Optical Coherence Tomography Angiography Evaluation of the Parafoveal Vasculature and Its Relationship With Ocular Factors

Colin S. Tan,1,2 Louis W. Lim,1 Vernon S. Chow,1 Isaac W. Chay,1 Shoun Tan,1 Kai Xiong Cheong,1 Gabriel T. Tan,1 and Srinivas R. Sadda3

1National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore
2Fundus Image Reading Center, National Healthcare Group Eye Institute, Singapore
3Doheny Eye Institute, University of California Los Angeles, Los Angeles, United States

Evaluation of the retinal vasculature is essential in the management of retinal conditions, in particular retinal vascular diseases. Among other parameters, the size and regularity of the foveal avascular zone (FAZ) have been shown to be of both diagnostic and prognostic value in retinal diseases.1–10 The FAZ has been reported to be enlarged in patients with diabetic retinopathy9 and retinal vein occlusions,11 while it is smaller among patients with foveal hypoplasia12 or albinism.13 For the past few decades, fluorescein angiography (FA) has been the most commonly used imaging modality for evaluation of the retinal microvasculature and its relationship with ocular factors.14–31

To understand the effects of retinal diseases on the FAZ, it is essential to first determine the variation of FAZ size and shape among healthy individuals. Earlier studies1–6,14–28 have reported significant variation of FAZ size and shape in normal eyes. Many of these studies, however, have been performed by using standard/conventional FA, which is only able to image the superficial retinal vessels, but not the deep retinal plexus.

Recent advances in optical coherence tomography (OCT) technology, in particular the increased scanning speed of OCT devices, as well as progress in image-processing algorithms, have allowed the development of OCT angiography (OCT-A), which is a noninvasive method of imaging the various vascular layers in the retina without the administration of intravenous dye.29,30 Another significant advantage of OCT-A over FA is the ability to image the deep retinal plexus, which can be viewed separately from the superficial plexus.29–31

Only a few studies have described the range of FAZ sizes measured with OCT-A.7–10,32–37 As ophthalmologists begin to use OCT-A devices to evaluate the vascular and FAZ characteristics of diseased eyes, it is imperative to have normative data for the size and characteristics of both the superficial and deep FAZ in order to better evaluate the impact of retinal diseases on these. Another key gap in our current knowledge is an understanding of the effects of demographic and ocular parameters such as spherical equivalent, axial length, retinal thickness, and choroidal thickness on the FAZ size. While some of these parameters have been evaluated individually,6,8,14,16,18,19,23,26,27,32,35 it is important to assess these factors comprehensively, to account for the potential interactions between these parameters. In addition, since high myopia is more prevalent among certain populations, such as Asians,38 it
would be useful to know how the FAZ varies among such individuals.

Our objectives were to determine the size and characteristics of the superficial and deep FAZ in normal, healthy adults by using OCT-A, and to ascertain the effects of demographic and ocular parameters on the FAZ.

METHODS

This was a prospective cohort study of 117 healthy volunteers with no ocular disease and included participants with high myopia (spherical equivalent –6 diopters [D] or higher) but no complications of myopia or other concurrent ocular diseases. The study was conducted at the National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore. Participants with high myopia, but otherwise healthy eyes, were specifically included to ascertain potential differences in FAZ parameters between high myopes and other participants. A trained retinal specialist reviewed the fundus of all participants to exclude ocular diseases. The study was approved by the Institutional Review Board of the National Healthcare Group and conformed to the tenets of the Declaration of Helsinki. Written, informed consent was obtained from all participants.

Imaging Protocol

All imaging modalities were performed using a standardized imaging protocol and were obtained sequentially at a standardized time between 12 PM to 2 PM to account for the potential effects of diurnal variation in ocular parameters, in particular choroidal thickness.39 The OCT scans were performed on both eyes by a trained operator under mesopic lighting conditions.

Optical coherence tomography angiography scans were performed with the AngioVue OCT-A system (Optovue, Fremont, CA, USA). A 3 × 3-mm angio-OCT scan (304 × 304 pixels) centered on the fovea was performed on each eye. Each B-scan was repeated at each fixed position, with two orthogonal OCT-A volume scans (horizontal and vertical) acquired to minimize motion artifacts. Split-spectrum amplitude decorrelation angiography was used to detect flow and produce the OCT-A en face images. Automated segmentation lines were used to divide the capillary bed into the superficial and deep layers. The superficial capillary plexus, defined as the region between the vitreoretinal interface and the outer border of the ganglion cell layer, was segmented with one boundary at 3 μm beneath the internal limiting membrane, and the other 15 μm beneath the inner plexiform layer. The deep capillary plexus, defined as the region between the inner border of the inner plexiform layer and the outer border of the outer plexiform layer, was segmented with the boundaries set at 15 and 69 μm, respectively, beneath the inner plexiform layer.

To assess macular and choroidal thicknesses, the Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) was used. A 62-line horizontal raster scan (30° × 25°, 9.2 mm × 7.6 mm) centered on the fovea was performed, with 25 frames averaged in each OCT B-scan to improve the image quality.

All OCT scans were reviewed by a fellowship-trained retinal specialist (CST) to ensure that the scans were centered on the fovea and of sufficient clarity to adequately visualize the retinal vessels (OCT-A) and the choroid-scleral boundary (Spectralis OCT).

Axial length was measured by using the IOL Master 700 (Carl Zeiss Meditec, Dublin CA, USA). Refractive error and keratometry were measured by using the Canon RK-F1 full autorefractor-keratometer (Canon, Inc., Tokyo, Japan).

Assessment of Foveal Avascular Zone

Grading of the OCT-A images was performed in a reading center under standardized lighting conditions. Optical coherence tomography angiography scans of the superficial and deep retinal vasculature were exported and independently assessed by two trained graders using ImageJ (version 1.49, National Institutes of Health, Bethesda, MD, USA) (Fig. 1). After the scale was set to 304 pixels/3 mm, superficial and deep FAZ boundaries were manually traced by the graders, and the FAZ area and characteristics were calculated by the software.

Subsequently, the segmentation lines of the OCT-A scans were modified by using the Optovue software to include the full thickness of the retina (Figs. 1C, 1F). The resultant full-thickness retina FAZ sizes were regraded by the same graders and the results compared with the measurements above. All FAZ sizes (superficial, deep, and full-thickness retina) were graded independently, without reference to the corresponding scans of different layers from the same eye.

Circularity represents the degree of resemblance of the region to a perfect circle, with a value of 1.0 denoting a perfect circle.40 Feret’s diameter is the maximum diameter of the FAZ and is also known as the maximum caliber.40 Feret’s angle refers to the angle that the maximum diameter makes with the horizontal meridian.40

Central subfield retinal thickness was measured with the Heidelberg Eye Explorer software, version 1.7.1.0, following manual adjustment of errors in segmentation boundaries. Central choroidal thickness was measured manually by using the calipers of the proprietary software, as previously described.41

Statistical Analysis

Statistical analysis was performed with IBM SPSS version 23 (SPSS, Inc., Chicago, IL, USA). Multiple linear regression analysis was performed to evaluate the relationship between FAZ size and ocular factors, while t-tests were used to compare means between groups. Intraclass correlation coefficients (ICCs) were used to assess the intergrader agreement between the graders.

RESULTS

Of the 117 participants, 64 were male and 53 were female, with a mean age of 22.5 (range, 21–30; SD ±1.4) years. The mean axial length was 25.4 mm, and ranged from 22.4 to 28.9 mm (SD ±1.3), while the mean spherical equivalent was −4.3 D (range, −15.5 D to +1.0 D; SD ±2.9). Among this cohort, 56 eyes (25.9%) had high myopia (defined as spherical equivalent of −6 D or higher).

The mean central subfield retinal thickness was 262.8 μm (range, 220–316 μm; SD ±17.7), while the mean central choroidal thickness was 312.4 μm (SD ±92.3), and ranged from 119 to 545 μm.

Superficial and Deep FAZ Characteristics

The characteristics of the superficial and deep FAZ, as well as the FAZ measured from the full-thickness retinal slab, are summarized in Table 1. The mean superficial FAZ area was 0.24 mm², and ranged from 0.04 to 0.48 mm² (Fig. 2). In contrast, the mean deep FAZ area was 0.38 mm² and ranged from 0.10 to 0.70 mm². Comparing all eyes, the deep FAZ was significantly larger than the superficial FAZ (mean difference 0.13 mm²; paired t-test, P < 0.001) (Fig. 3A). In all of the participants, no retinal vessels were visualized within the outer retinal layer.
When comparing the right and left eyes of participants, the superficial and deep FAZ sizes were strongly correlated (correlation coefficients of 0.95 and 0.88, respectively; Fig. 4), with mean differences between eyes of 0.004 mm² ($P = 0.146$) and 0.005 mm² ($P = 0.351$) for the superficial and deep FAZ, respectively.

The shape of the FAZ varied among participants, with some having a relatively circular shape, while others had more irregular boundaries (Fig. 2). The mean circularity index was 0.80 (range, 0.52–0.95) for the superficial FAZ, and 0.88 (range, 0.71–0.97) for the deep FAZ. The mean Feret’s diameter of the superficial FAZ was 0.65 mm, while it was 0.78 mm for the deep FAZ ($P < 0.001$). The axis of the longest diameter (Feret’s angle) was 90.7° for the superficial FAZ and 73.9° for the deep FAZ.

**Full-Thickness Retina Slab FAZ Area**

The characteristics of the FAZ measured by using a full-thickness retina slab are shown in Table 1. As illustrated in Figure 3B, full-thickness retina slab area showed a very strong correlation with superficial FAZ area (coefficient 0.992, $P < 0.001$).

**Table 1.** Measurements of Superficial and Deep Foveal Avascular Zones

<table>
<thead>
<tr>
<th></th>
<th>Superficial FAZ, Mean (Range)</th>
<th>Deep FAZ, Mean (Range)</th>
<th>Full-Thickness Retina FAZ, Mean (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAZ area, mm²</td>
<td>0.24 (0.04–0.48)</td>
<td>0.38 (0.10–0.70)</td>
<td>0.24 (0.03–0.49)</td>
</tr>
<tr>
<td>25th percentile</td>
<td>0.20</td>
<td>0.29</td>
<td>0.19</td>
</tr>
<tr>
<td>50th percentile</td>
<td>0.24</td>
<td>0.36</td>
<td>0.24</td>
</tr>
<tr>
<td>75th percentile</td>
<td>0.30</td>
<td>0.46</td>
<td>0.50</td>
</tr>
<tr>
<td>FAZ descriptives</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perimeter, mm</td>
<td>1.93 (0.70–2.95)</td>
<td>2.30 (1.31–3.33)</td>
<td>1.94 (0.68–2.80)</td>
</tr>
<tr>
<td>Circularity</td>
<td>0.80 (0.52–0.95)</td>
<td>0.88 (0.71–0.97)</td>
<td>0.79 (0.51–0.95)</td>
</tr>
<tr>
<td>Feret’s diameter, mm</td>
<td>0.65 (0.24–0.97)</td>
<td>0.78 (0.45–1.19)</td>
<td>0.65 (0.25–0.93)</td>
</tr>
<tr>
<td>Feret’s angle, deg</td>
<td>90.7 (1.4–178.5)</td>
<td>73.9 (2.9–175.5)</td>
<td>95.7 (1.5–179.0)</td>
</tr>
<tr>
<td>Comparison between eyes</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Difference in FAZ area, mm²</td>
<td>0.004 (0–0.11)</td>
<td>0.005 (0–0.21)</td>
<td>0.004 (0–0.11)</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>0.95</td>
<td>0.88</td>
<td>0.95</td>
</tr>
</tbody>
</table>
**Figure 2.** Optical coherence tomography angiogram of FAZ. (A) Small superficial FAZ. (B) Small deep FAZ. (C) Corresponding OCT scan illustrating the shape of the fovea, with a shallow foveal pit. Central retinal thickness is 297 μm. (D) Moderate-sized superficial FAZ. (E) Moderate-sized deep FAZ. (F) Optical coherence tomography scan showing a deeper foveal pit, with central retinal thickness of 257 μm. (G) Large superficial FAZ. (H) Large deep FAZ. (I) The foveal pit is very deep, with a central retinal thickness of 244 μm.

**Figure 3.** Correlations between FAZ areas. (A) Scatterplot of superficial FAZ area with deep FAZ area. The deep FAZ is consistently larger than the superficial FAZ of the same eye. (B) Scatterplot of superficial FAZ area with full retina thickness FAZ area. There is a strong correlation between the FAZ areas (correlation coefficient 0.992).
0.001), with a mean difference of 0.0005 mm² (P = 0.510). In contrast, full-thickness retina slab FAZ differed in size from the deep FAZ by 0.13 mm² (P < 0.001), with correlation coefficient of 0.698.

Factors Affecting FAZ Area

Females had a larger superficial (0.28 vs. 0.21 mm², P < 0.001) and deep FAZ (0.42 vs. 0.35 mm², P < 0.001) than males. Performing univariate linear regression on all eyes (Table 2), superficial, deep, and full retinal thickness FAZ areas had significant correlations with central subfield retinal thickness, sex, axial length, and spherical equivalent, but did not vary significantly with age or central choroidal thickness. The relationships between superficial and deep FAZ areas and central retinal thickness are illustrated in Figure 5.

By multiple linear regression analysis (Table 2), both superficial and deep FAZ areas varied significantly with central retinal thickness, sex, and spherical equivalent.

Separate Analysis of Eyes With and Without High Myopia

The cohort was subdivided into eyes with and without high myopia and analyzed separately (Table 2). In both groups, the FAZ in the superficial, deep, and full-retinal thickness layers were significantly larger in females than males.

Performing univariate analysis (Table 2), central retinal thickness and sex significantly affected the size of the superficial, deep, and full-retinal thickness FAZ for normal eyes. Among eyes with high myopia, in addition to these factors, both axial length and choroidal thickness affected the size of the deep FAZ.

On multivariate analysis for normal eyes, the significant factors affecting FAZ size for the superficial and full-thickness retinal layers were central retinal thickness and sex. For the deep FAZ area in normal eyes, only central retinal thickness remained significant on multivariate analysis.

For eyes with high myopia, central retinal thickness, sex, and choroidal thickness significantly affected the superficial and deep FAZ sizes on multivariate analysis.

Repeatability of FAZ Measurement

Measurement of FAZ area showed good intergrader (ICC, 0.997; 95% confidence interval, 0.988–0.999) and intragrader repeatability (ICC, 0.998; 95% confidence interval, 0.987–0.999) (Fig. 1).

DISCUSSION

In this study, we reported the characteristics of both the superficial and deep FAZ among healthy individuals and the relationship between the FAZ size and various ocular and demographic factors. On multivariate analysis, superficial and deep FAZ areas were found to be influenced by sex, central retinal thickness, and spherical equivalent in the overall cohort. However, when analyzing separately, the FAZ size in normal eyes was affected by central retinal thickness and sex only. Among eyes with high myopia, in addition to central retinal thickness and sex, central choroidal thickness also affected the superficial and deep FAZ size.

To date, there are only a few articles describing FAZ area measured with OCT-A,7–10,32–37 with the mean area of the superficial FAZ ranging from 0.25 to 0.304 mm²,8,32,34,37 while the deep FAZ ranges from 0.34 to 0.495 mm².8,32,34,37 Consistent with the findings of earlier studies, in our study, the mean superficial FAZ area was 0.24 mm², while the mean area of the deep FAZ was larger (0.38 mm²). It has been reported that the FAZ area in the superficial plexus is smaller than that of the deep retinal plexus, which is likely related to the anatomy of the retinal vasculature in the two layers. In this study, the superficial FAZ was consistently smaller than the deep FAZ (Fig. 5A).

It is important to note, however, that FAZ size among normal individuals appears to vary greatly at both the superficial and deep levels (Table 3).1–10,14–28,32–37 This
<table>
<thead>
<tr>
<th></th>
<th>All Eyes</th>
<th>Emmetropes and Low Myopes</th>
<th>High Myopes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate Linear Regression Analysis</td>
<td>Multiple Linear Regression Analysis</td>
<td>Univariate Linear Regression Analysis</td>
</tr>
<tr>
<td></td>
<td>Coefficient</td>
<td>$R^2$</td>
<td>$P$ Value</td>
</tr>
<tr>
<td>Superficial FAZ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.405</td>
<td>0.164</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Spherical equivalent, D</td>
<td>0.146</td>
<td>0.021</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>$-0.215$</td>
<td>0.046</td>
<td>$0.001$</td>
</tr>
<tr>
<td>Central subfield retinal thickness, μm</td>
<td>$-0.713$</td>
<td>0.508</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Central choroidal thickness, μm</td>
<td>0.078</td>
<td>0.006</td>
<td>0.236</td>
</tr>
<tr>
<td>Deep FAZ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.297</td>
<td>0.088</td>
<td>$&lt;0.001$</td>
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<tr>
<td>Spherical equivalent, D</td>
<td>0.158</td>
<td>0.025</td>
<td>$0.015$</td>
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<tr>
<td>Axial length, mm</td>
<td>$-0.221$</td>
<td>0.049</td>
<td>$0.001$</td>
</tr>
<tr>
<td>Central subfield retinal thickness, μm</td>
<td>$-0.430$</td>
<td>0.185</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Central choroidal thickness, μm</td>
<td>0.087</td>
<td>0.007</td>
<td>0.191</td>
</tr>
<tr>
<td>Full-thickness retinal slab FAZ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.420</td>
<td>0.176</td>
<td>$&lt;0.001$</td>
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<tr>
<td>Spherical equivalent, D</td>
<td>0.144</td>
<td>0.021</td>
<td>$0.028$</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>$-0.213$</td>
<td>0.046</td>
<td>$0.001$</td>
</tr>
<tr>
<td>Central subfield retinal thickness, μm</td>
<td>$-0.713$</td>
<td>0.509</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Central choroidal thickness, μm</td>
<td>0.067</td>
<td>0.004</td>
<td>0.311</td>
</tr>
</tbody>
</table>

* $P$ values in bold are statistically significant.
FIGURE 5. Variation of FAZ size with central retinal thickness. (A) Variation of superficial FAZ size with central retinal thickness. (B) Variation of deep FAZ size with central retinal thickness. (C) Variation of full retinal thickness FAZ size with central retinal thickness.
### Table 3. Summary of Studies Regarding FAZ Size and Correlation With Parameters in Normal Eyes Using OCT Angiography

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of Eyes</th>
<th>Age, Mean (Range), y</th>
<th>Superficial FAZ, Area, Mean (±SD), mm²</th>
<th>Deep FAZ, Area, Mean (±SD), mm²</th>
<th>Correlation With FAZ Mean Area</th>
<th>Correlation With FAZ Mean Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study</td>
<td>234</td>
<td>22.7 (21–30)</td>
<td>All eyes: 0.24 (0.08)</td>
<td>All eyes: 0.38 (0.12)</td>
<td>Superficial FAZ inverse</td>
<td>Superficial FAZ no relationship</td>
</tr>
<tr>
<td>Samara et al.</td>
<td>70</td>
<td>42 (12–76)</td>
<td>0.266 (0.097)</td>
<td>0.495 (0.227)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Samara et al.</td>
<td>32</td>
<td>70</td>
<td>0.266 (0.097)</td>
<td>0.495 (0.227)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shahlaee et al.</td>
<td>34</td>
<td>38 (26–72)</td>
<td>0.27 (0.101)</td>
<td>0.34 (0.116)</td>
<td></td>
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</tr>
<tr>
<td>Yu et al.</td>
<td>76</td>
<td>36 (24–59)</td>
<td>Overall: 0.474 (0.172)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Takase et al.</td>
<td>19</td>
<td>62.8 (38–81)</td>
<td>0.25 (0.06)</td>
<td>0.38 (0.11)</td>
<td></td>
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</tr>
<tr>
<td>Di et al.</td>
<td>85</td>
<td>53.81 (30–80)</td>
<td>Overall: 0.36 (0.11)*</td>
<td></td>
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</tr>
<tr>
<td>Freiberg et al.</td>
<td>25</td>
<td>60.41</td>
<td>Mean horizontal diameter: 573 µm (177)</td>
<td>Mean horizontal diameter: 659 µm (194)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mamm et al.</td>
<td>25</td>
<td>27.6 (21–35)</td>
<td>Overall: 0.262 (0.020)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kuehlewein et al.</td>
<td>19</td>
<td>38 (26–72)</td>
<td>0.30 (0.152)*</td>
<td>0.48 (0.162)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim et al.</td>
<td>2</td>
<td>46 (33–59)</td>
<td>Overall: 0.14 (0.150)*</td>
<td></td>
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</tr>
</tbody>
</table>

* The authors did not specify whether this was the superficial or deep FAZ.
variation must be considered and represents a significant challenge when assessing possible pathologic FAZ enlargement in the setting of retinal disease.

Since the FAZ areas vary considerably among healthy individuals, it is all the more important to understand the demographic or ocular factors that may potentially influence this. Many of the earlier studies describing FAZ area have not examined the influence of these factors on FAZ size, while a few have investigated only specific variables such as age, sex, central retinal thickness and volume. Similarly, in a study using standard FA, Tick et al. report a strong correlation between the FAZ size and retinal thickness. This is likely related to the foveal pit morphology, with deeper foveal pits resulting in a wider separation of the superficial retinal layers and hence a larger FAZ. Both of these articles, however, did not describe the effects of axial length or spherical equivalent as potential confounders.

In our study, we examined these relationships and found that spherical equivalent and axial length did not significantly affect FAZ area after accounting for central retinal thickness and sex. In an earlier study on FAZ size using FA, Bresnick et al. report that there is no relationship between spherical equivalent and the circumference or diameter of the FAZ. Similarly, several authors have reported no significant association between FAZ size and axial length. It is possible, however, that the apparent negative correlation of FAZ size with axial length observed on univariate analysis could be due to the lower optical magnification in eyes with greater axial length.

The effect of sex on FAZ size remains uncertain. An article by Yu et al. reports that superficial FAZ is larger among females than males. In contrast, Samar et al. have found no significant differences in FAZ size between the sexes, although the females in that study do have larger FAZ sizes (0.272 vs. 0.258 mm², P = 0.55). Differences in FAZ area between the sexes must be interpreted with caution, since there could be differences in ocular parameters such as central retinal thicknesses and spherical equivalent between the two groups, which may act as potential confounders. However, even after accounting for these differences, we found that sex remained a significant influence on both superficial and deep FAZ size on multivariate analysis.

Since the choroid plays an important role in the normal physiology of the eye, as well as in various ocular diseases, we aimed to examine the potential effects of choroidal thickness on FAZ size. The choroid would appear to be particularly relevant to the FAZ, since the central foveal retina would be primarily nourished by the choroid. To the best of our knowledge, this has not previously been studied. We found that choroidal thickness did not influence the size of the superficial or deep FAZ in eyes without high myopia. In eyes with high myopia, however, the choroidal thickness was a significant factor affecting both the superficial and deep FAZ areas. This may be the result of the underlying pathophysiologic characteristics of high myopia and warrants further investigation in subsequent studies.

In addition to the associations between ocular and demographic factors affecting FAZ area, another interesting finding is the strong correlation in FAZ size between contralateral eyes of participants, with mean differences between eyes of 0.004 and 0.005 mm² for the superficial and deep FAZ, respectively. This is an important observation, since in unilateral eye disease the FAZ area of the eye with ocular disease could potentially be compared with that of the fellow (normal) eye to determine whether it is truly abnormal.

In this study, in addition to assessment of the FAZ area, using standard settings on the OCT-A device, we used a novel approach by manually adjusting the segmentation boundaries to include the full thickness of the retina (Fig. 1). Optical coherence tomography angiography is known to be exquisitely sensitive to errors in segmentation, and by adjusting the boundaries, we were able to address the impact of potential variability in segmentation by obtaining just a single image of the vasculature in the entire retinal thickness. Using this approach, we had a very interesting finding: that the full-thickness retinal slab produces FAZ sizes that are very similar to that of the superficial retinal plexus, with a difference of only 0.0005 mm², and a high degree of correlation. This is a potentially useful approach in future studies to reduce the impact of variations in segmentation.

The strengths of this study included the large number of participants, which is important when performing multiple linear regression analysis. In addition, we examined a wide range of demographic and ocular factors, which may potentially affect FAZ size, and accounted for the possibility of interactions through multivariate analysis. We also included participants with a large range of refractive errors and retinal thicknesses, in order to fully examine the effects of these variables on FAZ size. This is of particular importance among some populations, such as Asians, with an increasing prevalence of high myopia. We found differences in the factors that affected FAZ size among eyes with high myopia compared to normal eyes.

Among the limitations, we had a narrow age range of the participants. However, we feel that this may confer an advantage. Since some studies have suggested that age influences FAZ size by 0.258 mm², P = 0.55), Differences in FAZ area between the sexes must be interpreted with caution, since there could be differences in ocular parameters such as central retinal thicknesses and spherical equivalent between the two groups, which may act as potential confounders. However, even after accounting for these differences, we found that sex remained a significant influence on both superficial and deep FAZ size on multivariate analysis.

Acknowledgments

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References


