Original Research

Variability of Foveal Avascular Zone Measurements Among Filipino Eyes Using Optical Coherence Tomography Angiography

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ABSTRACT

Objective: To determine the foveal avascular zone (FAZ) thickness and other FAZ measurements in eyes of healthy Filipino adults aged 20-49 years.

Methods: This single-center, cross-sectional, observational study evaluated 186 subjects (372 eyes) of Filipino adults 20 to 49 years of age. Using *Angioplex®*, the automated software of the optical coherence tomography angiography (OCTA) machine, the FAZ area, perimeter, circularity, vascular density, and perfusion in the superficial FAZ were recognized. Statistical analysis was done using SPSS version 23. The mean and standard deviation of the values of superficial capillary free zone measurements were calculated.

Results: The mean FAZ area was 0.297 ± 0.112 mm², the mean circularity was 0.667 ± 0.080, and the mean perimeter was 2.316 ± 0.80 mm. These parameters were all larger in the female population (p <0.001, p = 0.043 and p <0.001, respectively). No significant correlation was found between the FAZ area and age and between perimeter and age, but the circularity of the FAZ was inversely correlated with age (p = 0.002). The mean vessel density and vessel perfusion central were 9.767 ± 3.470 mm/mm² and 17.008 ± 6.457 %; both were significantly lower in the female population (p = 0.005 and p = 0.003). The mean central macular thickness (CMT) was 245.895 ± 20.769 μm. CMT was noted to be higher in the male population (p <0.001). The CMT was directly correlated with age (p = 0.024).

Conclusions: In eyes of healthy Filipino adults aged 20-49 years, females exhibited larger FAZ area, higher circularity, and lower CMT, compared to males. Additionally, females displayed lower central vessel density and perfusion. While FAZ area and perimeter remained stable with age, circularity decreased, and CMT increased.

Keywords: Filipino; foveal avascular zone; FAZ; optical coherence tomography angiography; OCTA

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Given the critical role of the foveal avascular zone (FAZ) in high-acuity vision and its association with various vision-impairing pathologies, researchers have actively sought reliable methods to quantify its size and shape. While established techniques like histology, immunohistochemistry, fluorescein angiography (FA), and indocyanine green angiography (ICGA) exist, an accurate and dependable approach for FAZ assessment remains a valuable pursuit. This would enhance the diagnosis and management of numerous retinal vascular disorders known to impact the FAZ.[1,2,3] Despite recent advancements in biomedical engineering and technology, FA remains the *de facto* standard for visualizing retinal microvasculature and the FAZ. However, FA presents limitations, including its invasive nature, time-consuming procedure, and potential adverse effects ranging from nausea to allergic reactions.[4]

The advent of optical coherence tomography angiography (OCTA) provides retina specialists with a dye-free, non-invasive tool for comprehensively evaluating the FAZ.[5] This technology offers the unique ability to assess both the superficial and deep capillary plexuses, allowing for a more detailed analysis of the FAZ compared to traditional methods.[6] Accurate evaluation of the retina's structural and vascular architecture, particularly the superficial capillary plexus (SCP) and deep capillary plexus (DCP), is essential for accurately diagnosing, treating, and prognosticating numerous retinal diseases.[7] Delineating the natural variation in FAZ size and shape in healthy individuals, and their association with demographic and ocular features, is crucial for accurately interpreting the impact of retinal diseases on the FAZ.[8]

Quantitative analysis of the FAZ, in terms of its size and shape, using OCTA potentially outperforms conventional qualitative assessments, in terms of uncovering early-stage macular diseases. While data exist for other populations, no published research has quantified the FAZ in healthy Filipino adult eyes using OCTA. Multiple studies reported larger FAZs in females compared to males,[9-10,13-15] conflicting evidences of correlation between age and FAZ area,[9,11,14] and, in terms of ethnicity, a smaller FAZ area in Caucasians versus Chinese individuals.[12] The lack of Filipino FAZ data made the present study necessary.

This study primarily aimed to define the FAZ in the eyes of healthy Filipino adults aged 20-49 years using the OCTA. Specifically, it sought to (1) quantify the average structural FAZ measurements in this population, and (2) investigate the influence of age, gender, and refractive error on these measurements.

METHODOLOGY

This single-center, cross-sectional, observational study recruited healthcare workers at Fatima University Medical Center, a tertiary private hospital in the Philippines, from February 1 to April 30, 2023. Eligible study participants were current hospital employees aged 20-49 years old with best-corrected visual acuity (BCVA) of 20/20, and refractive error within the –3.00 to +2.00 diopter (D) range, and without any ocular conditions or systemic diseases that could impact the FAZ.

The sample size was calculated based on the estimation of the population mean of FAZ diameter of the superficial capillary plexus. On the assumption that the standard deviation of the FAZ was 119.99, with a maximum allowable error of 30 and a reliability of 95%, the initial sample size was calculated to be 62 eyes.[10] The final sample size required to determine the effects of age and sex on FAZ measurements with 3 categories for age and 2 for sex was 372 eyes.

This study adhered to rigorous national and international ethical guidelines and was approved by the Institutional Ethics Review Board of Fatima University Medical Center. Signed informed consent was obtained from all study participants.

Study participants underwent BCVA determination using an ETDRS chart, tonometry, and slit-lamp examination of the anterior and posterior segments. The tests and examinations were performed by an independent ophthalmology resident, ensuring unbiased data collection.

This study utilized the Zeiss Cirrus 5000 HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA, USA) for OCTA measurements. One of three masked, trained technicians performed the scan on each study participant. The technician performed a 512 × 128 mm macular cube scan followed by a 3 × 3 mm OCTA scan. Only scans with signal strength quality

≥ 8 were included for analysis. An automated software, *Angioplex®*, calculated the FAZ area, perimeter, circularity, vascular density, and perfusion within the superficial FAZ layer. In cases where automatic FAZ identification failed, the FAZ area and intraretinal layers were manually retraced. The investigators also implemented manual measurements of the horizontal and vertical diameters of the FAZ using the instrument's internal calipers for scans that were identified and retraced by the *Angioplex®*. Examination of the macular cube scan confirmed the absence of any significant macular pathologies. Retinal measurements, including macular thickness and ganglion cell layer thickness, were subsequently extracted from the macular cube data. To ensure unbiased evaluation, two skilled readers, who were both vitreo-retina specialists, and blinded to the participants' identities and screening outcomes, conducted a comprehensive analysis of the compiled data. In cases of disagreement, the readers engaged in collaborative discussions to reach a unified interpretation.

Statistical analysis was done using SPSS version 23. Superficial capillary free zone measurements were reported in means and standard deviations. In the univariate analysis, analysis of variance was used to test differences in FAZ parameters among the age groups, while independent *t*-test was used to test differences in FAZ parameters among males and females. In the multivariate analysis, multiple linear regression was utilized. The level of significance was set at $p = 0.05$.

RESULTS

A total of 372 eyes of 186 health workers were included in the study. The mean age of the subjects was 27.35 ± 6.41 years (range: 20-49 years). Of the 186 health workers, 61 (32.8%) were males with a mean age of 28.07 ± 6.35, and 125 (67.2%) were females with a mean age of 27.01 ± 6.43 . The mean spherical equivalent for the whole group was –0.96 ± 1.14 D (range: –3.00 to +1.75 D). The demographic data are shown in Table 1. The overall structural characteristics of the FAZ in all subjects are shown in Table 2.

Table 1. Demographic characteristics of the study group (186 subjects, 372 eyes)

SUBJECTS		*n*	%
AGE GROUP	20 - 29 years	132	71.0
	30 - 39 years	40	21.5
	40 - 49 years	14	7.5
SEX	Male	61	32.8
	Female	125	67.2
EYES		*n*	%
SPHERICAL EQUIVALENT	–3.00 D	58	15.6
	–2.00 to –2.75 D	27	7.3
	–1.00 to –1.75 D	58	15.6
	–0.25 to –0.75 D	131	35.2
	0.00 D	57	15.3
	+0.25 to +0.75 D	34	9.1
	+1.00 to +1.75 D	7	1.9
LATERALITY	Right eye	186	50.0
	Left eye	186	50.0

Table 2. Overall structural characteristics of FAZ

Total Population, *n* = 372 eyes		
	Mean ± SD	Range
FAZ AREA (mm2)	0.297 ± 0.112	0.05 – 0.74
CIRCULARITY	0.667 ± 0.080	0.41 – 0.90
PERIMETER (mm)	2.316 ± 0.458	0.96 – 3.85
HORIZONTAL DIAMETER (μm)	625.040 ± 122.980	208.00 – 973.00
VERTICAL DIAMETER (μm)	614.777 ± 128 089	234.00 – 1006.00
VESSEL DENSITY CENTRAL (mm/mm2)	9.767 ± 3.470	2.30 – 22.10
VESSEL DENSITY INNER (mm/mm2)	20.389 ± 2.585	2.70 – 24.30
VESSEL DENSITY FULL (mm/mm2)	19.239 ± 2.357	8 00 – 23 10
VESSEL PERFUSION CENTRAL (%)	17.008 ± 6.457	3.80 – 45.00
VESSEL PERFUSION INNER (%)	36.798 ± 4.593	3.16 – 51.30
VESSEL PERFUSION FULL (%)	34.639 ± 4.239	16.20 – 47.20
CENTRAL MACULAR THICKNESS (μm)	245.895 ± 20.769	200.00 – 298.00
AVERAGE GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (μm)	84.610 ± 5.274	71.00 – 99.00
MINIMUM GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (μm)	82.056 ± 5.292	70 00 – 97.00

Table 3 shows the structural characteristics of FAZ of male and female eyes. Females had significantly larger FAZ area than males, 0.317 ± 0.114 vs. 0.255 ± 0.096 mm², respectively (p <0.001). Females also had higher FAZ circularity (0.673 ± 0.079 vs. 0.655 ± 0.082, $p = 0.043$), perimeter (2.389 ± 0.458 mm vs. 2.168 ± 0.422 mm, p <0.001), horizontal diameter (646.216 ± 116.585

μm vs. 581.648 ± 124.807 μm, p <0.001), and vertical diameter (636.184 ± 125.840 μm vs. 570.910 ± 121.782 μm , p <0.001) compared to males. Among males, the vessel density of the central area of the FAZ (males 10.540 ± 3.958 vs. females 9.389 ± 3.146 mm/mm², $p = 0.005$), and vessel perfusion of the central area (18.575 ± 7.740 vs. 16.243 ± 5.587 mm/mm², $p = 0.003$) were significantly higher than in females. Vessel densities of the inner and full area of the FAZ, and vessel perfusions of the inner and full area of the FAZ, were similar in both sexes (p = 0.383, 0.564, 0.704, and 0.949). The central macular thickness (CMT) (males 256.172 ± 21.946 vs. females 240.880 ± 18.212 μm, p <0.001) as well as the average ganglion cell layer + inner plexiform layer (GCL+IPL) thickness (85.648 ± 6.005 vs. 84.104 ± 6.8 μm, $p = 0.014$) and minimum ganglion cell layer + inner plexiform layer (GCL+IPL) thickness (83.475 ± 6.011 vs. 81.364 ± 4.764 μm, p = 0.001) were all significantly higher in males.

Table 3. Structural characteristics of FAZ by sex

	SEX				
	Male, *n* = 122 eyes		Female, *n* = 250 eyes		*p*-value
	Mean ± SD	Range	Mean ± SD	Range	
FAZ AREA (mm²)	0.255 ± 0.096	0.05 – 0.45	0.317 ± 0.114	0.07 – 0.74	<0.001*
CIRCULARITY	0.655 ± 0.082	0.43 – 0.81	0.673 ± 0.079	0.41 – 0.90	0.043*
PERIMETER (mm)	2.168 ± 0.422	0.96 – 3.13	2.389 ± 0.458	1.17 – 3.85	<0.001*
HORIZONTAL DIAMETER (μm)	581.648 ± 124.807	208.00 – 822.00	646.216 ± 116.585	308.00 – 973.00	<0.001*
VERTICAL DIAMETER (μm)	570.910 ± 121.782	300.00 – 821.00	636.184 ± 125.840	234.00 – 1006.00	<0.001*
VESSEL DENSITY CENTRAL (mm/mm²)	10.540 ± 3.958	2.30 – 21.40	9.389 ± 3.146	2.60 – 22.10	0.005*
VESSEL DENSITY INNER (mm/mm²)	20.211 ± 2.861	8.40 – 23.80	20.475 ± 2.440	2.70 – 24.30	0.383
VESSEL DENSITY FULL (mm/mm²)	19.128 ± 2.798	8.00 – 23.10	19.294 ± 2.113	11.60 – 23.10	0.564
VESSEL PERFUSION CENTRAL (%)	18.575 ± 7.740	3.90 – 45.00	16.243 ± 5.587	3.80 – 39.50	0.003*
VESSEL PERFUSION INNER (%)	36.668 ± 4.769	17.10 – 44.60	36.861 ± 4.513	3.16 – 51.30	0.704
VESSEL PERFUSION FULL (%)	34.616 ± 5.115	16.20 – 47.20	34.650 ± 3.749	19.90 - 40.80	0.949
CENTRAL MACULAR THICKNESS (μm)	256.172 ± 21.946	215.00 – 298.00	240.880 ± 18.212	200.00 – 287.00	<0.001*
AVERAGE GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (μm)	85.648 ± 6.005	71.00 – 99.00	84.104 ± 6.8	72.00 – 98.00	0.014*
MINIMUM GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (μm)	83.475 ± 6.011	70.00 – 97.00	81.364 ± 4.764	70.00 – 97.00	0.001*

*Difference is significant at $p \leq 0.05$

Table 4 shows the structural characteristics of FAZ by age. The circularity of the FAZ decreased with age (from 0.677 ± 0.079 to 0.643 ± 0.084, p = 0.002). However, there was no statistical significance in the FAZ area, perimeter, vessel density (inner, central, full), vessel perfusion (inner, central, full), and the average and minimum GCL+IPL thickness among the age groups. The CMT increased with age (from 244.265 ± 19.810 μm to 253.964 ± 18.602 μm, $p = 0.024$).

Table 4. Structural characteristics of FAZ by age

	Age Group	*n*	Mean	Standard Deviation	Range	*p*-value
FAZ AREA (mm²)	20 - 29	264	0.298	0.108	0.05 – 0.74	0.857
	30 - 39	80	0.296	0.127	0.06 – 0.66	
	40 - 49	28	0.286	0.111	0.09 – 0.70	
CIRCULARITY	20 - 29	264	0.677	0.079	0.44 – 0.90	0.002*
	30 - 39	80	0.645	0.080	0.41 – 0.82	
	40 - 49	28	0.643	0.084	0.43 – 0.77	
PERIMETER (mm)	20 - 29	264	2.316	0.447	0.96 – 3.85	0.583
	30 - 39	80	2.345	0.509	1.14 – 3.73	
	40 - 49	28	2.241	0.412	1.25 – 2.84	
HORIZONTAL DIAMETER (μm)	20 - 29	264	625.633	118.248	208 – 973	0.944
	30 - 39	80	625.738	137.310	251 – 957	
	40 - 49	28	617.464	128.008	294 – 786	
VERTICAL DIAMETER (μm)	20 - 29	264	618.091	125.132	234 – 942	0.475
	30 - 39	80	613.538	136.408	300 – 1006	
	40 - 49	28	587.071	132.555	331 – 985	
VESSEL DENSITY CENTRAL (mm/mm²)	20 - 29	264	9.614	3.149	2.30 – 22.10	0.395
	30 - 39	80	9.985	4.195	3.90 – 21.40	
	40 - 49	28	10.585	4.040	4.20 – 21.40	
VESSEL DENSITY INNER (mm/mm²)	20 - 29	264	20.400	2.635	2.70 – 24.30	0.373
	30 - 39	80	20.155	2.473	12.30 – 23.80	
	40 - 49	28	20.950	2.400	15.50 – 23.70	
VESSEL DENSITY FULL (mm/mm²)	20 - 29	264	19.252	2.334	8.00 – 23.10	0.346
	30 - 39	80	19.014	2.413	11.60 – 22.70	
	40 - 49	28	19.764	2.416	14.20 – 22.50	
VESSEL PERFUSION CENTRAL (%)	20 - 29	264	16.591	5.525	3.80 – 39.50	0.395
	30 - 39	80	17.834	8.543	6.70 – 45.00	
	40 - 49	28	18.579	7.470	14.20 – 22.50	
VESSEL PERFUSION INNER (%)	20 - 29	264	36.813	4.217	17.10 – 51.30	0.971
	30 - 39	80	36.860	4.404	22.90 – 44.60	
	40 - 49	28	36.484	7.728	3.16 – 42.60	
VESSEL PERFUSION FULL (%)	20 - 29	264	34.530	4.115	16.20 – 40.80	0.609
	30 - 39	80	34.753	4.623	21.40 – 47.20	
	40 - 49	28	35.339	4.336	25.60 – 40.40	
CENTRAL MACULAR THICKNESS (μm)	20 - 29	264	244.265	19.810	200 – 296	0.024*
	30 - 39	80	248.450	23.716	204 – 289	
	40 - 49	28	253.964	18.602	222 – 298	
AVERAGE GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (μm)	20 - 29	264	84.909	5.182	73 – 99	0.256
	30 - 39	80	84.125	4.697	71 – 91	
	40 - 49	28	83.179	7.237	72 – 97	
MINIMUM GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (μm)	20 - 29	264	82.345	5.153	70 – 97	0.164
	30 - 39	80	81.925	4.818	71 – 91	
	40 - 49	28	79.714	7.190	70 – 95	

*Difference is significant at $p \leq 0.0$

Table 5 shows the structural characteristics of the FAZ by spherical equivalent (SE). There was a significant difference in the FAZ area ($p = 0.008$) across the different SE ranges, with the highest among the –0.25 to –0.75 D group (0.320 ± 0.124 mm²) and the lowest among –2.00 to –2.75 D (0.246 ± 0.081 mm²). Circularity was also significantly different among the groups ($p = 0.001$) with the highest among the 0.00 D group (0.690 ± 0.086) and the lowest among +1.00 to +1.75 D (0.563 ± 0.049). However, there was no difference in perimeter among the groups. Significant differences among the SE groups were also seen in the vessel density of the inner and full area of the FAZ and vessel perfusion of the inner and full area of the FAZ. There was a significant difference in the CMT across the different SE ranges ($p < 0.001$), with the highest among –2.00 to –2.75 D (257.148 ± 16.212 μm) and the lowest among +0.25 to +0.75 D (238.853 ± 20.920 μm). There was also a significant difference in the average GCL+IPL thickness ($p < 0.001$) with the highest among +1.00 to +1.75 D (87.429 ± 4.860 μm) and the lowest among +0.25 to +0.75 D (83.177 ± 4.738 μm), and the minimum GCL+IPL thickness ($p < 0.001$), with the highest among +1.00 to +1.75 D (83.571 ± 4.756 μm) and the lowest among +0.25 to +0.75 D (79.971 ± 4.681 μm).

Table 5. Structural characteristics of FAZ by spherical equivalent

	Spherical equivalent	*n*	Mean	Standard Deviation	Range	*p*-value
FAZ AREA (mm²)	–3.00 D	58	0.275	0.096	0.06 – 0.52	0.008*
	–2.00 to –2.75 D	27	0.246	0.081	0.1 – 0.43	
	–1.00 to –1.75 D	58	0.274	0.097	0.11 – 0.6	
	–0.25 to –0.75 D	131	0.320	0.124	0.07 – 0.74	
	0.00 D	57	0.312	0.106	0.1 – 0.59	
	+0.25 to +0.75D	34	0.304	0.130	0.05 – 0.56	
	+1.00 to +1.75 D	7	0.277	0.070	0.18 – 0.37	
CIRCULARITY	–3.00 D	58	0.656	0.072	0.41 – 0.82	0.001*
	–2.00 to –2.75 D	27	0.633	0.080	0.47 – 0.77	
	–1.00 to –1.75 D	58	0.672	0.081	0.48 – 0.90	
	–0.25 to –0.75 D	131	0.670	0.076	0.45 – 0.82	
	0.00 D	57	0.690	0.086	0.43 – 0.81	
	+0.25 to +0.75D	34	0.678	0.082	0.49 – 0.81	
	+1.00 to +1.75 D	7	0.563	0.049	0.52 – 0.65	
PERIMETER (mm)	–3.00 D	58	2.258	0.422	1.14 – 3.13	0.254
	–2.00 to –2.75 D	27	2.184	0.378	1.6 – 2.94	
	–1.00 to –1.75 D	58	2.256	0.446	1.56 – 3.85	
	–0.25 to –0.75 D	131	2.378	0.499	1.17 – 3.77	
	0.00 D	57	2.353	0.399	1.66 – 3.54	
	+0.25 to +0.75D	34	2.292	0.529	0.96 – 3.15	
	+1.00 to +1.75 D	7	2.467	0.248	2.1 – 2.69	
HORIZONTAL DIAMETER (µm)	–3.00 D	58	608.000	122.003	251 – 864	0.094
	–2.00 to –2.75 D	27	573.667	87.033	444 – 765	
	–1.00 to –1.75 D	58	611.345	105.950	395 – 852	
	–0.25 to –0.75 D	131	638.061	127.017	308 – 957	
	0.00 D	57	649.877	118.649	357 – 973	
	+0.25 to +0.75D	34	620.500	159.275	208 – 900	
	+1.00 to +1.75 D	7	654.000	81.699	566 – 750	
VERTICAL DIAMETER (µm)	–3.00 D	58	594.500	114.676	314 – 864	0.073
	–2.00 to –2.75 D	27	558.000	122.800	300 – 765	
	–1.00 to –1.75 D	58	600.328	103.259	393 – 838	
	–0.25 to –0.75 D	131	632.641	140.835	234 – 1006	
	0.00 D	57	634.983	110.939	397 – 878	
	+0.25 to +0.75D	34	615.765	156.790	300 – 835	
	+1.00 to +1.75 D	7	617.857	108.333	442 – 728	
VESSEL DENSITY CENTRAL (mm/mm²)	–3.00 D	58	8.886	3.675	2.3 – 21.4	0.142
	–2.00 to –2.75 D	27	11.315	4.262	4.7 – 21.4	
	–1.00 to –1.75 D	58	9.7931	2.775	3.8 – 18.8	
	–0.25 to –0.75 D	131	10.017	3.412	2.8 – 22.1	
	0.00 D	57	9.295	3.130	2.6 – 17.1	
	+0.25 to +0.75D	34	9.997	4.156	4.3 – 19.3	
	+1.00 to +1.75 D	7	8.914	1.694	5.8 – 11.3	
VESSEL DENSITY INNER (mm/mm²)	–3.00 D	58	18.398	3.859	2.7 – 23	0.001*
	–2.00 to –2.75 D	27	20.130	1.783	16.7 – 22.5	
	–1.00 to –1.75 D	58	20.462	2.089	12.8 – 23.9	
	–0.25 to –0.75 D	131	20.945	1.959	14.7 – 24	
	0.00 D	57	21.079	2.104	15 – 23.7	
	+0.25 to +0.75D	34	20.503	2.578	12.3 – 24.3	
	+1.00 to +1.75 D	7	20.686	2.277	16.3 – 23	
VESSEL DENSITY FULL (mm/mm²)	–3.00 D	58	17.605	3.168	8 – 22.1	0.002*
	–2.00 to –2.75 D	27	19.137	1.939	15.6 – 22.1	
	–1.00 to –1.75 D	58	19.297	1.996	12.1 – 22.8	
	–0.25 to –0.75 D	131	19.719	1.899	14 – 22.7	
	0.00 D	57	19.746	2.100	14 – 22.5	
	+0.25 to +0.75D	34	19.294	2.583	11.6 – 23.1	
	+1.00 to +1.75 D	7	19.329	2.182	15.1 – 21.4	
VESSEL PERFUSION CENTRAL (%)	–3.00 D	58	15.369	6.409	3.9 – 36.1	0.091
	–2.00 to –2.75 D	27	19.730	7.559	8.8 – 37.6	
	–1.00 to –1.75 D	58	17.259	5.881	6.5 – 45	
	–0.25 to –0.75 D	131	17.482	6.569	4.7 – 44.4	
	0.00 D	57	16.118	5.667	3.8 – 30.9	
	+0.25 to +0.75D	34	17.209	7.288	6.8 – 34.1	
	+1.00 to +1.75 D	7	15.400	3.072	9.9 – 20	
	–3.00 D	58	34.469	5.319	17.1 – 41.4	0.018*
	–2.00 to –2.75 D	27	36.793	3.167	30.1 – 41.5	

VESSEL PERFUSION INNER (%)	–1.00 to –1.75 D	58	37.102	3.722	24.2 – 44.6	
	–0.25 to –0.75 D	131	37.648	3.848	20.8 – 51.3	
	0.00 D	57	37.182	5.955	3.16 – 42.6	
	+0.25 to +0.75D	34	36.535	4.410	22.9 – 42.3	
	+1.00 to +1.75 D	7	35.843	5.451	28.2 – 41.5	
VESSEL PERFUSION FULL (%)	–3.00 D	58	32.143	5.526	16.2 – 39	0.016*
	–2.00 to –2.75 D	27	34.856	3.439	28.1 – 41	
	–1.00 to –1.75 D	58	34.786	4.006	22.8 – 47.2	
	–0.25 to –0.75 D	131	35.366	3.657	19.9 – 46.8	
	0.00 D	57	35.398	3.700	25.8 – 40.4	
	+0.25 to +0.75D	34	34.371	4.378	21.4 – 40.8	
	+1.00 to +1.75 D	7	34.757	4.050	27 – 38.4	
CENTRAL MACULAR THICKNESS (µm)	–3.00 D	58	255.224	20.021	215 – 298	<0.001*
	–2.00 to –2.75 D	27	257.148	16.212	219 – 289	
	–1.00 to –1.75 D	58	247.155	19.690	216 – 287	
	–0.25 to –0.75 D	131	242.527	19.165	200 – 291	
	0.00 D	57	241.912	23.241	202 – 296	
	+0.25 to +0.75D	34	238.853	20.920	204 – 273	
	+1.00 to +1.75 D	7	244.429	22.963	222 – 279	
AVERAGE GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (µm)	–3.00 D	58	83.931	4.848	74 – 93	<0.001*
	–2.00 to –2.75 D	27	83.741	5.668	75 – 98	
	–1.00 to –1.75 D	58	83.190	5.596	71 – 99	
	–0.25 to –0.75 D	131	86.428	5.078	74 – 98	
	0.00 D	57	83.491	4.874	72 – 97	
	+0.25 to +0.75D	34	83.177	4.738	74 – 90	
	+1.00 to +1.75 D	7	87.429	4.860	80 – 92	
MINIMUM GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (µm)	–3.00 D	58	81.931	5.157	72 – 91	<0.001*
	–2.00 to –2.75 D	27	81.630	5.100	74 – 97	
	–1.00 to –1.75 D	58	80.621	5.357	70 – 97	
	–0.25 to –0.75 D	131	83.786	5.209	72 – 96	
	0.00 D	57	80.930	5.039	70 – 95	
	+0.25 to +0.75D	34	79.971	4.681	72 – 87	
	+1.00 to +1.75 D	7	83.571	4.756	76 – 88	

*Difference is significant at $p \leq 0.05$

Table 6 shows the results of multivariate analysis using multiple linear regression. Compared to males, females had significantly larger FAZ area (0.061 mm², $p = 0.001$), perimeter (0.219 mm, $p = 0.001$), horizontal diameter (64.230 µm, $p = 0.001$), and vertical diameter (63.613 µm, $p = 0.001$). However, the vessel density (–1.103%, $p = 0.013$) and vessel perfusion (–2.207%, $p = 0.007$) of the central area of the FAZ were significantly lower in females. The CMT (–14.564 µm, $p = 0.001$) as well as the average GCL+IPL thickness (–1.698 µm, $p = 0.008$) and minimum GCL+IPL thickness (–2.282 µm, $p = 0.002$) were also significantly lower in females. The circularity (–0.022, $p = 0.002$) of the FAZ decreased with age, in contrast to CMT which increased with age (4.317 µm, $p = 0.002$). For every +1.00 D increase in SE, there were corresponding increases in the following FAZ parameters: FAZ area by 0.016 mm² ($p = 0.001$), circularity by 0.007 ($p = 0.045$), perimeter by 0.044 mm ($p = 0.030$), horizontal diameter by 14.720 µm ($p = 0.015$), vertical diameter by 16.051 µm ($p = 0.002$), inner vessel density by 0.674 mm/mm² ($p = 0.001$), full vessel density by 0.529 mm/mm² ($p = 0.001$), inner vessel perfusion by 0.649% ($p = 0.004$), and full vessel perfusion by 0.708% ($p = 0.003$). However, there was a corresponding decrease in CMT by –5.281 µm for every +1.00 D increase in SE ($p = 0.001$).

DISCUSSION

Variations in the FAZ region and retinal vasculature are associated with diverse pathologies, prompting interest in OCTA as a non-invasive diagnostic tool with significant potential. However, while studies have explored FAZ area and vascular characteristics in various ethnicities, there was a lack of published data from a healthy Filipino adult population.

Table 6. Multivariate analysis of FAZ parameters

	Sex		Age Group		Spherical equivalent	
FAZ Parameters	B coefficient (95% CI)	*p*-value	B coefficient (95% CI)	*p*-value	B coefficient (95% CI)	*p*-value
FAZ AREA (mm^2)	0.061 (0.039, 0.082)	0.001*	–0.003 (–0.019, 0.015)	0.794	0.016 (0.006, 0.026)	0.001*
CIRCULARITY	0.015 (–0.003, 0.033)	0.105	–0.022 (–0.038, –0.007)	0.002*	0.007 (0.00,0.014)	0.045*
PERIMETER (mm)	0.219 (0.124, 0.316)	0.001*	–0.003 (–0.080, 0.074)	0.937	0.044 (0.006, 0.083)	0.030*
HORIZONTAL DIAMETER (μm)	64.230 (34.887, 91.028)	0.001*	0.127 (–20.839, 21.062)	0.991	14.720 (3.611, 25.805)	0.015*
VERTICAL DIAMETER (μm)	63.613 (38.589, 90.532)	0.001*	–9.153 (–29.822, 12.203)	0.382	16.051 (4.156, 28.793)	0.002*
VESSEL DENSITY CENTRAL (mm/mm^2)	–1.103 (–1.921, –0.294)	0.013*	0.353 (–0.240, 0.944)	0.240	0.026 (–0.306, 0.340)	0.872
VESSEL DENSITY INNER (mm/mm^2)	0.247 (–0.275, 0.779)	0.365	–0.002 (–0.440, 0.390)	0.996	0.674 (0.410, 0.949)	0.001*
VESSEL DENSITY FULL (mm/mm^2)	0.154 (–0.370, 0.679)	0.571	0.005 (–0412, 0.422)	0.974	0.529 (0.267, 0.817)	0.001*
VESSEL PERFUSION CENTRAL (%)	–2.207 (–3.758, –0.707)	0.007*	0.904 (–0.166, 2.031)	0.108	0.009 (–0.595, 0.636)	0.979
VESSEL PERFUSION INNER (%)	0.152 (–0.836, 1.27)	0.761	–0.184 (–1.413, 0.733)	0.736	0.649 (0.222, 1.072)	0.004*
VESSEL PERFUSION FULL (%)	0.048 (–0.933, 0.959)	0.945	0.227 (–0.402, 0.871)	0.542	0.708 (0.293, 1.134)	0.003*
CENTRAL MACULAR THICKNESS (μm)	–14.564 (–18.551, –10.485)	0.001*	4.317 (1.155, 6.936)	0.002*	–5.281 (–6.910, –3.481)	0.001*
AVERAGE GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (μm)	–1.698 (–2.888, -0.589)	0.008*	–1.040 (–2.096, 0.109)	0.054	0.412 (–0.054, 0.851)	0.084
MINIMUM GANGLION CELL LAYER + INNER PLEXIFORM LAYER THICKNESS (μm)	–2.282 (–3.447, –1.174)	0.002*	–1.201 (–2.184, –0.180)	0.020*	0.138 (–0.306, 0.572)	0.544

For each parameter, 1000 bootstrap samples were generated.
For gender groups, positive B coefficient indicates higher values in females. For age groups, positive B coefficient indicates higher values in older age groups. For spherical equivalent groups, positive B coefficient indicates increasing values with more positive spherical equivalent.
*Difference is significant at $p \leq 0.05$

Previous studies reported FAZ area, perimeter, and circularity values for the superficial capillary plexus in Asian populations. These values varied slightly depending on the machine used. The current study found similar FAZ measurements compared to these prior studies.[11,19-20] Findings in the study led the researchers to conclude that the FAZ's perimeter and area both have a correlation with sex. Similar to earlier studies in other ethnic groups, the female group in the present study sample had higher mean FAZ area and perimeter values than the male group.[9,11-16]

The study by Verma *et al.* showed that the FAZ area and perimeter increased significantly with age, while the FAZ circularity decreased significantly with age.[17] Another study found that the FAZ area and perimeter increased with age until 40 years, and then decreased in older age groups, while the FAZ circularity showed no significant correlation with age.[18] The current study did not find any significant correlation between either FAZ area or perimeter with age, but FAZ circularity did decrease with age (Table 4). All these studies suggest that age may affect the size and shape of the FAZ, but the results may vary depending on the OCTA device, measurement method, and population characteristics. The changes in the FAZ parameters with age may reflect the physiological or pathological alterations in the retinal microvasculature and macular structure. In this study, the mean vessel density and vessel perfusion (central, inner, and full) were lower compared to those in a study done among the Irish population.[15] The current study also showed that women's central vessel density and perfusion were significantly lower than those of men. However, there were conflicting results in the literature regarding vessel density and gender. Wang *et al.* found that the central vessel density and perfusion of men were lower than those of women,[21] whereas Yilmaz *et al.* did not find any significant link between either central vessel density or perfusion with gender.[22]

This study showed that CMT was lower in women than in men, which was consistent with previously published data.[23-24] Samara *et al.* speculated that while CMT linked adversely with FAZ area, a finding that has been reported elsewhere, a thicker retina may have a smaller FAZ because of increased metabolic demands.[25-26] These conclusions were supported by the current investigation, which found that males, who had higher CMT than females, also had statistically higher central vascular density and perfusion, and smaller FAZ area (Table 3). This shows that a smaller avascular zone is necessary for a higher retinal thickness since a thicker retina needs more blood vessels and perfusion. The current study found that the CMT increased with aging, while an earlier study showed a general trend of central macular thinning with aging.[27] Zhou *et al.* reported that the FAZ area was significantly smaller in emmetropic eyes than in myopic or hyperopic eyes, and it was positively correlated with the spherical equivalent.[23] Another study found that the spherical equivalent was significantly correlated with the area and perimeter of the superficial FAZ, but not with the acircularity and circularity indexes.[28] These studies suggested that refractive error may affect the size of the FAZ, but not necessarily its shape.

This pioneering study examined FAZ characteristics in the eyes of healthy Filipino adults aged 20-49 years. Females exhibited larger FAZ area, higher circularity, and thinner CMT compared to males. In addition, females displayed lower central vessel density and perfusion. While FAZ area and perimeter remained stable with age, circularity decreased, and CMT increased. These findings highlight population-specific FAZ variations, emphasizing the importance of ethnicity-tailored interpretations of OCTA data in health and disease. The study acknowledges limitations such as the following: potential recall bias; results not generalizable (the participants were employed individuals who thus belonged only to working age groups and may not fully represent the entire Filipino population); the study participants were deemed "healthy" based only on health status interview, without vetting by an internist; and the study only considered refractive errors in their spherical equivalent forms. Intraocular pressure of eyes, although measured, was not utilized in this study. Interobserver agreement among readers was not measured. Nevertheless, considering known FAZ variations across ethnicities, this research provides valuable data for Filipino eyes and highlights the importance of using consistent measurement methods across different groups in future research.

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