Asymmetry of Macular Vessel Density in Bilateral Early Open-angle Glaucoma With Unilateral Central 10-2 Visual Field Loss

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Open-angle glaucoma (OAG) is an optic neuropathy characterized by progressive damage of retinal ganglion cells (RGCs) and their axons. Macula has the highest RGC density, with ~50% of RGCs located in this region. Macula has the highest RGC density, with ~50% of RGCs located in this region. This anatomic structure makes macula an important position for early detection of structural and vascular changes in glaucoma. Previous studies have found that macula was involved in the early glaucomatous damage. The pathogenesis of OAG remains unknown, but mounting studies have suggested that vascular factors played an important role in the development and progression of glaucoma. Optical coherence tomography angiography (OCTA) based on the split-spectrum amplitude-decorrelation angiography algorithm can quantitatively and qualitatively visualize the decreased vessel density in glaucomatous eyes with high repeatability.

Few studies investigated the intraeye and intereye asymmetry of the macular vessel density in glaucomatous eyes. However, these 2 studies used 24-2 visual field to assess the visual function of glaucoma. Although central 24-2 or 30-2 visual field test pattern is widely used in clinical setting for assessing glaucomatous function loss, De Moraes et al found that commonly used glaucoma staging systems including Hodapp-Parrish-Anderson, visual field index, and Brusini staging systems, which are based on 24-2 or 30-2 visual field test results, might fail to detect the presence of glaucomatous macular damage and underestimate the disease severity. Previous study found that 24-2 visual field could miss central visual field loss manifested in 10-2 visual field. It is not surprising, because the test points of 10-2 visual field space every 2 degrees, which are denser than those of 24-2/30-2 visual field test pattern (grid 6 degrees). More points of 10-2 visual field test pattern are tested within the macular region and could be more accurate to reflect the functional damage of macula.

OAG is generally a bilateral disease that manifests asymmetric glaucomatous optic nerve damage and visual field loss. To understand the characteristics of early glaucomatous damage in macula, the current study investigated the differences of macular microvasculature between the perimetrically affected eyes and the unaffected eyes, and between the hemifields in glaucomatous eyes with single-hemifield visual field loss, based on central 10-2 visual field, which might provide insight into the pathophysiological mechanism of glaucoma.

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MATERIALS AND METHODS

This prospective cross-sectional study was conducted at the Department of Glaucoma, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China, between January 2019 and May 2019. The study protocol was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Zhongshan Ophthalmic Center. Written informed consent was obtained from all participants.

All participants underwent comprehensive ocular examinations including best-corrected visual acuity, refraction, intraocular pressure (IOP) measurement by Goldmann applanation tonometry, slit-lamp examination, gonioscopy, dilated fundus examination with 90-D lens, stereoscopic disc photography (Nonmyd WX; Kowa Inc., Tokyo, Japan), central corneal thickness measurement by spectral-domain optical coherence tomography (SD-OCT) (RTVue OCT; Optovue Inc., Fremont, CA) with an additional anterior lens, visual field examinations, and SD-OCT and OCTA imaging.

Blood pressure including systolic blood pressure and diastolic blood pressure was measured in the left brachial artery at the height of heart by an automatic blood pressure instrument (Model: HM-7136; Omron Inc., Japan). Mean ocular perfusion pressure is two thirds of the mean artery pressure minus IOP, where mean artery pressure is calculated as two thirds of the diastolic blood pressure plus one third of the systolic blood pressure.

Study Subjects

Consecutive patients diagnosed as bilateral early OAG with 10-2 visual field loss in 1 eye and intact 10-2 visual field result in the contralateral eye, were included in this study. OAG patients of this study consist of juvenile-onset open-angle glaucoma (JOAG) and primary open-angle glaucoma (POAG, also known as adult-onset OAG) patients. The common inclusion criteria for OAG in the current study were the presence of glaucomatous optic disc changes (neuroretinal rim thinning, excavation, notching, or retinal nerve fiber layer defect) confirmed by 2 glaucoma experts (J. H. and H.X.) on both dilated fundus examination and stereoscopic optic disc photographs, a history of untreated IOP > 21 mm Hg, above 18 years old. The major difference between JOAG and POAG is the age of glaucoma onset: the age of glaucoma patient is younger than 35 years old, and the age of POAG patient is 35 years or older. Visual field results were not used for the definition of OAG. Although the definition of early stage of OAG was based exclusively upon the 30-2 visual field test with mean deviation better than −6.0 dB in at least 2 consecutive and repeatable visual field tests. Central 10-2 visual field loss was defined as a cluster of 3 continuous points (5%, 5%, 1%; 5%, 2%, 2%; or worse) within 1 hemifield on the pattern deviation or total deviation plot based on cluster criteria, and the points of the cluster were allowed to lie on the edge of the visual field plot. 15,19 Healthy participants were recruited from hospital staff, who were required to have no family history of glaucoma, IOP < 21 mm Hg, normal optic nerve appearance, and normal 10-2 and 30-2 visual fields which were defined as pattern standard deviation within the 95% confidence limits and glaucoma hemifield test result within normal limits, in both eyes. Only 1 eye in 1 healthy participant was randomly selected.

Common inclusion criteria for all participants were age above 18 years, open-angle on gonioscopy, best-corrected visual acuity ≥ 20/40, refractive error between +3.0 and −6.0 D. Exclusion criteria were coexisting ocular diseases, such as retinal disease, nonglaucomatous optic neuropathy, uveitis; a medical history of systemic disease, such as diabetes mellitus, hypertension; an intraocular surgery except for uncomplicated cataract surgery 6 months before enrollment; and presence of significant media opacities which prevented from obtaining high-quality images.

Visual Field Tests

All participants underwent visual field examinations using central 30-2 and central 10-2 pattern with Swedish Interactive Threshold Algorithm in a standard condition (Humphrey Field Analyzer II; Carl Zeiss Meditec Inc., Dublin, CA). 30-2 visual field test and 10-2 visual field test were performed on the same day. 10-2 visual field test was performed after 30-2 visual field test with a rest period of at least 15 minutes. Only reliable visual field results, defined as fixation losses < 20%, false-positive rates < 15%, false-negative rates < 30%, were included in the current study. We further categorized 10-2 visual field defects as single-hemifield defect (superior or inferior hemifield) and bilateral hemifields defect (Fig. 1). The eyes with single-hemifield defect were selected for further intrasubject analyses.

SD-OCT and OCTA Imaging

Imaging of fundus ultrastructure and microvasculature were acquired with a RTVue-XR Avanti SD-OCT system with Angiovue (Optovue Inc.). Dilation was performed before imaging. The Optic Nerve Head Scan protocol was used to measure circumpapillary retinal nerve fiber layer (cpRNFL) thickness and rim area, which centered on the optic disc along a 3.45 mm diameter circle. The ganglion cell complex scan protocol, which centered 1 mm temporal to the fovea and covered a 7 mm diameter circular area, was used to measure macular ganglion cell complex (mGCC) thickness.

High-density Angio Retina 6×6-mm protocol was used to cover the macula. We analyzed the superficial vessel density, which extended from inner limiting membrane to inner plexiform layer (9 μm below). Vessel density measurement was automatically obtained with built-in software (Optovue Inc.; software version: 2017.1.0.151). Macular whole image vessel density was measured in a 6×6-mm² area. Parafoveal vessel density was measured within an annulus with inner diameter of 1 mm and outer diameter of 3 mm. Perifoveal vessel density was measured within an annulus with inner diameter of 3 mm and outer diameter of 6 mm. Vessel density was defined as the total area occupied by the vessels.

Poor quality images showing scan quality <7/10, vitreous floaters artifacts or segmental errors were excluded. 5,20

Statistical Analysis

Statistical analyses were performed using SPSS software (version: 20.0; SPSS Inc., Chicago, IL). Continuous variables were presented as means (95% confidence interval). χ² Test was used to compare categorical variables such as sex. The sample size of this study was relatively small, therefore, nonparametric tests was used. Mann-Whitney test was used to compare the differences between healthy eyes and 10-2 visual field affected eyes, and between healthy eyes and 10-2 visual field unaffected eyes. Wilcoxon signed ranks test was used to compare the intereye differences between 10-2 visual field affected eyes and 10-2 visual field unaffected fellow eyes, and the intrasubject differences between affected hemifields and unaffected hemifields in perimetrically...
affected eyes with single-hemifield. $P$-value $< 0.05$ was considered statistically significant. Bonferroni correction was applied for multiple comparisons. $P$-value $< 0.017$ ($0.05/3$) was considered statistically significant in multiple comparisons.

RESULTS

Thirty-two eyes of 16 patients with bilateral early OAG and unilateral 10-2 visual field loss and 13 eyes of 13 healthy participants met the inclusion criteria and were included in the current study. There were 8 patients aged 20 to 35 years old, diagnosed as JOAG; and 8 patients older than 35 years old, diagnosed as POAG. The demographic and ocular characteristics of healthy eyes and OAG eyes are described in Table S1 (Supplemental Digital Content 1, http://links.lww.com/IJG/A398). There were no significant differences between OAG patients and healthy participants concerning age, sex, and mean ocular perfusion pressure (all $P > 0.05$). The axial length of 10-2 perimetrically affected eyes was longer than 10-2 perimetrically unaffected eyes, while the difference was borderline significant [24.2 (23.5, 24.8) mm vs. 24.1 (23.5, 24.8) mm; $P = 0.017$]. As expected, all results of cpRNFL thickness of the perimetrically affected eyes were thinner compared with unaffected eyes and healthy eyes (all $P < 0.017$), while only average and inferior mGCC thicknesses of the affected eyes were thinner compared with the unaffected eyes ($P = 0.001$ and 0.001, respectively). No optic disc hemorrhage was found in any patients of this study.

Superficial macular vessel density measurements in healthy, perimetrically affected and unaffected eyes are shown in Table S2 (Supplemental Digital Content 1, http://links.lww.com/IJG/A398). All results of the macular vessel densities of the affected eyes, except for nasal parafoveal vessel density ($P = 0.028$), were significantly decreased compared with healthy eyes (all $P < 0.017$). All results of macular vessel densities of the unaffected eyes, except for superior and nasal parafoveal vessel density, nasal perifoveal vessel density (all $P > 0.017$), were significantly lower compared with healthy eyes (all $P < 0.017$). The intereye analyses showed that macular whole image vessel density of the affected eyes was comparable to the unaffected eyes [44.7% (42.8%, 46.6%) vs. 46.6% (45.1%, 48.0%); $P = 0.028$]. In regard to the vessel density in different areas of the macula, we found that average and all quadrants’ parafoveal vessel densities of the affected eyes were comparable to the unaffected eyes (all $P > 0.017$). However, inferior perifoveal vessel densities of the affected eyes were significantly lower than the unaffected eyes ($P = 0.007$).

Twelve eyes with single-hemifield loss from 16 eyes with 10-2 visual field loss were selected for further intraeye analyses. Comparisons of visual field, structural, microvascular results in the hemispheres corresponding to the affected hemifields and the unaffected hemifields in glaucomatous eyes with single-hemifield 10-2 visual field loss are summarized in Table S3 (Supplemental Digital Content 1, http://links.lww.com/IJG/A398). As expected, mean sensitivity of the unaffected hemifields was significantly lower than the affected hemifields ($P = 0.007$).

FIGURE 1. Examples of 30-2 and 10-2 visual field loss in 3 representative eyes. All visual field results are presented in right eye view. 30-2 and 10-2 visual fields of the same column derived from the same eye. All 3 eyes presented visual field loss within the central 10 degrees on 30-2 visual field deviation plots, and spatially corresponded well with 10-2 visual field. Left: the superior hemifields were abnormal on both 30-2 and 10-2 visual fields. Middle: the inferior hemifields were abnormal on both 30-2 and 10-2 visual fields. Right: both superior and inferior hemifields were abnormal on both 30-2 and 10-2 visual fields. Figure 1 can be viewed in color online at www.glaucomajournal.com.
lager than the affected hemifields [32.6 (31.7, 33.5) dB vs. 31.6 (31.0, 32.3) dB, \( P = 0.004 \)]. The mGCC thickness of the unaffected hemifields was significantly larger compared with the affected hemifields [89.0 (84.8, 93.2) \( \mu \text{m} \) vs. 78.4 (73.0, 83.8) \( \mu \text{m} \); \( P = 0.005 \)]. Macular whole image vessel density and perifoveal vessel density of the unaffected hemifields were significantly larger than the affected hemifields [46.3% (44.5%, 48.1%) vs. 43.8% (40.6%, 47.0%), 47.0% (45.4%, 48.6%) vs. 43.0% (40.2%, 47.1%); \( P = 0.026 \) and 0.023, respectively]. Although parafoveal vessel density of the unaffected hemifields was comparable to the affected hemifields [49.3% (46.5%, 52.2%) vs. 48.0% (44.7%, 51.4%); \( P = 0.239 \)].

Representative cases of a healthy eye, and 2 eyes of a patient with bilateral early primary open-angle glaucoma and unilateral 10-2 visual field loss. Macular vessel density of the healthy eye (top) was significantly denser and distributed more evenly compared with the unaffected eye (middle), and affected eye (bottom) which showed superior hemifield visual field loss in both 30-2 and 10-2 tests. In addition, a well-defined inferior arcuate macular microvascular defect spatially corresponded well with macular ganglion cell complex (GCC) thinning and 10-2 visual field defect in the affected eye. RNFL indicates retinal nerve fiber layer.

**FIGURE 2.** Representative cases of a healthy eye, and 2 eyes of a patient with bilateral early primary open-angle glaucoma and unilateral 10-2 visual field loss. Macular vessel density of the healthy eye (top) was significantly denser and distributed more evenly compared with the unaffected eye (middle), and affected eye (bottom) which showed superior hemifield visual field loss in both 30-2 and 10-2 tests. In addition, a well-defined inferior arcuate macular microvascular defect spatially corresponded well with macular ganglion cell complex (GCC) thinning and 10-2 visual field defect in the affected eye. RNFL indicates retinal nerve fiber layer.

**DISCUSSION**

To the best of our knowledge, this is the first study investigating the intraeye and intereye asymmetry of macular vessel density in bilateral early OAG eyes with unilateral 10-2 visual field loss. In the current study, we found that macular vessel density was significantly decreased even in 10-2 perimetrically unaffected glaucoma eyes. The intereye and intraeye analyses showed that significant damage of macular vessel density was present in perifoveal but not parafoveal area in early OAG. In addition, the damage of macular vessel density spatially corresponded to mGCC damage and visual field damage.

Macula has the highest density of RGC and is crucial for daily visual function such as reading and driving. The vessels supplying nutrition for the macula to meet their high metabolism derive from the central retinal artery and contain exclusively the capillaries and small vessels (arterioles and venules). Previous studies found that central 10-2 visual field could be more accurate to reflect the function and the glaucomatous damage of macula when compared with 24-2/30-2 visual field. Therefore, the current study adopted 10-2 rather than 24-2/30-2 visual field to investigate the differences between the perimetrically affected eyes and the unaffected eyes in the same patient, and the differences between the hemifields in the same glaucomatous eye with single-hemifield visual field loss.

In regard to the structural changes in OAG eyes with unilateral 24-2 visual field loss, previous studies found that perimetrically unaffected eyes had smaller rim area, thinner cpRNFL and mGCC when compared with healthy eyes. Similarly, we found that rim area, cpRNFL, and mGCC of glaucomatous eyes with unaffected 10-2 visual field were significantly decreased compared with healthy eyes. Our results indicated that significant structural damage occurred even in glaucomatous eyes with unaffected 10-2 visual field.

With the application of OCTA, the vessel density in whole image area and in various areas of macula could be non-invasively quantified with high repeatability. Previous study found that parafoveal vessel density of 24-2 visual field unaffected eyes was comparable to the contralateral affected eyes, and was significantly lower than healthy eyes. Similarly, average parafoveal vessel density of the 10-2 visual field unaffected eyes was comparable to the affected eyes and was significantly lower than healthy eyes in the current study, which indicated that significant microvascular damage of macula occurred in eyes without detectable 10-2 visual field loss. Previous studies qualitatively observed significant vessel dropout in peripheral area but not in parafoveal area. Furthermore, we conducted quantitative research and found that inferior parafoveal vessel density of the affected eyes was significantly lower than the unaffected eyes. Moreover, we found that inferior mGCC thicknesses of the affected eyes was also thinner than the unaffected eyes. These findings suggested that the damage of parafoveal vessel density, especially in inferior quadrant, was more significant and spatially corresponded to the structural damage in early OAG.

Glaucmatous eyes with single-hemifield loss are good research objects for investigating the association between damage of retinal microvasculature and structural damage of macula, and between damage of retinal microvasculature and visual field loss. A previous study compared the hemi-field differences of the macular vessel density in early to moderate OAG eyes with single-hemifield defect of 24-2 visual field, and found that parafoveal vessel density of the
unaffected hemifields was significantly higher than the affected hemifields. Although we found comparable parafoveal vessel density between the unaffected hemifields and the affected hemifields in early OAG. The probable explanation accounting for this discrepancy may due to different inclusion criteria between the 2 studies. The current study, which was based on 10-2 visual field loss, included exclusively the early glaucoma and focused on the glaucomatous damage on macula. This finding suggested that parafoveal vessel density might not be involved in the very early damage of glaucoma. However, it was interesting to find that perifoveal vessel density and mGCC thickness of the affected hemifields were lower and thinner, respectively, compared with the unaffected hemifields. This finding further suggested that the damage of perifoveal vessel density was more prominent in early OAG, and macular microvascular defect spatially corresponded to structural damage and visual field loss.

The average age of glaucoma patients of this study is relatively young when compared with previous studies. Eight of 16 early OAG patients were younger than 35 years old. These OAG patients can be also diagnosed as JOAG which is characterized by the presence of OAG in patients younger than 35 years old. Overall, the current study comprises both the JOAG and adult-onset OAG (POAG), which represent a relative full spectrum of OAG. Therefore, the results and conclusions of this study may not be generalizable to the exclusive adult-onset OAG (POAG) patients.

A previous study found that eyes with visual field defect within 10 degree had a higher incidence of optic disc hemorrhage. Similarly, a recent study by Shakla et al found that optic disc hemorrhage was significantly correlated with the presence and progression of both 24-2 and 10-2 visual field defects. Although we found no optic disc hemorrhage in any patients of this study, we recommend the careful scrutinization of the central visual field using 10-2 visual field test in glaucoma patients with optic disc hemorrhage.

There are some limitations to the current study. First, sample size was relatively small in this study. However, the differences of variable parameters were considerably compared within intereyes and intraeyes. This approach is advantageous in improving the statistical power because it avoids the effect of confounding factors on vessel density measurement such as age, sex, and anatomic variabilities. Second, we cannot determine the cause-effect relationship between microvascular damage and structural damage because of the nature of cross-section of this study. Longitudinal study is needed to resolve this issue.

In conclusion, significant macular microvascular damage was present even in glaucomatous eyes without detectable 10-2 visual field loss. The damage of perifoveal vessel density, especially in inferior quadrant, was more prominent in early glaucoma. Macular microvascular damage spatially corresponded to structural and visual field damages. Further study is needed to investigate the cause-effect relationship between microvascular damage and structural damage in early OAG patients.

REFERENCES

1. Weinreb RN, Leung CK, Crowston JG, et al. Primary open-angle glaucoma. Nat Rev Dis Primers. 2016;2:16067.
2. Curcio CA, Allen KA. Topography of ganglion cells in human retina. J Comp Neurol. 1990;300:5–25.
3. Hood DC, Raza AS, de Moraes CG, et al. Glaucomatous damage of the macula. Prog Retin Eye Res. 2013;32:1–21.
4. Kim YK, Ha A, Na KI, et al. Temporal relation between macular ganglion cell-inner plexiform layer loss and peripapillary retinal nerve fiber layer loss in glaucoma. Ophthalmology. 2017;124:1056–1064.
5. Hou H, Moghimi S, Zangwill LM, et al. Macula vessel density and thickness in early primary open-angle glaucoma. Am J Ophthalmol. 2019;199:120–132.
6. Edlinger FSM, Schrens-Hoesl LM, Mardin CY, et al. Structural changes of macular inner retinal layers in early normal-tension and high-tension glaucoma by spectral-domain optical coherence tomography. Graeefes Arch Clin Exp Ophthalmol. 2018;256:1245–1256.
7. Flammer J, Mozaffarifar M. What is the present pathogenetic concept of glaucomatous optic neuropathy? Surv Ophthalmol. 2007;52(suppl 2):S162–S173.
8. Yanagi M, Kawasaki R, Wang JJ, et al. Vascular risk factors in glaucoma: a review. Clin Exp Ophthalmol. 2011;39:252–258.
9. Jia Y, Tan O, Tokayer J, et al. Split-spectrum amplitude decorrelation angiography with optical coherence tomography. Opt Express. 2012;20:4710–4725.
10. Van Melkebeke L, Barbosa-Breda J, Huygens M, et al. Optical coherence tomography angiography in glaucoma: a review. Ophthal Clin. 2018;60:139–151.
11. Venugopal JP, Rao H, Weinreb RN, et al. Repeatability and comparability of peripapillary vessel density measurements of high-density and non-high-density optical coherence tomography angiography scans in normal and glaucoma eyes. Br J Ophthalmol. 2019;103:949–954.
12. Yarmohammadi A, Zangwill LM, Manalastas PIC, et al. Peripapillary and macular vessel density in patients with primary open-angle glaucoma and unilateral visual field loss. Ophthalmology. 2018;125:578–587.
13. Yarmohammadi A, Zangwill LM, Diniz-Filho A, et al. Peripapillary and macular vessel density in patients with glaucoma and single-hemifield visual field defect. Ophthalmology. 2017;124:709–719.
14. De Moraes CG, Sun A, Jarukasetphon R, et al. Association of macular visual field measurements with glaucoma staging systems. JAMA Ophthalmol. 2019;137:139–145.
15. De Moraes CG, Hood DC, Thenappan A, et al. 24-2 visual fields miss central defects shown on 10-2 tests in glaucoma suspects, ocular hypertensives, and early glaucoma. Ophthalmology. 2017;124:1449–1456.
16. Grillo LM, Wang DL, Ramachandran R, et al. The 24-2 visual field test misses central retinal damage confirmed by the 10-2 visual field test and optical coherence tomography. Trans Vis Sci Technol. 2016;5:15.
17. Danford ID, Verkuil LD, Choi DJ, et al. Characterizing the “POAGome”: a bioinformatics-driven approach to primary open-angle glaucoma. Prog Retin Eye Res. 2017;58:89–114.
18. Weinreb RN, Grajevski A, Papadopoulos M, Grigg J, Freedman S, eds. Childhood Glaucoma. Amsterdam: Kugler Publications; 2013.
19. Traynis I, De Moraes CG, Raza AS, et al. Prevalence and nature of early glaucomatous defects in the central 10° of the visual field. JAMA Ophthalmol. 2014;132:291–297.
20. Wu Z, Huang J, Dustin L, et al. Signal strength is an important determinant of accuracy of nerve fiber layer thickness measurement by optical coherence tomography. J Glaucoma. 2009;18:213–216.
21. Kur J, Newman EA, Chan-Ling T. Cellular and physiological mechanisms underlying blood flow regulation in the retina and choroid in health and disease. Prog Retin Eye Res. 2012;31:377–406.
22. Da Pozzo S, Fanni D, Paoloni M, et al. Retinal nerve fibre layer perimeter of perimetrically unaﬀected eyes of glaucoma patients: an optical coherence tomography study. Clin Exp Ophthalmol. 2009;37:217–222.
23. Zangalli CS, Ahmed OM, Waisbourd M, et al. Segmental analysis of macular layers in patients with unilateral primary open-angle glaucoma. J Glaucoma. 2016;25:e401–e407.
24. Koustenis A Jr, Harris A, Gross J, et al. Optical coherence tomography angiography: an overview of the technology and an assessment of applications for clinical research. Br J Ophthalmol. 2017;101:16–20.

25. Takusagawa HL, Liu L, Ma KN, et al. Projection-resolved optical coherence tomography angiography of macular retinal circulation in glaucoma. Ophthalmology. 2017;124:1589–1599.

26. Chen HS, Liu CH, Wu WC, et al. Optical coherence tomography angiography of the superficial microvasculature in the macular and peripapillary areas in glaucomatous and healthy eyes. Invest Ophthalmol Vis Sci. 2017;58:3637–3645.

27. Park SC, De Moraes CG, Teng CC, et al. Initial parafoveal versus peripheral scotomas in glaucoma: risk factors and visual field characteristics. Ophthalmology. 2011;118:1782–1789.

28. Shukla AG, Sirinek PE, De Moraes CG, et al. Disc hemorrhages are associated with the presence and progression of glaucomatous central visual field defects. J Glaucoma. 2020;29:429–434.