eyes that were negative on ultrasound B-scan.[16] Based on these results, we proposed that EDI OCT may be a possible new reference standard for diagnostic evaluation and monitoring of ONHD.[16]

The prevalence of ONHD has been reported as 0.34% to 3.7% in hospital-based studies using clinical ophthalmoscopy[5,17,18] and as 1.0%[19] and 2.0%[20] in histologic studies.

http://dx.doi.org/10.1016/j.ophtha.2016.10.035
ISSN 0161-6420/16

The purpose of this study was to determine the prevalence of ONHD in clinically normal subjects using EDI OCT, with its better ONHD detection ability compared with conventional diagnostic methods. In addition to the qualitative diagnostic criteria from our previously reported study,[16] we attempted to establish a quantitative criterion for the length of isolated hyperreflective bands to strengthen the reliability of ONHD diagnosis. We also evaluated the associations of ONHD with age, gender, and axial length.

Methods

This prospective, cross-sectional, observational study was approved by the New York Eye and Ear Infirmary of Mount Sinai Institutional Review Board. Written informed consent was obtained from all subjects, and the study adhered to the tenets of the Declaration of Helsinki.

Participants: Clinically Normal Subjects

We recruited healthy volunteers from a variety of sources; for example, spouses of glaucoma patients, volunteers in the hospital and their friends, and hospital workers' relatives or friends who wanted a free comprehensive eye examination. All subjects provided a detailed medical and ocular history and underwent slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, dilated optic disc and fundus examination, and standard automated perimetry (Humphrey Visual Field Analyzer, 24-2 SITA-standard strategy; Carl Zeiss Meditec, Inc, Dublin, CA). Also, an infrared optic disc photograph was taken and circumpapillary retinal nerve fiber layer thickness was measured along the 3.4-mm-diameter circle using spectral-domain OCT (Spectralis; Heidelberg Engineering GmbH, Dossenheim, Germany).

Clinically normal subjects were required to have best-corrected visual acuity better than 20/40, intraocular pressure between 10 and 21 mmHg, normal anterior segments with open iridocorneal angles, normal optic disc and fundus appearance, normal visual field, normal retinal nerve fiber layer thickness and profile, no afferent pupillary defect, and no apparent ocular or systemic conditions that could affect the optic nerve or retina.

For enrolled clinically normal subjects, EDI OCT was performed as described below. The optic nerve head diameter along the long axis of the optic disc was measured using the built-in measurement tool of the OCT machine. Additionally, ultrasound B-scan (OTI-Scan; Ophthalmic Technologies, Toronto, Canada) of the optic nerve head was performed and axial length was measured (IOLMaster; Carl Zeiss Meditec, Inc). Axial length was not measured in a subset of clinically normal subjects due to operator unavailability, machine unavailability, and poor subject cooperation.

Enhanced Depth Imaging Optical Coherence Tomography to Detect Optic Nerve Head Drusen

For EDI OCT to detect ONHD, we used the method described in our previous study.[16] In brief, serial horizontal and vertical cross-sectional scans (interval between scans, ~30 μm) of the optic nerve head were obtained in both eyes of each enrolled subject using EDI OCT (Spectralis; Heidelberg Engineering GmbH). The OCT was set to image a 15×10-degree rectangle for horizontal scans (and a 10×15-degree rectangle for vertical scans) centered on the optic disc. Each rectangle was imaged with 97 scans, and each scan had 20 OCT frames averaged. To evaluate the reproducibility of OCT findings, the same imaging protocol was repeated for subjects who agreed to have a second set of EDI OCT scans. The EDI OCT scans shown in this study are negative images with the Bruch membrane appearing black rather than white and with vascular shadows appearing as white vertical streaks.

Enhanced Depth Imaging Optical Coherence Tomography Criteria for Optic Nerve Head Drusen

Based on the results of our previous study,[16] we defined ONHD in EDI OCT scans as horizontal hyperreflective band(s) perpendicular to the OCT beam with or without a signal-poor core (Fig 1), except those that occur in pairs along the course of vessels representing the anterior and posterior vascular walls. Also, to strengthen the reliability of ONHD diagnosis, we attempted to establish an additional criterion for the length of isolated hyperreflective bands.

First, we separately recruited patients with clinically definite ONHD in either eye from the glaucoma and neuro-ophthalmology referral practices at the New York Eye and Ear Infirmary of Mount Sinai. Clinically definite ONHD were defined as discrete or coalescent, refractile, beige, rounded bodies within or at the margin of the optic disc on dilated optic disc examination. All subjects underwent the same aforementioned examinations as healthy volunteers.

We excluded eyes with previous intraocular surgery (except uncomplicated cataract extraction), ocular trauma, visually significant cataract with best-corrected visual acuity of 20/40 or less, or systemic or ocular conditions other than ONHD known to affect the optic nerve head structure or visual field (e.g., glaucoma, ischemic optic neuropathy, optic neuritis, and papilledema).

For enrolled patients with clinically definite ONHD, EDI OCT and ultrasound B-scan of the optic nerve head were performed as described above. All horizontal and vertical EDI OCT scans were carefully reviewed for isolated horizontal hyperreflective bands without a signal-poor core. All ONHD with isolated hyperreflective bands detected in horizontal EDI OCT scans were confirmed by vertical EDI OCT scans at the same location, and vice versa. The length of all isolated hyperreflective bands was measured in both horizontal and corresponding vertical EDI OCT scans using the Spectralis OCT software's measuring tool (Fig 1); the 2 measurements were averaged and used as the length of the band. The measurements for all isolated hyperreflective bands were analyzed and the "mean minus 2 standard deviations" value was used as the minimum length of isolated hyperreflective bands of ONHD in clinically normal subjects. We believe that establishing the minimum length of horizontal hyperreflective bands will reduce false-positive results caused by speckle noise and artifacts that are shorter than the hyperreflective ONHD bands.

Then, for clinically normal subjects, all horizontal and vertical EDI OCT scans were carefully reviewed for horizontal hyperreflective bands with or without a signal-poor core. The length of all isolated hyperreflective bands without a signal poor core was measured in both horizontal and corresponding vertical EDI OCT scans using the Spectralis OCT software's measuring tool; the 2 measurements were averaged and used as the length of the band.

Statistical Analysis

For all analyses, parametric or nonparametric tests were utilized based on the normality test. The mean length of isolated hyperreflective bands in horizontal EDI OCT scans was compared with that in corresponding vertical scans in clinically normal eyes using the Mann−Whitney U test. Spearman correlation analysis was performed between ONHD band lengths in horizontal EDI OCT scans and those in vertical EDI OCT scans at the same location in clinically normal eyes. Mean length of isolated hyperreflective