Original Article

Macular and Peripapillary Vascular Densities in Non-Glaucomatous Eyes of Patients with Unilateral Glaucoma

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Abstract

Objectives: Our purpose was to investigate vascular alterations in the non-glaucomatous eyes of patients with unilateral primary open angle glaucoma using optical coherence tomography angiography and to evaluate the role of vascular damage in glaucoma pathogenesis.

Materials and Methods: This cross-sectional study included 60 eyes of 30 patients with unilateral glaucoma (63.4 ± 8.8 years) and 30 eyes of 30 healthy subjects (65.6 ± 9.1 years). Three groups were formed: group A, affected eyes of unilateral glaucoma patients; Group B, non-glaucomatous eyes of unilateral glaucoma patients; and group C, healthy controls.

Results: When group A was compared with groups B and C, significant differences were detected in rim area, cup volume, mean cup/disc ratio, and retinal nerve fiber layer thickness parameters ($p<0.001$ for all). No significant difference was detected between groups B and C ($p>0.05$ for all). In peripapillary and macular vessel density (VD) comparisons, all parameters except intradisc VD were found to be lower in group A ($p<0.0167$ for all). No statistically significant difference was detected between groups B and C ($p>0.05$ for all).

Conclusion: The VD values in eyes with glaucoma were found to be lower than in the other two groups. However, no difference was observed between the non-glaucomatous eyes of glaucoma patients and those of healthy individuals. Thus, the results did not support our hypothesis that VD alterations would be observed in the fellow eyes of patients with unilateral glaucoma if the vascular pathway were responsible in the pathogenesis of glaucoma.

Keywords: Primary open-angle glaucoma, optical coherence tomography angiography, vascular density

Introduction

In the pathogenesis of glaucoma, it is thought that damage occurs through mechanical, immunological, and vascular pathways.[1,2,3] The vascular pathway theory has become very popular in recent years.[4,5] Vascular dysfunction in the optic nerve head (ONH) and peripapillary retina is believed to be important in the pathogenesis of primary open-angle glaucoma (POAG).[6,7]

Optical coherence tomography angiography (OCTA) is a non-invasive angiography device that does not require a fluorescent substance.[8] The use of OCTA has become common in both the diagnosis and follow-up of glaucoma in recent years.[9]

Our hypothesis was that detecting vascular insufficiency in the peripapillary or macular area in the unaffected (and presumed intact) eyes of patients with unilateral glaucoma would support the vascular pathway theory of glaucoma pathogenesis. Therefore, in this study we investigated vascular changes in the unaffected eyes of patients with unilateral POAG using OCTA. The relationships between vessel density (VD) values and both structural and functional tests were also evaluated.

Materials and Methods

This cross-sectional study was conducted in Başkent University Hospital by analyzing the information of patients who presented between January 2018 and April 2019. The ethics committee of our university approved the project (no. KA19/59), and the research was carried out in accordance with the principles of the Helsinki Declaration. Written informed consent to participate in this research was obtained from all subjects.

The study included 60 eyes of 30 patients with unilateral POAG and 30 eyes of 30 healthy individuals. Best corrected visual acuity, spherical equivalent (SE), intraocular pressure

(IOP), and biomicroscopic anterior segment, dilated fundus, and gonioscopic examination findings were recorded. Peripapillary and macular OCT and OCTA were performed.

Patients who had undergone surgery except uncomplicated cataract surgery; had cataracts, vitreous opacity, or corneal cloudiness; had an SE greater than +/-6 diopters (D); had a history of any retinal pathology that may affect the accuracy of measurements; or had exfoliation syndrome and other causes of secondary open-angle glaucoma were excluded. As pseudoexfoliation glaucoma is generally asymmetric, all patients were examined by slit-lamp biomicroscopy after pupil dilation to avoid any misdiagnosis. All included patients had high IOP before treatment; normotensive patients were excluded. Subjects who had systemic disorders that could interfere with OCT and OCTA results were also excluded.

The inclusion criteria for the POAG group were as follows: an open angle in gonioscopy, glaucomatous optic nerve damage in both clinical examination and OCT, and a glaucomatous visual field (VF) defect confirmed on two consecutive reliable tests (fixation loss rate ≤20%, false-positive and false-negative error rates ≤25%). Glaucomatous VF defect was defined as a VF change fulfilling two or more of the following criteria: 1) outside the normal limits on the Glaucoma Hemifield Test, 2) three abnormal points with a probability of being normal of $p<5\%$ and one with $p<1\%$ by pattern deviation, or 3) a pattern standard deviation (PSD) of $p<5\%$. In addition, the unaffected contralateral eye had to have an IOP <21 mmHg, open angle on gonioscopy, normal-appearing optic disc, and normal VF. The OCT disc, retinal nerve fiber layer thickness (RNFLT) and ganglion cell analysis (GCA) findings of these unaffected eyes were compatible with the patients' ages. The age-matched control group also had an open angle on gonioscopy, IOP <21 mmHg, normal-appearing optic disc, and normal OCT disc, RNFLT, GCA, and VF. The affected eyes of unilateral glaucoma patients were defined as group A, their unaffected eyes as group B, and the healthy control group eyes as group C.

OCTA images were obtained using the RTVue XR Avanti (Optovue; version 2017.1.0.151, Fremont, CA, USA) device, which can scan 70,000 A-mode images per second using 840 nm wavelength light. Retinal vascular structures in the scanned area were segmented automatically by the AngioVue software. Patients with signal strength above 6/10 were included.

Disc OCTA measurements were performed using 2 mm and 4 mm diameter rings based on the disc center. A 4.5x4.5 mm area comprised the whole image area. The area within the 2 mm ring is defined as the intrapapillary region and the area between the 2 mm and 4 mm rings as the peripapillary area. For the determination of the radial peripapillary capillary (RPC) network, the software automatically divides the measurement area into four layers. RPC measurements are determined by the density measurements of the region between the internal limiting membrane (ILM) and the lower limit of the retinal nerve fiber layer (RNFL). Capillary densities were used to evaluate the vascular network of the RNFL.

To evaluate the superficial plexus responsible for supplying the ganglion cell layer in a 6x6 mm area in macular OCTA measurements, a layer with an upper limit of the ILM and lower limit 10 μm below the inner plexiform layer was automatically created. Anatomical structures were defined by three concentric rings centered on the fovea. The innermost 1 mm diameter circle represents the fovea, the annulus between the middle 3 mm diameter ring and the innermost 1 mm ring represents the parafovea, and the annulus between the outermost 6 mm diameter ring and the middle 3 mm diameter ring represents the perifovea. A 6x6 mm area comprises the whole image area.

Optic nerve cup-to-disc ratio, rim area, and disc area values, RNFLT values, and GCA measurements consisting of minimum and mean ganglion cell layer and inner plexiform layer (GCL + IPL) thickness values were obtained automatically by a Cirrus HD spectral domain OCT device (Carl Zeiss Meditec, Dublin, CA, USA). Patients with a signal strength ≥6/10 were included.

Patients who had a 24-2 visual interactive measurement (24-2 Swedish interactive thresholding algorithm) with a Humphrey automated VF device (Humphrey Field Analyzer II 750) were included. Mean deviation (MD) and PSD values were recorded.

IOP measurements were made by two glaucoma specialists (S.G.G. and Ü.E.) between 8:30 and 10:30 a.m. with a Goldmann applanation tonometer mounted on a slit lamp (Takagi slit lamp microscope SM-70N, Takagi Inc., Manchester, UK) with fluorescein under topical anesthesia.

Statistical Analysis

IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY) was used for the analysis. Descriptive statistics were used to summarize the data. Analytical evaluations were made to compare the groups. In the hypothesis tests, Pearson chi-square test was used to compare qualitative variables, Mann-Whitney U test was used to compare continuous quantitative variables between independent groups, and the Kruskal-Wallis analysis of variance (H test) was used to compare continuous quantitative variables among more than two groups. For variables that had significant differences between groups, a Bonferroni-adjusted Mann-Whitney U test was performed with adjusted alpha value taken as 0.0167. A Spearman's rank correlation test was used to investigate the correlation between VD and structural and VF parameters. The data were checked for normal distribution by Kolmogorov-Smirnov test. $P<0.05$ was considered significant.

Results

Both eyes of 30 patients with unilateral POAG were included. Demographic and clinical features are given in Table 1. The groups were similar in age, gender, lens status, visual acuity, IOP, and SE $(p>0.05)$. In group A, 10 patients followed a drug regimen with one active substance, 11 patients with two active substances, 6 patients with three active substances, and 3 patients with four active substances. All patients' IOP values were below 21 mmHg with treatment.

The mean MD and PSD values in group A were -7.64±6.33 decibels (dB) and 6.17±3.95 dB, respectively. These values were significantly different than those in groups B and C (p<0.001 for all) (Table 1). Groups B and C had similar values for both parameters (p=0.99 and p=0.98, respectively).

The values obtained by OCT are shown in Table 2. Except for disc area, all optic disc parameters, RNFLT, and mean and minimum GCL + IPL thickness values differed significantly in group A compared to both group B and group C (p<0.001 for all values except disc area). No significant difference was found between groups B and C (p>0.05).

Peripapillary and macular VD measurements of the groups are presented in Table 3. All parameters except inside disc vessel density (IDVD) were found to be significantly higher in groups B and C than in group A (p<0.0167 for all), but there was no statistically significant difference between groups B and C (p>0.05).

Correlations between OCT and VD values are examined in Table 4. Mean RNFLT correlated with peripapillary VD (PPVD) values in all three groups, while mean whole image PPVD (WI-PPVD) measurements showed significant correlation with RNFLT in groups A and B. In all groups, both mean and minimum GCL + IPL thickness correlated with PPVD and WI-PPVD values.

Whole image macular VD (WI-MVD) values showed significant correlation with mean RNFLT and mean GCL + IPL thickness values only in group A (p=0.02, r=0.42 and p=0.007, r=0.48, respectively). Minimum GCL + IPL thickness and WI-MVD values were correlated in groups A and B (p=0.04, r=0.37 and p=0.03, r=0.38, respectively) (Table 4).

Table 5 shows correlations between VF values and mean RNFLT, mean GCL + IPL thickness, WI-PPVD, PPVD, WI-MVD, and parafoveal VD (PFVD) values in groups A and B. In group A, MD values were correlated with all parameters (p<0.05) except mean RNFLT. Similarly, PSD negatively correlated with all parameters in group A (p<0.05).

Table 1. Demographic structures and clinical features of the groups							
	Group A	Group B	Group C	*p* ‡	*p1*	*p2*	*p3*
Age (years) *	63.4±8.8	63.4±8.8	65.6±9.1		-	0.35	-
Gender (n women/men)†	17/13	17/13	18/12		-	0.87	-
Lens status (n pseudophakic/phakic)†	12/18	7/23	13/17		0.35	0.22	0.45
Spherical equivalent (diopters)	-0.6±1.6	-0.6±1.51	-0.13±1.5	0.35	-	-	-
Visual acuity (Snellen)	0.84±0.22	0.92±0.12	0.91±0.10	0.37	-	-	-
Intraocular pressure (mmHg)	18.03±5.39	15.6±3.11	17.03±2.53	0.07	-	-	-
Mean deviation (dB)	-7.64±6.33	-0.90±0.83	-0.76±0.64	**<0.001**	**<0.001**§	**<0.001**§	0.99§
Pattern standard deviation (dB)	6.17±3.95	2.05±1.06	1.94±0.72	**<0.001**	**<0.001**§	**<0.001**§	0.98§
*Mann-Whitney U test, †Pearson chi-square test, ‡Kruskal-Wallis H test, §Bonferroni-adjusted Mann-Whitney U test; p1: Group A vs. group B, p2: Group A vs. group C, p3: Group B vs. group C							

Table 2. Retinal nerve fiber layer thickness and ganglion cell analysis of the groups							
	Group A	Group B	Group C	*p*	*p1*	*p2*	*p3*
Rim area (mm²)	0.90±0.23	1.22±0.16	1.29±0.24	**<0.001**	**<0.001**	**<0.001**	0.47
Disc area (mm²)	2.39±0.34	1.77±0.27	1.75±0.25	**0.67**	-	-	-
Cup volume (mm³)	0.31±0.21	0.14±0.1	0.14±0.16	**<0.001**	**<0.001**	**<0.001**	0.31
Mean cup/disc ratio	0.68±0.11	0.53±0.11	0.46±0.17	**<0.001**	**<0.001**	**<0.001**	0.13
Vertical cup/disc ratio	0.69±0.12	0.49±0.11	0.45±0.16	**<0.001**	**<0.001**	**<0.001**	0.70
Mean RNFLT (µm)	70.1±11.57	90.4±7.08	91.43±8.71	**<0.001**	**<0.001**	**<0.001**	0.59
Inferior RNFLT (µm)	83.50±23.05	115.80±11.7	116.66±13.65	**<0.001**	**<0.001**	**<0.001**	0.63
Nasal RNFLT (µm)	61.90±10.9	69.40±10.33	70.56±11.03	**<0.001**	**<0.001**	**<0.001**	0.76
Superior RNFLT (µm)	69.80±17.36	74.26±8.67	111.73±15.19	**<0.001**	**<0.001**	**<0.001**	0.98
Temporal RNFLT (µm)	55.50±11.95	70.90±13.8	66.70±9.91	**<0.001**	**<0.001**	**<0.001**	0.41
Minimum GCL + IPL (µm)	59.36±10.5	77.20±6.37	78.20±4.95	**<0.001**	**<0.001**	**<0.001**	0.65
Mean GCL + IPL (µm)	67.80±8.39	79.50±6.40	80.40±4.79	**<0.001**	**<0.001**	**<0.001**	0.59
RNFLT: Retinal nerve fiber layer thickness, GCL + IPL: Ganglion cell layer+internal plexiform layer thickness. P: Kruskal-Wallis H test, p1: Group A vs. group B, p2: Group A vs. group C, p3: Group B vs. group C (Bonferroni-adjusted Mann-Whitney U test)							

Table 3. Peripapillary and macular vessel density measurements of the groups

	Group A	Group B	Group C	*p*	*p1*	*p2*	*p3*
WI-PPVD	39.73±5.91	48.42±3.71	48.82±2.52	**<0.001**	**<0.001**	**<0.001**	0.94
PPVD	40.97±7.33	51.4±3.92	51.06±3.05	**<0.001**	**<0.001**	**<0.001**	0.89
IDVD	43.67±6.52	46.38±6	45.88±5.27	**0.13**	-	-	-
SH-PPVD	41.06±7.5	47.70±8.8	51.67±3.11	**<0.001**	**<0.001**	**<0.001**	0.68
IH-PPVD	41.07±8.7	51.50±4.0	51.62±3.26	**<0.001**	**<0.001**	**<0.001**	0.76
I-PPVD	43.60±10.79	52.26±5.29	53.96±3.68	**<0.001**	**<0.001**	**<0.001**	0.15
N-PPVD	39.20±9.35	53.3±7.83	50.86±5.19	**<0.001**	**<0.001**	**<0.001**	0.15
S-PPVD	38.83±10.85	50.80±5.18	51.60±4.28	**<0.001**	**<0.001**	**<0.001**	0.62
T-PPVD	42.80±9.8	50.96±5.56	51.16±7.08	**<0.001**	**0.002**	**<0.001**	0.35
WI-MVD	40.10±4.79	46.12±4.62	47.27±3.49	**<0.001**	**<0.001**	**<0.001**	0.51
PFVD	42.11±5.84	47.59±6.60	48.75±4.58	**<0.001**	**0.001**	**<0.001**	0.62
SH-PFVD	42.13±6.56	47.32±7.13	51.67±3.11	**<0.001**	**0.003**	**<0.001**	0.69
IH-PFVD	42.09±5.55	47.92±6.33	51.65±3.26	**<0.001**	**<0.001**	**<0.001**	0.56
I-PFVD	42.93±5.57	48.05±7.34	49.44±5.64	**<0.001**	**0.002**	**<0.001**	0.55
N-PFVD	41.84±6.13	45.66±10.6	47.83±5.52	**<0.001**	**0.005**	**<0.001**	0.80
S-PFVD	42.46±7.45	47.67±7.3	48.81±5.78	**<0.001**	**0.009**	**0.001**	0.54
T-PFVD	41.09±7.32	47.67±6.37	48.90±4.40	**<0.001**	**<0.001**	**<0.001**	0.38

PPVD: Peripapillary vessel density, IDVD: Intradisc vessel density, PFVD: Parafoveal vessel density, MVD: Macular vessel density, WI: Whole image, SH: Superior hemisphere, IH: Inferior hemisphere, S: Superior quadrant, T: Temporal quadrant, I: Inferior quadrant, N: Nasal quadrant. *P*: Kruskal-Wallis H test, *p1*: Group A vs. group B, *p2*: Group A vs. group C, *p3*: Group B vs. group C (Bonferroni-adjusted Mann-Whitney U test)

Discussion

In this study we investigated the peripapillary and macular VDs in patients with unilateral POAG and healthy individuals. VD in POAG has been investigated in the literature before. Toshev et al.[10] observed lower PPVD values in POAG than in ocular hypertension. Similarly, Nascimento et al.[11] found that POAG patients had lower PPVD than healthy controls. In our study, we observed that PPVD values in eyes with glaucoma were lower than in fellow unaffected eyes and the control group, except for IDVD. Yip et al.[12] found that macular VDs decreased with PPVD in glaucoma, and that PPVD was superior in distinguishing healthy and glaucomatous eyes. Triolo et al.[13] compared healthy individuals to those with glaucoma or suspected glaucoma and found a decrease in PPVD but not in macular VD. In our study, we observed that all macular VDs were lower in glaucomatous eyes than in fellow unaffected eyes and the control group. No significant difference was observed in any macular VD or PPVD parameters between the fellow unaffected eyes of the patients and the control group. Therefore, there were no data supporting our hypothesis that there is a vascular predisposition in the pathogenesis of POAG.

In a study investigating the effect of optic disc perfusion and VD on glaucoma progression, Wang et al.[1] found that PPVD and RNFLT values showed high correlation. Chung et al.[14] also found PPVD and RNFLT values to be correlated and showed that the diagnostic ability of VD in glaucoma was similar to that of RNFLT measurements. In our study, the mean RNFLT and PPVD values were correlated in all three groups, as were GCA

parameters and PPVDs. Wang et al.[1] found a high correlation between PPVD and ganglion cell complex (GCC) measurements and reported that GCA showed a much stronger relationship with optic disc perfusion and VDs than other structural tests.

In our study, a correlation between mean RNFLT and WI-MVD values was only observed in group A. When GCA values were analyzed with macular VDs, a correlation was only found between mean GCL + IPL thickness and WI-MVD in group A. In group A and group B, a weak correlation was found between minimum GCL + IPL thickness and WI-MVD. Triolo et al.[13] did not find a correlation between GCC and macular VDs in their study of glaucoma patients.

In light of the information we obtained, we think that PPVD values are superior to macular VD values for glaucoma diagnosis and follow-up. WI-PPVD and PPVD values especially are correlated with RNFLT and GCA values. We believe that PPVD measurements may be important in the early diagnosis and treatment follow-up of glaucoma.

Poli et al.[15] investigated the correlation of peripapillary and macular VDs with GCC thickness, RNFLT values, and VF indices and found the highest correlation with PPVD. Chen et al.[16] found that VF values showed the highest correlation with WI-PPVD, followed by PPVD. They also concluded that macular VD values showed lower correlation with VF parameters than GCC thickness and RNFLT. Wang et al.[1] also obtained similar results, and found that optic disc perfusion parameters and VDs showed higher correlations with MD, RNFLT, and GCC thickness values. In our study, WI-MVD, PFVD, WI-PPVD,

Table 4. Correlation analysis of vessel density values and optical coherence tomography parameters in all groups		Group A	Group B	Group C
Mean RNFLT vs. WI-PPVD	p	0.002	0.02	0.11
	r	0.54	0.44	0.30
Mean RNFLT vs. PPVD	p	0.005	0.03	0.04
	r	0.50	0.40	0.38
Mean GCL + IPL vs. WI-PPVD	p	0.001	0.01	0.02
	r	0.58	0.46	0.43
Mean GCL + IPL vs. PPVD	p	0.002	0.001	0.001
	r	0.54	0.57	0.56
Minimum GCL + IPL vs. WI-PPVD	p	0.004	0.01	0.05
	r	0.51	0.45	0.37
Minimum GCL+IPL vs. PPVD	p	0.005	0.001	0.02
	r	0.50	0.58	0.42
Mean RNFLT vs. WI-MVD	p	0.02	0.77	0.26
	r	0.42	0.06	0.21
Mean RNFLT vs. PFVD	p	0.48	0.98	0.23
	r	0.14	0.006	0.23
Mean GCL + IPL vs. WI-MVD	p	0.007	0.05	0.16
	r	0.48	0.36	0.26
Mean GCL + IPL vs. PFVD	p	0.14	0.21	0.44
	r	0.28	0.24	0.15
Minimum GCL + IPL vs. WI-MVD	p	0.04	0.04	0.08
	r	0.37	0.38	0.33
Minimum GCL + IPL vs. PFVD	p	0.17	0.13	0.22
	r	0.26	0.28	0.23

RNFLT: Retinal nerve fiber layer thickness, PPVD: Peripapillary vessel density, WI: Whole image, GCL + IPL: Ganglion cell layer + internal plexiform layer, MVD: Macular vessel density, PFVD: Parafoveal vessel density. Spearman's rank correlation coefficient test was used. p: Statistical significance of correlation coefficient, r: Spearman's correlation coefficient

Table 5. Correlation of peripapillary vessel density, parafoveal vessel density, retinal nerve fiber layer thickness, and ganglion cell analysis measurements with visual field MD-PSD values		Group A	Group B
WI-PPVD vs. MD	p	<0.001	0.15
	r	0.69	0.27
PPVD vs. MD	p	<0.001	0.19
	r	0.61	0.25
WI-MVD vs. MD	p	0.001	0.52
	r	0.56	0.12
PFVD vs. MD	p	0.001	0.97
	r	0.59	-0.008
Mean RNFLT vs. MD	p	0.05	0.08
	r	0.36	0.33
Mean GCL + IPL vs. MD	p	0.03	0.16
	r	0.36	0.27
WI-PPVD vs. PSD	p	<0.001	0.20
	r	-0.74	-0.24
PPVD vs. PSD	p	<0.001	0.80
	r	-0.62	-0.05
WI-MVD vs. PSD	p	0.004	0.92
	r	-0.51	-0.02
PFVD vs. PSD	p	0.03	0.62
	r	-0.41	0.09
Mean RNFLT vs. PSD	p	0.02	0.14
	r	-0.42	-0.28
Mean GCL + IPL vs. PSD	p	0.026	0.74
	r	-0.41	-0.05

PPVD: Peripapillary vessel density, WI: Whole image, MD: Mean deviation, MVD: Macular vessel density, PFVD: Parafoveal vessel density, RNFLT: Retinal nerve fiber layer thickness, GCL + IPL: Ganglion cell layer + internal plexiform layer, PSD: Pattern standard deviation. Spearman's rank correlation coefficient test was used. p: Statistical significance of correlation coefficient, r: Spearman's correlation coefficient

and PPVD values were correlated with both MD and PSD values in eyes with glaucoma, similar to the literature. The correlation of RNFLT and GCA values with MD and PSD values were examined along with VDs, and the strongest correlations for both MD and PSD were with WI-PPVD, followed by PPVD.

One of the interesting results of our study is that although IDVD was found to be lower in eyes with glaucoma, it did not differ statistically from healthy eyes like other parameters. As previously noted, the crowding of large vessels and the narrowness of the scanned area may have hindered accurate assessment of the superficial disc microcirculation.[17] In the study by Chung et al.,[14] VDs in the ONH, peripapillary, and macular regions in glaucomatous eyes were found to be significantly lower than those in healthy eyes. The authors stated that the VD parameters, with the exception of IDVD, were significantly correlated with OCT parameters and VF indices. IDVD again showed poor diagnostic ability.[14] Nascimento et al.[11] found that superficial ONH VD did not differ between glaucoma patients and healthy subjects, but POAG eyes showed a significantly lower VD in the deep ONH. In our study, IDVD was measured in the superficial layer where the RPC network was examined. Studies have shown that the posterior lamina cribrosa is the primary damaged area and the central area of the lamina cribrosa was more vulnerable to reduced blood supply following IOP elevation in glaucoma.[18,19] However, there are studies that have found a decrease in superficial ONH VD in eyes with glaucoma.[20,21] These differing results may be caused by differences in the determination of the superficial layer, whether the great vessels are excluded or not, and the use of different OCTA devices and processing algorithms.

Mangouritsas et al.[17] recently showed a significantly lower mean PPVD and WI-PPVD in eyes with unilateral preperimetric glaucoma compared with normal fellow eyes and reported that

mean PPVD and WI-PPVD were not significantly higher in healthy controls than in fellow eyes. The results of this study are consistent with ours. Structural tests of fellow eyes were also normal, as in our study. We consider this evidence that in glaucoma, vascular findings do not appear much earlier than structural tests can identify. In the future, prospective studies could investigate the transformation of unilateral patients over time into bilateral glaucoma to provide a better understanding of whether the vascular pathway has an effect on the development of POAG.

Yarmohammadi et al.[22] conducted a study to characterize VD in POAG patients with unilateral VF loss. They observed that mean RNFLT, GCC thickness, and rim area measurements in the unaffected eyes of POAG patients were higher than in their affected fellow eyes and lower than in healthy eyes. The unaffected eyes of POAG patients also showed lower VD in both the peripapillary and macular regions compared to healthy eyes. However, the method of this study was slightly different from our study. Patients had a glaucomatous VF defect in one eye and normal VF in the other eye, and the appearance of the optic disc was not considered in the determination of eligibility for patients in the POAG group. The lower VD in perimetrically unaffected fellow eyes in their study suggests that OCTA can detect microvascular changes in eyes at high risk of developing glaucoma before there is detectable VF damage. Our study included patients with unilateral POAG to determine whether vascular changes started before structural changes and whether POAG patients had a vascular predisposition. The unaffected eyes of the POAG patients in our study had normal optic disc appearance and their peripapillary and macular structural tests were consistent with their age. Thus, the unaffected eyes in our study were perimetrically and structurally normal. This methodological difference was a notable variance between the two studies in comparing unaffected eyes with healthy eyes.

Study Limitations

The low number of patients can be considered a limitation in this study. However, it should be remembered that POAG is often bilateral. Unilaterality is rare, and patients with additional diseases that may affect OCTA were excluded from the study.

In addition, the IOP values of the glaucomatous eyes of the patients included in the study were under control with antiglaucomatous therapy. The use of antiglaucomatous drops by the patients is another limiting factor of this study. However, the IOP values of the eyes in all groups were below 21 mmHg, thereby minimizing the effect of IOP on the vasculature.

Conclusion

In our study, microvascular changes were not observed in the unaffected eyes of individuals with unilateral glaucoma. In other words, there was no evidence supporting the presence of a vascular predisposition in the pathogenesis of POAG. However, a definite judgement can only be reached through prospective follow-up of these eyes. To gain a better understanding of the vascular pathogenesis of glaucoma, we believe observing changes in the vascular structures in eyes which are developing glaucoma during follow-up visits would be a suitable approach. In our study, VDs were correlated with structural and functional glaucoma examinations, and a high correlation with PPVDs in glaucomatous eyes was observed. Monitoring PPVD may be important in diagnosing suspected glaucoma patients or following glaucoma patients in cases with diseases that adversely affect GCA measurements. In addition, we believe that monitoring PPVD is useful for early diagnosis and detection of progression in disc anomalies. Our findings that VF tests showed higher correlation with PPVD measurements than with RNFLT or GCA are important in terms of clinical approach. In advanced cases with a base effect in structural analysis or incompatibility of the VF, OCTA may be especially useful as a reliable examination in follow-up.

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