Glaucoma

An Optical Coherence Tomography Angiography Study of the Relationship Between Foveal Avascular Zone Size and Retinal Vessel Density

Junki Kwon,¹ Jaewan Choi,² Joong Won Shin,¹ Jiyun Lee,¹ and Michael S. Kook¹

¹Department of Ophthalmology, University of Ulsan, College of Medicine, Asan Medical Center, Seoul, Korea
²Central Seoul Eye Center, Seoul, Korea

Purpose. To assess the relationship between the size of the foveal avascular zone (FAZ; area and perimeter) and vessel density (VD) at various retinal regions using optical coherence tomography angiography (OCTA) in patients with open-angle glaucoma (OAG).

Methods. In this retrospective cross-sectional study, OAG eyes were grouped according to the presence/absence of central visual field (CVF) defects. A control group of normal eyes was also included. OCTA images were obtained from the optic nerve (4.5 × 4.5 mm²) and macular (3 × 3 mm²) area, in which VDs were measured in the circumpapilla, parafovea, and fovea regions. Partial correlation analyses between FAZ parameters representing size and VDs at different retinal regions were performed. The correlation between FAZ parameters and macular ganglion cell-inner plexiform layer thickness (mGCIPLT) and CVF mean sensitivity (MS) was also assessed. For spatial correspondence, correlations between FAZ parameters and corresponding VD, mGCIPLT, and CVF-MS measurements were assessed at each hemiretina.

Results. A total of 126 OAG eyes and 40 controls were reviewed. Overall, FAZ parameters showed statistically significant correlations with VDs measured at the fovea, parafovea, and circumpapilla (FAZ area: r = −0.603, −0.385, −0.256; P < 0.001, < 0.001, and 0.003, respectively). These correlations were observed regardless of the presence of CVF defects (all P < 0.05). FAZ size showed significant spatial correlations with VD, mGCIPLT, and CVF-MS measurements at each hemiretina.

Conclusions. OCTA-derived FAZ area and perimeter showed statistically significant correlations with VDs measured at various retinal locations with spatial correspondence in OAG.

Keywords: foveal avascular zone, vessel density, OCT angiography

Glaucomatous optic neuropathy (GON) is characterized by progressive retinal ganglion cell (RGC) death and axonal loss.¹ ² Blood flow insufficiency and/or abnormal microcirculation in the optic nerve head (ONH) and retina is thought to play an important role in some patients with glaucoma.³–⁷ To assess the microcirculation in the eye, different types of imaging modalities have been studied, including fluorescein angiography (FA), Heidelberg retina flowmeter, and color Doppler. Although FA has been widely used to detect vascular pathology in the retina, it does not provide a direct observation of the microvasculature within various layers of the retina and ONH. Moreover, FA does not provide a quantitative assessment of the microcirculation in various regions of the retina. Recent studies have described the use of non-invasive retinal microvasculature imaging, known as optical coherence tomography angiography (OCTA). This approach uses differences between B-scans to generate contrast associated with the motion of red blood cells (RBCs) through the microvasculature at various locations in the eye.⁸ ⁹ OCTA therefore enables detailed and reproducible images of the retinal microvasculature networks to be obtained with a high level of resolution.¹⁰

The foveal avascular zone (FAZ) is the round, capillary-free zone within the macula. Measurements of FAZ size (area and perimeter) using OCTA have been shown to be highly reproducible in patients with microcirculatory deficiency involving the macula, such as diabetic retinopathy, as well as in healthy individuals.⁹ ¹¹ Using OCTA images of the superficial vascular network, our group has previously reported an enlarged FAZ area in the perifoveal region, which was spatially correlated with central visual field (CVF) loss in glaucoma patients.¹² Furthermore, our subsequent study demonstrated that the FAZ area and perimeter showed significant diagnostic value in discriminating glaucomatous eyes with CVF defects from normal eyes.¹³ Indeed, FAZ perimeter was seen to have a similar glaucomatous diagnostic value to conventional structural parameters, such as the circumpapillary retinal nerve fiber layer (cpRNFL) or macular ganglion cell-inner plexiform layer (mGCIPL) thickness.¹³ These findings suggest the potential role of OCTA-derived FAZ area or perimeter as a novel parameter for the detection of glaucoma patients in a clinical setting.

The macula is the only structure in the eye where the RGC layer is more than a single layer of cells thick, containing up to seven layers of RGC bodies.¹⁴ ⁰ In terms of spatial location, RGCs are mainly located in the central 4.5 mm diameter region of the macula.¹⁵ Glaucoma patients often present with the loss of macular RGCs and nerve fiber layer thickness in the presence
of CVF loss, even at early stages of the disease. Using OCTA, Rao et al. have demonstrated that macular vessel density (VD) in the parafoveal region (central 1-3 mm diameter zone) was reduced in patients with glaucoma compared with healthy eyes. Moreover, glaucomatous change in VD has been detected by serial OCTA measurements in the macular region in patients with primary open-angle glaucoma (POAG), suggesting the potential role of macular VD measurement to detect and monitor microvascular changes in glaucoma.

At present, although it is known that both FAZ size and retinal VD measurements are altered in glaucoma patients, the relationship between microvasculature changes in the FAZ and VD measurements at various retinal locations is unknown. We hypothesized that clarification of this relationship would provide an additional insight into the clinical utility of FAZ size (area or perimeter) in the detection and possible monitoring of glaucoma. In the present study, we have, therefore, investigated the relationships between the FAZ size and VD measurements obtained with OCTA at different retinal locations, including the circumpapillary, parafoveal, and foveal regions in a series of healthy and glaucomatous eyes. The relationship was further evaluated according to the involvement of CVF defects in glaucoma patients. As the FAZ is formed by the superficial vascular complex (SVC) in the central region of the macula, and the location of visual field (VF) defects (i.e., central versus peripheral) may influence the correlation between FAZ parameters and VDs derived from various retinal locations.

**METHODS**

**Participants**

This cross-sectional, retrospective study was approved by the Institutional Review Board of the Asan Medical Center and adhered to the tenets of the Declaration of Helsinki. The medical records of patients who visited the glaucoma clinic of the Asan Medical Center between November 2016 and November 2017 were reviewed retrospectively. Open-angle glaucoma (OAG) eyes and normal control eyes were analyzed consecutively. Inclusion criteria for all participants were age >18 years, best-corrected visual acuity (BCVA) of 20/40 or better, and refractive error (RE) within -10 to +3 diopters (D) sphere and -3 to +5 D cylinder. Exclusion criteria included the presence of any media opacities that resulted in poor quality OCTA images, myopia greater than -8 diopters, and possible monitoring of glaucoma. In the present study, we have, therefore, investigated the relationships between the FAZ size and VD measurements obtained with OCTA at different retinal locations, including the circumpapillary, parafoveal, and foveal regions in a series of healthy and glaucomatous eyes. The relationship was further evaluated according to the involvement of CVF defects in glaucoma patients, as the FAZ is formed by the superficial vascular complex (SVC) in the central region of the macula, and the location of visual field (VF) defects (i.e., central versus peripheral) may influence the correlation between FAZ parameters and VDs derived from various retinal locations.

**OCTA Image Acquisition and Processing**

OCTA images were obtained from both the circumpapillary and macular areas. At first, a 4.5 × 4.5 mm² area, centered on the ONH, was captured with default segmentation of radial peripapillary capillary (RPC) provided by the manufacturer. The RPC layer slab included the area from the internal limiting membrane (ILM) to the nerve fiber layer (NFL). Whole image VD (wVD) was obtained over the entire 4.5 × 4.5 mm² scan field. The intrinsic viewing software (version 2016.2.0.35) provided circumpapillary vessel density (cpVD) in a region defined as a 750 µm-wide elliptical annulus extending from the optic disc boundary, based on the 360° global area and 6-sectoral area, according to the Garway-Heath map (superotemporal, ST; temporal, T; inferotemporal, IT; inferonasal, IN; nasal, N; superonasal, SN).

OCTA images from the macula were captured from a 3 × 3 mm² field of view centered on the fovea in a superficial slab that extended from the ILM to the posterior boundary of the inner plexiform layer (IPL). In this macula OCTA image, four vascular parameters were derived: macular wVD, parafoveal vessel density (pVD), foveal vessel density (fVD), and FAZ size consisting of area and perimeter. VDs were provided by intrinsic viewing software. Macular wVD was measured in the entire 3 × 3 mm² field. pVD was measured in an annular region with an inner diameter of 1 mm and outer diameter of 3 mm centered on the fovea. Global and hemiretinal (superior and inferior) pVD was calculated. The fVD was measured in the most central circular region with a diameter of 1 mm centered on the fovea. Measurements of the FAZ area and perimeter have been described in detail elsewhere. Briefly, two independent raters performed FAZ measurements twice while masked to each other’s results, as well as to the clinical information for each participant, including the presence of glaucoma and location of VF defect. Macular OCTA images were loaded into an image analysis program...
1.82), and 

\[ q = \frac{D_m}{C_0} \]

\[ = \frac{1}{0.01306(23.95 - 1.82)}, \]

where \( D_m \) and \( q \) are the image magnification factor of the imaging system and the eye, respectively. The \( q \) of the OCT system (Optovue, Inc.) is 3.460, which can be calculated from \[ 1/0.01306(23.95 - 1.82) \].

In brief, before the analysis of the repeatability coefficients, the FAZ area and perimeter, Littmann’s method was used to correct the ocular magnification by each AL.34-38 Details of the formula are provided elsewhere.34,35-37 In brief, the between-rater repeatability analysis was performed using repeatability coefficient and measurement error, with previous studies.34,43-45 Repeatability coefficient was calculated as 2.77\text{average within-subject standard deviation (} \sigma_{w} \text{)}, and measurement error was calculated as 1.96\text{standard deviation (} \sigma \text{)}. The 95% confidence intervals of repeatability coefficient were calculated as 1.96\text{average within-subject standard deviation (} \sigma_{w} \text{)}. The 95% confidence intervals of repeatability coefficient were calculated as 1.96\text{standard deviation (} \sigma \text{)}.

### Statistical Analysis

To examine the bias/agreement between the two raters, a Bland-Altman plot analysis was performed for FAZ area and perimeter. In addition, intra-rater repeatability analysis was performed using repeatability coefficient and measurement error, as in previous studies.34,43-45 Repeatability coefficient was calculated as 2.77\text{average within-subject standard deviation (} \sigma_{w} \text{)}, and measurement error was calculated as 1.96\text{standard deviation (} \sigma \text{)}. The 95% confidence intervals of repeatability coefficient were calculated as 1.96\text{average within-subject standard deviation (} \sigma_{w} \text{)}. The 95% confidence intervals of repeatability coefficient were calculated as 1.96\text{standard deviation (} \sigma \text{)}.

Comparisons between OAG eyes and normal controls were made using independent \( t \) tests or \( \chi^2 \) tests as appropriate. Since the FAZ area and macular VD were significantly correlated with age (positive and negative, respectively),46-47 age was adjusted for all correlation analyses between FAZ parameters and VDs at various retinal locations. Therefore, to evaluate the relationship between FAZ size (area, perimeter) and VD measurements at various retinal locations (wiVD, cpVD, pfVD, and pVD), quantitative correlations were assessed in all eyes as well as each subgroup (CVF + and CVF -), using partial correlation analysis while using AL-corrected FAZ size according to the Littmann’s formula and adjusting for age effect. Normal eyes were included in all correlation analyses. Partial correlation analyses between FAZ parameters and other structural/functional parameters (cpRNFLT, mGCIPLT, and MS) were also assessed in the overall and subgroups of OAG eyes after controlling for age.42 For the correlation between FAZ size and visual function, retinal sensitivity was expressed in both linear (1/L) and dB scales. In this study, the absolute value of correlation coefficient below 0.19 was regarded as very weak, 0.2 to 0.39 as weak, 0.4 to 0.59 as moderate, 0.6 to 0.79 as strong, and 0.8 to 1.0 as very strong correlation.48,49

For the evaluation of spatial correspondence between the FAZ size and vascular/structural/functional parameters, the correlation between FAZ area and perimeter and various variables (cpVD, pfVD, cpRNFLT, mGCIPLT, and CVF MS) was assessed at each hemiretina (i.e., superior and inferior hemiretina) separately. For example, the superior FAZ area and perimeter in the superior hemiretina were matched to cpVD at the ST sector, pfVD at the superior hemiretina, cpRNFLT at the superior quadrant, mGCIPLT at the superior hemiretina, MS of 26 test points in the inferior hemi-VF, and MS of two central points in the inferior hemi-VF (Fig. 1). All reported \( P \) values are two-sided and values of \( P < 0.05 \) were considered to indicate statistical significance. All statistical analyses were performed using statistical software (SPSS software version 18.0 for Windows; SPSS, Inc., Chicago, IL, USA) and R program version 3.1.2 (R Foundation, Vienna, Austria).

### Results

A total of 182 eyes (137 OAG, 45 normal) met the initial inclusion criteria and the quality of the OCT/OCTA images was subsequently checked. Of these, 16 eyes (11 OAG, 5 normal) were excluded because of insufficient image quality; 166 eyes were, therefore, included in the final analysis (126 OAG, 40 normal). Of the 126 OAG eyes, 67 (from 67 subjects) were CVF + and 59 (from 59 subjects) were CVF -. All participants were Korean.

Figure 2 shows the Bland-Altman plots for FAZ area and perimeter between the two raters. Intra-rater repeatability analyses results are summarized in Table 1. Repeatability coefficient and measurement error of FAZ area and perimeter was greater than those of FAZ area.
Table 2 summarizes the demographics, ocular characteristics, and measurement data from the VF test, SD-OCT, and OCTA of the entire OAG, CVF+; CVF-/C0; and normal groups. Both the CVF+ and CVF-/C0 groups had significantly higher baseline IOP than the normal group (P < 0.001 and 0.014, respectively). Sex proportion, CCT, SE, and AL showed no significant differences between the glaucoma subgroups and the normal group, with the exception that the age of the participants was higher in the CVF+ group than the normal group. As expected, both CVF+ and CVF-/C0 groups showed significant differences compared with the normal group in terms of VF parameters (including MD, PSD, and MS), SD-OCT measurements (cpRNFLT and mGCIPLT), and OCTA-derived variables, including wiVDs of the disc and macula and cpVD. In addition, the CVF+ group showed significantly lower pfVD and fVD, larger FAZ area, and greater FAZ perimeter than the normal group (all P < 0.05). The differences of FAZ parameters between groups (CVF+ versus normal) were larger than repeatability coefficients, which suggested that these differences were not simply due to the variability of the measurements. Although the CVF-/C0 group also showed lower pfVD and IVd, larger FAZ area, and greater FAZ perimeter than the normal group, the differences were not statistically significant (all P > 0.05).

Table 3 shows the correlation between FAZ parameters and VDs at different retinal locations (disc whole image, circum-papilla, macula whole image, parafovea, and fovea). For the overall 166 eyes, FAZ area and perimeter showed a significant negative correlation with all VF measurements obtained with OCTA (all P < 0.01). Of note, the degree of correlation between FAZ parameters and IVd measurements at different retinal locations showed a similar order to the degree of locational adjacency to the fovea (i.e., the degree of correlation between FAZ parameters and VD measurements was highest between FAZ parameters and IVd, followed by that between FAZ parameters and cpVD. A similar trend in association between FAZ parameters and VD measurements at various retinal locations was also noted in the CVF+ group, with the correlation being strongest with the fovea. Of interest, this trend was also observed in the CVF-/C0 group.

Table 4 illustrates the relationship between FAZ parameters and various structural and functional indices representing glaucoma severity. FAZ area and perimeter showed a significant negative correlation with SD-OCT parameters (cpRNFLT and mGCIPLT), as well as with the VF-MS of all 52 points and the central four points in the overall group (166 eyes) regardless of retinal sensitivity scale, after adjusting for age. A similar trend was also observed in the CVF+ group. However, in the CVF-/C0 group, only FAZ area showed a significant negative correlation with cpRNFLT and mGCIPLT. In terms of the relationship between FAZ parameters and functional indices, there was no significant correlation between FAZ parameters and any central VF-MS values in the CVF-/C0 group, while there were significant correlations between FAZ parameters and VF-MS values (global and central) in the CVF+ group.

Regarding spatial correspondence, Table 5 summarizes the results of correlation analyses for each hemiretina. For the overall group of 166 eyes, FAZ area and perimeter showed a significant negative correlation with all VF measurements obtained with OCTA (all P < 0.01). Of note, the degree of correlation between FAZ parameters and IVd measurements at different retinal regions showed a similar order to the degree of locational adjacency to the fovea (i.e., the degree of correlation between FAZ parameters and VD measurements was highest between FAZ parameters and IVd, followed by that between FAZ parameters and cpVD. A similar trend in association between FAZ parameters and VD measurements at various retinal locations was also noted in the CVF+ group, with the correlation being strongest with the fovea. Of interest, this trend was also observed in the CVF-/C0 group.
perimeter showed a significant correlation with all OCTA, SD-OCT, and VF-derived parameters, including cpVD, pVd, cpRNFLT, and mGCIPLT at the inferior hemiretina, and MS of the central two points and MS of the global 26 points at the superior hemi-VF (all \( P < 0.05 \)).

**Representative Case**

Figure 3 shows a representative case from the glaucoma cohort; 24-2 VF testing showed that glaucomatous VF defects involving the CVF area and MS were lower in the superior hemi-VF than in the inferior hemi-VF, especially in the central...
two points. Based on macular OCTA imaging, the FAZ area and perimeter were greater in the inferior hemiretina than in the superior hemiretina. VDs at the parafovea and circumpapilla provided by intrinsic automatic software were lower in the inferior hemiretina than in the superior hemiretina. The
difference between the superior hemiretina and inferior hemiretina was greater in the pVD (4.00%) than in the cpVD (2.45%). SD-OCT also showed lower mGCIPLT and cpRNFLT in the inferior hemiretina than in the superior hemiretina. The
Central visual field defects subgroup, 107 eyes (40 normal + 67 OAG-+). No central visual field defects subgroup, 99 eyes (40 normal + 59 OAG-). The FAZ area and perimeter showed significant negative correlation with superiormost hemiretinal FAZ parameter (superior or inferior hemiretina) values, thus indicating the relationship between FAZ size enlargement and reduction of superficial VF measurements at various retinal locations in patients with glaucoma.

In normal eyes, the FAZ diameter range is about 0.4 to 0.5 mm, as determined by previous histologic or fluorescein angiographic studies. In patients with glaucoma, the FAZ area is reported to be enlarged compared with that in normal controls, which ranged from 0.360 to 0.435 mm² 12,13,24. In the current study consisting of Korean patients, the mean FAZ area was 0.583 and 0.431 mm² for normal control and OAG eyes, respectively, which is similar to measurements seen in previous studies.

In this study, FAZ area and perimeter showed the highest correlations with VO measurements at the fovea (degree of correlation: moderate to strong), which is defined as a 1-mm diameter circular area. Histologically, the border of the FAZ is formed by a single-layered capillary arcade that lies within the ganglion cell layer (GCL). The FAZ area is highly sensitive to ischemic events and is enlarged in conditions such as old age, diabetic retinopathy, RVO, and sickle cell disease.16,47,55–56. The diameter of the FAZ is ~400 μm in normal eyes. A recent study found that the FAZ area was ~0.373 to 0.577 mm² in normal eyes with ICCs >0.9.55. In the present study, the mean FAZ area was 0.467 mm², 0.393 mm², and 0.385 mm² for the 300 CVF–, 0.327 mm², and normal groups, respectively. The area of the fovea in normal eyes is ~0.785 mm², and the area of the fovea should, therefore, be large enough to contain the FAZ border. Consequently, it is not unexpected that FAZ parameters and VO showed a strong negative correlation.

The FAZ area and perimeter showed a significant negative correlation with macular wVD and pVD (degree of correla-

**Table 3. Age-Adjusted Partial Correlations Between the FAZ (Area and Perimeter) and VD Density at Different Retinal Regions**

<table>
<thead>
<tr>
<th></th>
<th>wiVD Disc, %</th>
<th>cpVD, %</th>
<th>wiVD Macula, %</th>
<th>pVD, %</th>
<th>fVD, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All 166 eyes (40 normal + 126 OAG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAZ area, mm²</td>
<td>−0.274 (0.001)</td>
<td>−0.256 (0.003)</td>
<td>−0.268 (0.002)</td>
<td>−0.385 (&lt;0.001)</td>
<td>−0.603 (&lt;0.001)</td>
</tr>
<tr>
<td>FAZ perimeter, mm</td>
<td>−0.279 (0.005)</td>
<td>−0.260 (0.005)</td>
<td>−0.244 (&lt;0.001)</td>
<td>−0.302 (&lt;0.001)</td>
<td>−0.443 (&lt;0.001)</td>
</tr>
<tr>
<td>Central visual field defects subgroup, 107 eyes (40 normal + 67 CVF–)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAZ area, mm²</td>
<td>−0.260 (0.021)</td>
<td>−0.240 (0.030)</td>
<td>−0.191 (0.079)</td>
<td>−0.302 (0.007)</td>
<td>−0.530 (&lt;0.001)</td>
</tr>
<tr>
<td>FAZ perimeter, mm</td>
<td>−0.269 (0.018)</td>
<td>−0.247 (0.025)</td>
<td>−0.2187 (0.054)</td>
<td>−0.242 (0.030)</td>
<td>−0.387 (&lt;0.001)</td>
</tr>
<tr>
<td>No central visual field defects subgroup, 99 eyes (40 normal + 59 OAG–)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAZ area, mm²</td>
<td>−0.257 (0.030)</td>
<td>−0.311 (0.008)</td>
<td>−0.360 (0.002)</td>
<td>−0.459 (&lt;0.001)</td>
<td>−0.652 (&lt;0.001)</td>
</tr>
<tr>
<td>FAZ perimeter, mm</td>
<td>−0.293 (0.012)</td>
<td>−0.354 (0.002)</td>
<td>−0.321 (0.005)</td>
<td>−0.411 (&lt;0.001)</td>
<td>−0.530 (&lt;0.001)</td>
</tr>
</tbody>
</table>

Values with statistical significance are shown in bold. Data are presented as age-adjusted partial correlation coefficient (P value).

**Table 4. Age-Adjusted Partial Correlations Between the FAZ (Area and Perimeter) and SD-OCT and VF Parameters**

<table>
<thead>
<tr>
<th></th>
<th>cpRNFLT, μm</th>
<th>mgGCIPLT, μm</th>
<th>Whole VF MS, 1/L</th>
<th>Whole VF MS, dB</th>
<th>Central 4 Points MS, 1/L</th>
<th>Central 4 Points MS, dB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total 166 eyes (40 normal + 126 OAG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAZ area, mm²</td>
<td>−0.263 (0.001)</td>
<td>−0.336 (&lt;0.001)</td>
<td>−0.281 (0.002)</td>
<td>−0.290 (&lt;0.001)</td>
<td>−0.256 (0.002)</td>
<td>−0.333 (&lt;0.001)</td>
</tr>
<tr>
<td>FAZ perimeter, mm</td>
<td>−0.237 (0.004)</td>
<td>−0.294 (&lt;0.001)</td>
<td>−0.297 (&lt;0.001)</td>
<td>−0.291 (&lt;0.001)</td>
<td>−0.287 (&lt;0.001)</td>
<td>−0.340 (&lt;0.001)</td>
</tr>
<tr>
<td>Central visual field defects subgroup, 107 eyes (40 normal + 67 CVF–)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAZ area, mm²</td>
<td>−0.285 (0.007)</td>
<td>−0.372 (&lt;0.001)</td>
<td>−0.327 (0.002)</td>
<td>−0.287 (0.006)</td>
<td>−0.287 (0.007)</td>
<td>−0.347 (0.001)</td>
</tr>
<tr>
<td>FAZ perimeter, mm</td>
<td>−0.231 (0.010)</td>
<td>−0.338 (0.001)</td>
<td>−0.338 (0.001)</td>
<td>−0.283 (0.007)</td>
<td>−0.313 (0.002)</td>
<td>−0.345 (0.001)</td>
</tr>
<tr>
<td>No central visual field defects subgroup, 99 eyes (40 normal + 59 OAG–)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAZ area, mm²</td>
<td>−0.219 (0.047)</td>
<td>−0.235 (0.031)</td>
<td>−0.231 (0.044)</td>
<td>−0.271 (0.012)</td>
<td>−0.162 (0.142)</td>
<td>−0.170 (0.106)</td>
</tr>
<tr>
<td>FAZ perimeter, mm</td>
<td>−0.198 (0.072)</td>
<td>−0.275 (0.061)</td>
<td>−0.265 (0.025)</td>
<td>−0.297 (0.007)</td>
<td>−0.170 (0.121)</td>
<td>−0.174 (0.117)</td>
</tr>
</tbody>
</table>

Values with statistical significance are shown in bold. Data are presented as age-adjusted partial correlation coefficient (P value).
### Correlations Between FAZ Parameters and Other Retinal Measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>mGCIPLT</th>
<th>cpRNFLT</th>
<th>Global 26 Points MS</th>
<th>Central 2 Points MS</th>
<th>Sup Central 2 Points MS</th>
<th>Inf Central 2 Points MS</th>
<th>Inferior hemiretina (with sup hemi-VF)</th>
<th>Superior hemiretina (without sup hemi-VF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inf FAZ area, mm$^2$</td>
<td>-0.274 (0.006)</td>
<td>-0.386 (0.003)</td>
<td>-0.360 (&lt;0.001)</td>
<td>-0.357 (&lt;0.001)</td>
<td>-0.318 (0.001)</td>
<td>-0.345 (&lt;0.001)</td>
<td>-0.274 (0.006)</td>
<td>-0.386 (0.003)</td>
</tr>
<tr>
<td>Inf FAZ perimeter, mm</td>
<td>-0.287 (0.001)</td>
<td>-0.306 (0.001)</td>
<td>-0.318 (0.001)</td>
<td>-0.325 (0.001)</td>
<td>-0.304 (0.001)</td>
<td>-0.335 (&lt;0.001)</td>
<td>-0.287 (0.001)</td>
<td>-0.306 (0.001)</td>
</tr>
<tr>
<td>Sup FAZ area, mm$^2$</td>
<td>-0.198 (0.034)</td>
<td>-0.179 (0.024)</td>
<td>-0.219 (0.020)</td>
<td>-0.223 (0.017)</td>
<td>-0.231 (0.016)</td>
<td>-0.234 (0.020)</td>
<td>-0.198 (0.034)</td>
<td>-0.179 (0.024)</td>
</tr>
<tr>
<td>Sup FAZ perimeter, mm</td>
<td>-0.190 (0.041)</td>
<td>-0.189 (0.042)</td>
<td>-0.219 (0.020)</td>
<td>-0.223 (0.017)</td>
<td>-0.231 (0.016)</td>
<td>-0.234 (0.020)</td>
<td>-0.190 (0.041)</td>
<td>-0.189 (0.042)</td>
</tr>
</tbody>
</table>

Values with statistical significance are shown in bold. Data are presented as age-adjusted partial correlation coefficient ($r_C$).

### Correlations Between FAZ Area and Other Retinal Measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>mGCIPLT</th>
<th>cpRNFLT</th>
<th>Global 26 Points MS</th>
<th>Central 2 Points MS</th>
<th>Sup Central 2 Points MS</th>
<th>Inferior hemiretina (with sup hemi-VF)</th>
<th>Superior hemiretina (without sup hemi-VF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inf FAZ area, mm$^2$</td>
<td>0.256 (0.003)</td>
<td>-0.360 (&lt;0.001)</td>
<td>-0.357 (&lt;0.001)</td>
<td>-0.318 (0.001)</td>
<td>-0.345 (&lt;0.001)</td>
<td>-0.274 (0.006)</td>
<td>-0.386 (0.003)</td>
</tr>
<tr>
<td>Inf FAZ perimeter, mm</td>
<td>0.256 (0.003)</td>
<td>-0.360 (&lt;0.001)</td>
<td>-0.357 (&lt;0.001)</td>
<td>-0.318 (0.001)</td>
<td>-0.345 (&lt;0.001)</td>
<td>-0.274 (0.006)</td>
<td>-0.386 (0.003)</td>
</tr>
<tr>
<td>Sup FAZ area, mm$^2$</td>
<td>0.198 (0.034)</td>
<td>-0.179 (0.024)</td>
<td>-0.219 (0.020)</td>
<td>-0.223 (0.017)</td>
<td>-0.231 (0.016)</td>
<td>-0.234 (0.020)</td>
<td>-0.198 (0.034)</td>
</tr>
<tr>
<td>Sup FAZ perimeter, mm</td>
<td>0.190 (0.041)</td>
<td>-0.189 (0.042)</td>
<td>-0.219 (0.020)</td>
<td>-0.223 (0.017)</td>
<td>-0.231 (0.016)</td>
<td>-0.234 (0.020)</td>
<td>-0.190 (0.041)</td>
</tr>
</tbody>
</table>

Values with statistical significance are shown in bold. Data are presented as age-adjusted partial correlation coefficient ($r_C$).
words, OAG eyes without CVF defects may have relatively intact FAZ architecture as well as CVF MS measurements, which may lead to a lack of correlation between FAZ parameters and central VF MS measurements. Our findings suggest that the OCTA-derived FAZ area or perimeter may be a useful parameter for monitoring VF changes in glaucoma patients with CVF defects.

Of note, significant topographic correlations were seen between FAZ size and OCTA, SD-OCT, and VF-derived parameters in both the inferior hemiretina (with superior hemi-VF) and superior hemiretina (with inferior hemi-VF). These findings may confirm our previous observations, which showed that the mean FAZ area derived from OCTA in the hemiretinal segments corresponding to VF defects is significantly larger than that in the hemiretinal segments without VF defects in glaucomatous eyes with hemifield CVF defects. Moreover, the current study demonstrates that good topographic correlations also exist between changes in FAZ size and OCTA-derived VD measurements at the circumpapilla and parafovea. Therefore, our findings suggest that vascular structural/functional deficits in glaucomatous eyes and perifoveal microvascular damage are spatially correlated throughout various retinal locations.

We acknowledge that this study has several limitations. The first relates to the method of measuring the FAZ parameters. We assessed FAZ size by marking the border of vessels from OCTA images using ImageJ software, as previously validated. Although excellent reproducibility was observed in this study and has been reported in previous studies, it is possible that measurement error or inter-rater variability may exist and act as a confounding variable. While we corrected the ocular magnification effect from different ALs in the measurement of FAZ size using Littmann’s formula, the use of OCTA-derived VD measurements remains a possible source of error in our correlation analyses. In this study, we set the cutoff value of OCTA image quality at SSI >48, as used in many previous studies. Venugopal et al. recently reported that SSI value had a significant effect on the repeatability of VD measurement by OCTA. The mean SSI values of our cohort were relatively high, being close to 60, and there was no significant difference among groups in terms of SSI values. Therefore, we do not consider that SSI had a significant impact on our correlation analyses. In this study, we evaluated the central visual function using VF 24-2 testing. As Hood et al. proposed, glaucomatous damage to the macula can be missed or underestimated with standard VF tests using a 6° grid, such as VF 24-2 testing. Furthermore, none of the test points used in VF 24-2 testing corresponded to the FAZ topographically due to the smaller size of the FAZ. In this study, we focused on the innermost four points of VF 24-2 testing that correspond to the central 25° area, where RGCs are concentrated, to investigate whether a correlation between FAZ size and VF retinal sensitivity exists. However, VF 10-2 testing with foveal threshold value may yield more accurate measurement of central visual function and more accurate topographic correspondence with FAZ size than the VF 24-2 test. Since this study demonstrated a significant correlation between FAZ size and IVD and pIVD, we can deduce the vascular status of the macula through the observation of FAZ size. Finally, our study participants are the same race (Koreans). Previous studies revealed that foveal pit morphology showed differences between races, and FAZ size had significant correlation with foveal fit morphology. Therefore, the utility of FAZ size may be complicated or limited in a clinic where patients from various races are examined.

In conclusion, when measured with OCTA, FAZ area and perimeter showed a significant correlation with VDs at the fovea, parafovea, and circumpapilla, with the strongest correlation being noted in the fovea, followed by the parafovea and circumpapilla. FAZ size (area and perimeter) showed a significant correlation with cpRNFLT/mGCIPLT and central and global visual function measured by the innermost 4 and 52 points of VF 24-2 testing in the OAG eyes, with spatial correspondence. These findings suggest that FAZ size may be a potential vascular biomarker representing macular RGC status and central visual function in patients with glaucoma.

Acknowledgments

Disclosure: J. Kwon, None; J. Choi, None; J.W. Shin, None; J. Lee, None; M.S. Kook, None

References

FAZ and Retinal Vessel Density by OCT Angiography


