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Parapapillary Choroidal Microvasculature Dropout in Glaucoma

A Comparison between Optical Coherence Tomography Angiography and Indocyanine Green Angiography

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Purpose: To investigate whether the parapapillary choroidal microvasculature dropout (MvD) determined by optical coherence tomography angiography (OCTA) in glaucomatous eyes indicates a true perfusion defect and whether the MvD accurately represents the area of nonperfusion.

Design: Observational case series.

Participants: Thirty primary open-angle glaucoma (POAG) patients with choroidal MvD as determined by OCTA and 13 POAG patients without this dropout.

Methods: Peripapillary circulation was evaluated using both OCTA and indocyanine green angiography (ICGA). For OCTA, the choroidal microvasculature was evaluated using 4.5×4.5-mm choroid–disc vessel density maps of OCTA images of the optic nerve head. An MvD was identified in OCTA by the presence of a capillary dropout. A filling defect observed in ICGA was defined as a perfusion defect ($_{ICG}$PD).

Main Outcome Measures: The topographic correlations between MvD and $_{ICG}$PD determined based on their circumferential extent, location, and area.

Results: The $_{ICG}$PD was observed as a sectoral filling defect in the 30 POAG patients exhibiting MvD and appeared identical to the MvD in terms of the shape and location. The circumferential extent, location, and area of $_{ICG}$PD did not differ from those of the MvD (all $P > 0.05$). The $_{ICG}$PD was not found in any of the eyes not having the MvD.

Conclusions: A localized MvD observed in the parapapillary choroid using OCTA coincided with the $_{ICG}$PD detected by ICGA. These findings indicate that OCTA accurately images impaired parapapillary choroidal circulation. *Ophthalmology 2017;■:1–9 © 2017 by the American Academy of Ophthalmology*

Glaucoma is a multifactorial disease whose precise mechanism remains elusive.[1] Although increased intraocular pressure (IOP) is considered the greatest risk factor for the development[2] and progression[3–5] of glaucoma, studies have shown that compromised ocular blood flow[6–10] or decreased perfusion in the retina and choroid[11–16] are associated with glaucoma. These findings suggest that glaucomatous optic neuropathy also can be vasogenic in origin.

Optical coherence tomography angiography (OCTA) is a new imaging technique that enables visualization of the retinal and choroidal microvasculature. Recent studies using OCTA have demonstrated decreased vascularity in the optic nerve head[17,18] and parapapillary retina[19–23] in glaucoma patients. The decreased vascularity in OCTA was correlated topographically with hemifield visual field (VF) defects.[19,20] Noteworthy is the parapapillary choroidal microvasculature dropout (MvD) recently demonstrated in glaucomatous eyes.[20,23] This finding is in line with previous fluorescein angiography[13,24–27] or indocyanine green angiography (ICGA)[15,16] studies that demonstrated impaired filling of the parapapillary choroid in glaucoma. The choroidal microvasculature within the peripapillary area is of particular clinical interest[23] because it is downstream from the short posterior ciliary artery,[13,15,28–30] which also perfuses the prelaminar tissue and lamina cribrosa.[28–30]

Because of its noninvasive nature, OCTA can expedite studies investigating the relevance of parapapillary microvascular compromise in the pathophysiologic features of glaucomatous optic neuropathy. However, it should be established first that OCTA can accurately detect the area of the compromised perfusion, that is, whether the MvD identified by OCTA indicates a true perfusion defect and whether the OCTA-detected MvD involves the total area of nonperfusion.

Indocyanine green angiography provides reliable information about the choroidal vascular bed and is used as the standard method to assess the choroidal circulation. We conducted this study to examine the peripapillary microvasculature using both OCTA and ICGA to confirm whether the MvD identified by OCTA represents a true perfusion defect and whether the areas of vascular impairment

http://dx.doi.org/10.1016/j.ophtha.2017.03.039
ISSN 0161-6420/17

identified by the 2 techniques are consistent. To the best of our knowledge, there is no study in the literature investigating the peripapillary choroidal circulation using both OCTA and ICGA in the same study population.

Methods

This prospective study investigated the peripapillary circulation using OCTA and ICGA in consecutive primary open-angle glaucoma (POAG) patients who were enrolled in the Investigating Glaucoma Progression Study, which is an ongoing prospective study of glaucoma patients at the Glaucoma Clinic of Seoul National University Bundang Hospital Glaucoma Clinic. Of the patients in the Investigating Glaucoma Progression Study, those who agreed to undergo ICGA and had both ICGA and OCTA results were selected for the study. Written informed consent to participate was obtained from all participants. The study protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital and it followed the tenets of the Declaration of Helsinki.

All participants underwent comprehensive ophthalmic examinations that included best-corrected visual acuity, Goldmann applanation tonometry, a refraction test, slit-lamp biomicroscopy, gonioscopy, stereo disc photography and red-free fundus photography (EOS D60 digital camera; Canon, Utsunomiyashi, Tochigiken, Japan), central corneal thickness measurement (Orbscan II; Bausch & Lomb Surgical, Rochester, NY), axial length measurement (IOLMaster version 5; Carl Zeiss Meditec, Dublin, CA), spectral-domain optical coherence tomography (Spectralis; Heidelberg Engineering, Heidelberg, Germany), standard automated perimetry (Humphrey Field Analyzer II 750, 24-2 Swedish interactive threshold algorithm; Carl Zeiss Meditec), OCTA (AngioVue; Optovue, Fremont, CA), and ICGA (Heidelberg Retinal Angiograph 2; Heidelberg Engineering). Clinical history also was obtained from participants, including demographic characteristics, presence of cold extremity or migraine, and other systemic diseases. Systolic and diastolic blood pressures (BPs) were measured at the time of OCTA. Mean arterial pressure and ocular perfusion pressure were calculated based on the following equations: mean arterial pressure = diastolic BP + 1/3 (systolic BP − diastolic BP; ocular perfusion pressure = mean arterial pressure − IOP at the time of OCTA.

Primary open-angle glaucoma was defined as the presence of an open iridocorneal angle, signs of glaucomatous optic nerve damage (i.e., neuroretinal rim thinning, notching, or a retinal nerve fiber layer [RNFL] defect), and a glaucomatous VF defect. A glaucomatous VF defect was defined as a defect conforming with one or more of the following criteria: (1) results outside normal limits on a glaucoma hemifield test, (2) 3 abnormal points with a $P < 0.05$ probability of being normal and 1 abnormal point with $P < 0.01$ by pattern deviation, or (3) a pattern standard deviation of $P < 0.05$ confirmed on 2 consecutive reliable tests (fixation loss rate ≤20% and false-positive and false-negative error rates ≤25%). The normal controls had an IOP of 21 mmHg or less, no history of increased IOP, an optic disc with a normal appearance, and normal VF results.

Eyes were required to have a record of untreated IOP, which was measured before the initiation of ocular hypotensive treatment or was identified in the referral notes. In patients with an untreated IOP of 21 mmHg or less, the diurnal variation was measured during office hours (9 AM to 5 PM). In patients who were undergoing

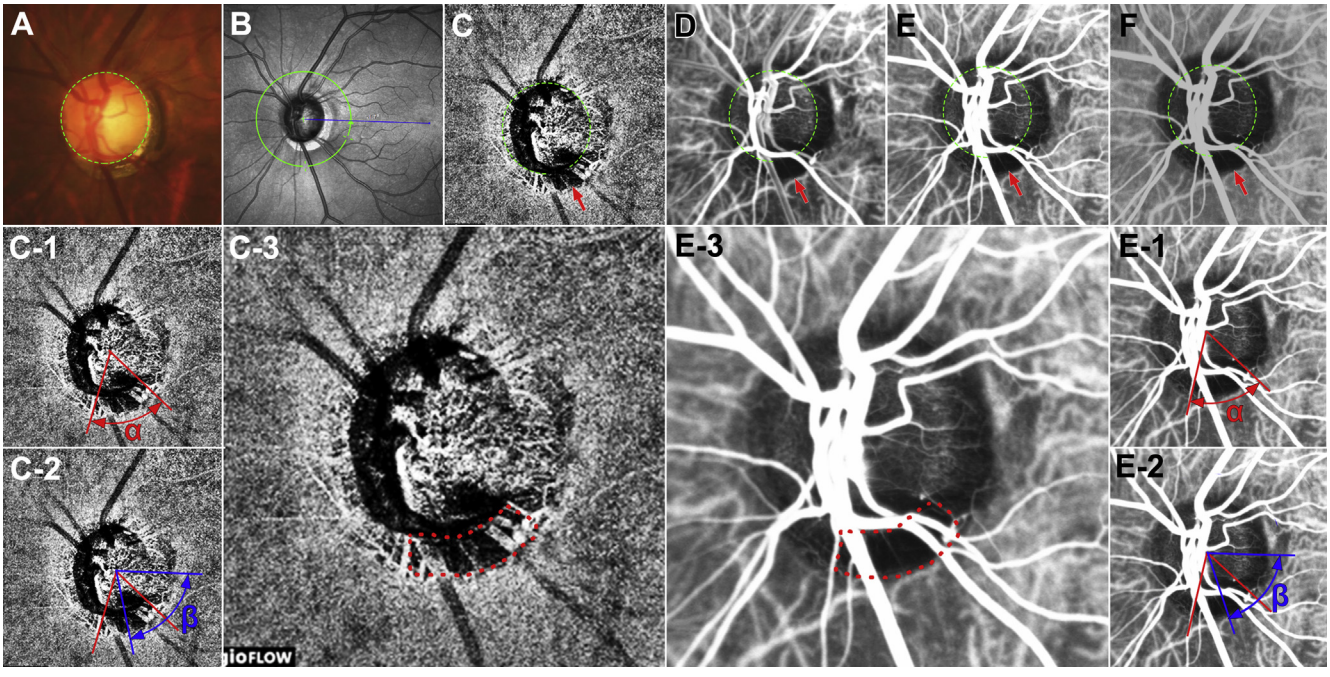

Figure 1. Determination of the circumferential extent and location and of the area of the microvasculature dropout: (**A**) color disc photograph, (**B**) infrared fundus image indicating the fovea-disc axis (*blue line*), (**C**) optical coherence tomography angiography (OCTA) image of the choroidal layer, and indocyanine green angiography (ICGA) images in (**D**) the retinal arteriovenous (at 20 seconds after dye injection), (**E**) peak (at 51 seconds), and (**F**) late (at 3 minutes 23 seconds) phases in a glaucomatous eye with a choroidal microvasculature dropout (MvD). **C-3**, **E-3**, Magnified views of (**C**) and (**E**), respectively, revealing that the vascular dropout shown by choroidal OCTA and ICGA are nearly identical. **A**, **C**–**F**, *Dashed lines* indicate the optic disc margin. *Arrows* indicate vascular impairments in (**C**) choroidal OCTA (MvD) and (**D**–**F**) ICGA ($_{ICG}$PD). α Is the angular extent of the (**C-1**) MvD and (**E-1**) $_{ICG}$PD, and β is the location of the (**C-2**) MvD and (**E-2**) $_{ICG}$PD relative to the fovea-disc axis. Areas demarcated by the *red dashed line* indicate the area of the (**E-3**) MvD and (**E-3**) $_{ICG}$PD.