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Original Article

Optical Coherence Tomography Angiography Findings in Primary Open-Angle and Pseudoexfoliation Glaucoma

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Abstract

Objectives: To compare the optical disc and macular vascular density values of patients with glaucoma and healthy individuals by using optical coherence tomography angiography and evaluate the relationship between structural and functional test results and vascular density.

Materials and Methods: The study included 128 eyes in total: 31 with pseudoexfoliation glaucoma (PEG), 55 with primary open-angle glaucoma (POAG) and similar visual field defects, and 42 healthy eyes. Whole image peripapillary vessel density (wpVD), intradisc vessel density (idVD), peripapillary vessel density (pVD), whole image macular vessel density (wmVD), and parafoveal vessel density (pfVD) values were compared between the groups. Correlations between visual field findings, retinal nerve fiber layer (RNFL) and optic nerve head measurements and peripapillary and macular vascular density were analyzed.

Results: In the PEG and POAG groups, wpVD, idVD, wmVD, and pfVD values were significantly lower in than the control group. In the PEG group, wpVD was found to be significantly lower than the POAG group ($p<0.001$). There was no significant difference between the PEG and POAG groups in wmVD and pfVD except for nasal pfVD. There were strong positive correlations between RNFL thickness and pVD in the glaucoma groups ($p<0.001$). Significant correlations were found between visual field mean deviation and pattern standard deviation values and peripapillary and macular vessel density values in the glaucoma groups.

Conclusion: Vascular density values were lower in glaucoma patients compared to normal individuals, and there is a strong correlation between structural and functional tests and vessel density values. The lower vascular density in the PEG group compared to the POAG group indicates that vascular damage may be more common in PEG patients.

Keywords: Optical coherence tomography angiography, vessel density, primary open-angle glaucoma, pseudoexfoliation glaucoma, visual field

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Introduction

Glaucoma is a group of optic neuropathies characterized by progressive degeneration of the retinal ganglion cells. It is the leading cause of irreversible blindness worldwide.[1] Primary open-angle glaucoma (POAG) is the most common type of open-angle glaucoma, and its pathophysiology and factors involved in its progression are not fully understood. However, damage to the retinal ganglion cells and their axons is known to occur in the early stage, and progression of this damage results in vision loss. Risk factors for POAG include high intraocular pressure (IOP), advanced age, and central corneal thinning.[2,3] Vascular dysfunction in the optic nerve head and peripapillary region is thought to play a role in the pathogenesis of POAG.[4] Pseudoexfoliation syndrome is an age-related systemic disorder characterized by the accumulation of white fibrogranular material (pseudoexfoliation material) in the extracellular matrix of different tissues in the body.[5] Pseudoexfoliation syndrome is associated with the accumulation of small white deposits in the anterior segment of the eye, most often at the pupil margin and on the anterior lens capsule. Contact between the lens and iris during pupil movement results in pseudoexfoliation material being scraped from the anterior lens surface and collecting in the trabecular network.[6] Pseudoexfoliation glaucoma (PEG) is one of the most common causes of open-angle glaucoma.[7,8]

The relationship between retinal microvascularity and glaucoma progression has previously been investigated using various methods such as fundus fluorescein angiography, indocyanine green angiography, scanner laser angiography, and laser Doppler flowmeter.[9,10,11,12] Although these methods have demonstrated impaired optic nerve head circulation in the pathogenesis of glaucoma, they have not been adopted as standard examinations in glaucoma diagnosis because of their low reproducibility and potential adverse effects.[13]

Optical coherence tomography angiography (OCTA) is a noninvasive, high-resolution, fluorescence-free angiography technique that has become widespread in recent years.[14] OCTA detects blood flow based on the motion contrast of red blood cells in the vessels. Unlike fundus fluorescein angiography, it does not require the use of any intravenous contrast agent.[15] OCTA allows the examination of vessel density in different layers of the retina, including the macula and optic nerve head.[16,17,18] In addition, the microvascular structure of the retina can be evaluated quantitatively and reproducibly using a special software called split-spectrum amplitude-decorrelation angiography.[19,20,21]

Previous studies have demonstrated low vessel density in the optic nerve head and peripapillary region in eyes with POAG.[17,20,22] Similarly, there are also studies showing that macular vessel density is lower in eyes with glaucoma compared to normal eyes.[23,24] However, of the studies comparing POAG and PEG patients in the literature, most investigated either the peripapillary region or the macular region.[25,26]

The present study aimed to investigate both peripapillary and macular vessel density parameters in POAG and PEG patients with OCTA and compare these data with a normal control group to evaluate the vascular changes that occur in glaucomatous optic neuropathy. In addition, we aimed to examine the relationship of vascular density values with retinal nerve fiber layer thickness (RNFLT), optic nerve head parameters, and visual field, which are widely used in the diagnosis and follow-up of glaucoma.

Materials and Methods

This prospective observational study was conducted in the glaucoma unit of the ophthalmology department of Ankara Training and Research Hospital. Ethical approval was obtained from the Ankara Training and Research Hospital Ethics Committee (no: 102, date: 01 October 2019), and all study procedures were carried out in accordance with the Declaration of Helsinki.

POAG was diagnosed based on the presence of open angle on gonioscopy, typical glaucomatous appearance of the optic disc on fundus examination, glaucomatous RNFL thinning on OCT, and visual field findings. PEG was diagnosed in the presence of similar findings plus pseudoexfoliation material detected on biomicroscopic and gonioscopic examination.

The study included 55 POAG eyes, 31 PEG eyes, and one eye of 42 healthy individuals. Inclusion criteria were age of 40-80 years; absence of systemic diseases with potential vascular manifestations, such as diabetes mellitus and arterial hypertension; no previous surgical history other than uncomplicated cataract surgery; absence of any ocular pathology other than glaucoma; Snellen best corrected visual acuity of 0.5 or better; absence of cataract, vitreous opacity, or corneal haze severe enough to interfere with signal strength during imaging; and less than ±5 diopters spherical and ±3 diopters cylindrical refractive error. The control group included individuals with no ophthalmologic disease or family history of glaucoma. The affected eyes of patients with unilateral disease and the right eyes of patients with bilateral disease and control subjects were included in the study.

All study participants underwent objective refraction measurement with Huvitz MRK-3100 (Huvitz, Korea), best corrected visual acuity measurement using Snellen chart, slit-lamp biomicroscopic examination, IOP measurement with Goldmann applanation tonometry, and central corneal thickness and axial length measurement with optical biometry AL-Scan (Nidek Co., Ltd., Gamagori, Japan).

After pupil dilation with 0.5% tropicamide, detailed fundus examination and RNFLT measurement were performed with spectral domain OCT device (SD-OCT, Heidelberg Engineering, Germany). Macular OCT 6x6 mm retinal angiography and optic nerve head-centered 4.5 x 4.5 mm disc angiography were then performed using the AngioVue device (RTVue-XR, Fremont, California, USA; software version 2017.1.0.151).

The OCTA system performs optic disc measurements using two circles 2 mm and 4 mm in diameter centered on the optic disc. A 4.5x4.5 mm field is used as the total image area. The area within the 2-mm circle is considered the intrapapillary zone and the area between the 2-mm and 4-mm circles is considered

the peripapillary zone. Whole image peripapillary vessel density (wpVD) measurements are evaluated in the entire 4.5x4.5 mm image area. To detect the radial peripapillary capillary plexus, the software automatically segments the region of interest into four layers, and radial peripapillary capillary plexus measurements are obtained as the vessel density in the area between the internal limiting membrane and the lower boundary of the RNFL. The software used in the study allows measurement of both vessel density in only the capillary plexus and total density ratios in the capillary plexus and large vessels. In order to evaluate the microvasculature in this study, we used capillary vessel density as the study parameter instead of the total vessel density in the measured areas. The software also automatically obtains peripapillary, intrapapillary, superior and inferior hemisphere peripapillary, and capillary densities in the inferior, nasal, superior, and temporal quadrants (Figure 1).

A 6x6 mm macular scan can also be obtained with the OCTA software. To evaluate the superficial plexus, which supplies the ganglion cell layer, a layer between the upper boundary of the internal limiting membrane to the lower boundary 10 µm below the inner plexiform layer is automatically segmented. A 9-zone map is automatically centered on the fovea to create quadrants. This map consists of 3 concentric circles, with the innermost 1-mm diameter area representing the fovea. The area between the central zone and the middle 3-mm diameter circle represents the parafovea, and the area between the middle circle and outer 6-mm diameter circle represents the perifovea. Whole image macular vessel density (wmVD) is calculated from the entire 6x6 mm scan area. In our study, we analyzed the vascular densities of the superficial plexus, which provides the blood supply for the ganglion cells, in the parafoveal area, where this layer is densest. The parameters analyzed were wmVD, average parafoveal VD, VD in the superior and inferior halves of the parafoveal ring, and superficial plexus VD in the inferior, nasal, temporal, and superior quadrants of the parafoveal ring (Figure 2).

Glaucoma patients underwent 24-2 visual field measurements (24-2 Swedish interactive thresholding algorithm) performed using a Humphrey Field Analyzer II 750 (Carl Zeiss Meditec). Those with false-negative and false-positive rates below 30% were included in the study. The mean deviation (MD) and pattern standard deviation (PSD) values of the patients were included in the study.

Statistical Analysis

SPSS Statistics version 22.0 software package (IBM Corp, Armonk, NY, USA) was used. When analyzing the data, qualitative data were expressed as frequency and percentage. Quantitative data were expressed using mean and standard deviation values as descriptive statistics. The Kolmogorov-Smirnov test was used to determine whether data were normally distributed. Normally distributed quantitative data were analyzed using Student's t-test for comparisons between 2 groups and one-way analysis of variance (ANOVA) for comparisons among 3 or more groups. One-way ANOVA was followed by the least significant difference method for multiple pairwise comparisons. Non-normally distributed quantitative data were analyzed using Mann-Whitney U test for comparisons between 2 groups and Kruskal-Wallis test for comparisons among 3 or more groups. The Conover-Iman method was used for multiple pairwise comparisons of data analyzed by Kruskal-Wallis test. Pearson or

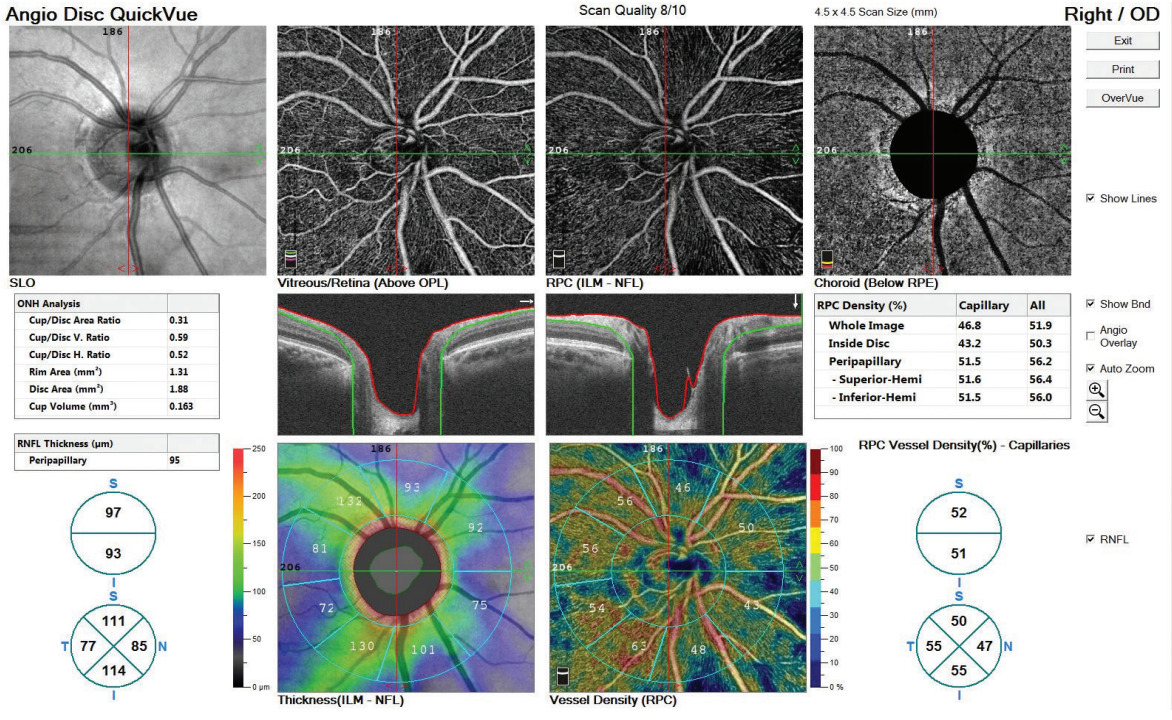

Figure 1. Image of 4.5x4.5 mm disc scan of the right eye of a patient with primary open-angle glaucoma

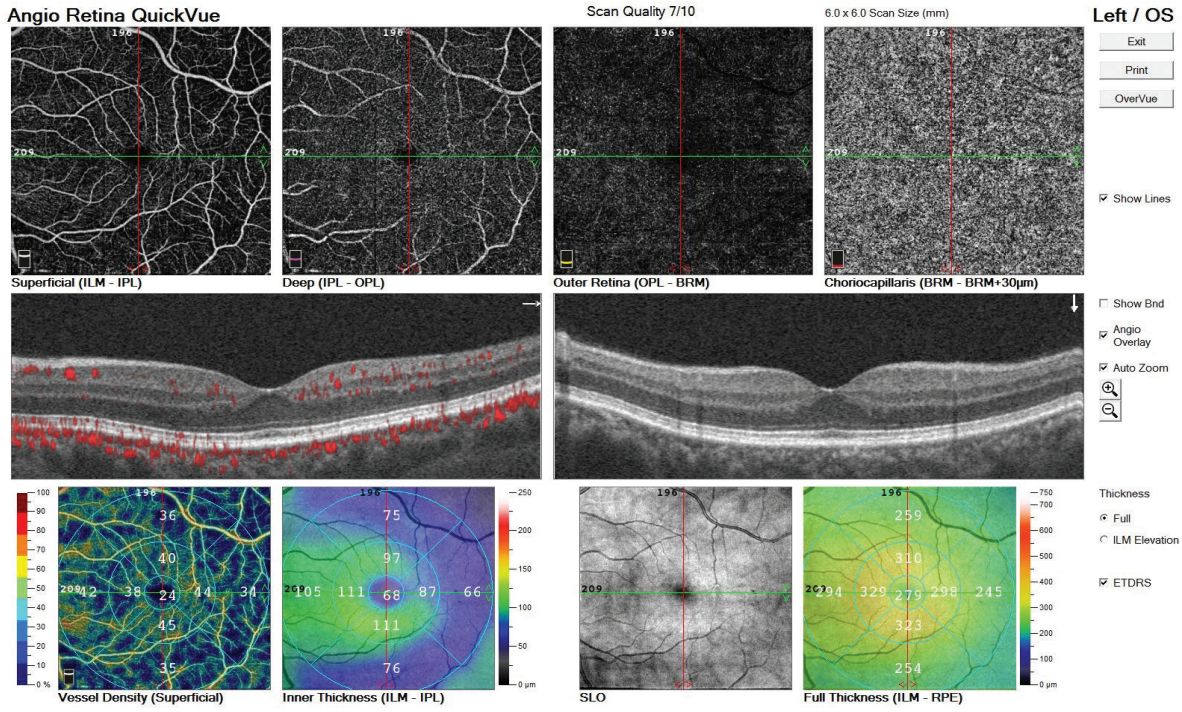

Figure 2. Image of a 6x6 mm macular optical coherence tomography angiography scan of the left eye a patient with pseudoexfoliation glaucoma

Spearman correlation analysis was used to evaluate relationships between quantitative data. Partial correlation analysis was performed to identify relationships between variables while controlling for age. All statistical calculations were evaluated within a 95% confidence interval and at a significance level of $p<0.05$.

Results

Demographic and Ocular Characteristics

The study included single eyes of a total of 128 individuals: 31 (24.2%) PEG patients, 55 (43.0%) POAG patients, and 42 (32.8%) controls. The demographic and ocular characteristics of the study participants are shown in Table 1.

Vascular Characteristics

Radial peripapillary capillary densities are compared in Table 2. WpVD, intradisc vessel density (idVD), and peripapillary vessel density (pVD) (all quadrants) were significantly higher in the control group than the glaucoma groups. There was no significant difference between the glaucoma groups in terms of idVD. However, wpVD and pVD (except in the nasal quadrant) were significantly higher in the POAG group compared to the PEG group.

Macular vessel density values are compared in Table 3. The control group had significantly higher wmVD and parafoveal vessel density (pfVD) (all quadrants) values than the glaucoma groups. There was no statistically significant difference between the glaucoma groups in terms of macular vessel density (except for pfVD in the nasal quadrant).

Peripapillary and macular vascular density values of patients with mild glaucoma of both types are compared in Table 4. WpVD, peripapillary vascular density in the inferior hemisphere (pVD-IH), and pVD values in the inferior and nasal quadrants were found to be significantly lower in the PEG group than the POAG group. The other parameters did not differ significantly between the groups.

Correlations Between Vascular, Structural, and Functional Parameters

Table 5 shows the correlation between RNFLT and pVD values in the glaucoma and control groups. Statistically significant positive correlations were detected in all quadrants in the whole patient group. RNFLT and pVD were significantly correlated in the temporal quadrant in the PEG group and the superior and temporal quadrants in the POAG group. In the control group, there was significant correlation in the average, superior, and inferior quadrant values.

Table 6 shows the correlation between MD and PSD values and pVD, wmVD, and pfVD values in the glaucoma groups. The strongest correlations were between MD and wmVD in the PEG group and between MD and pVD in the POAG group ($p=0.001$ and $p=0.004$, respectively).

Table 1. Demographic and ocular characteristics

	Groups			p value
	PEG (n=31)	POAG (n=55)	Control group (n=42)	
Age (years)[β]	68.06±7.73	62.29±8.80	56.93±6.56	<0.001
Male/female (n)	15/16	20/35	22/20	0.257
BCVA (Snellen decimal)[β]	0.95±0.09	0.94±0.10	0.99±0.05	0.013c
IOP (mmHg)[β]	16.35±5.78	16.04±2.76	12.98±2.23	<0.001[b,c]
AL (mm)*	23.22±0.98	23.37±0.93	23.15±0.89	0.493
CCT (µm)*	525.55±30.50	542.95±31.74	524.12±33.06	0.007[a,c]
RNFLT (µm)[β]	82.10±15.84	91.81±16.62	102.98±8.62	<0.001[a,b,c]
C/D ratio	0.55±0.16	0.52±0.17	0.39±0.14	<0.001[b, c]
Rim area (mm)^2	1.36±0.36	1.54±0.36	1.67±0.33	0.002[a,b]
MD (dB)	-5.30±5.92	-4.18±4.73		0.128
Glaucoma stage				
Mild (MD >6 dB)	22 (78.6%)	42 (84.0%)		0.679
Moderate (MD 6-12 dB)	4 (14.3%)	4 (8.0%)		
Severe (MD <12 dB)	2 (7.1%)	4 (8.0%)		

PEG: Pseudoexfoliative glaucoma, POAG: Primary open-angle glaucoma, BCVA: Best corrected visual acuity, IOP: Intraocular pressure, AL: Axial length, CCT: Central corneal thickness, MD: Mean deviation, C/D: Cup/disc. Data expressed as mean ± SD (standard deviation) or n (%). Pairwise comparisons were performed using *one-way ANOVA for normally distributed data and [β]Kruskal-Wallis test for non-normally distributed data. LSD or Conover-Iman test was used for multiple comparisons between groups. Statistically significant differences in [a]PEG vs. POAG, [b]PEG vs. control, [c]POAG vs. control.

Table 2. Comparison of radial peripapillary capillary densities between the glaucoma and control groups

	Groups			p value
	PEG (n=31)	POAG (n=55)	Control group (n=42)	
wpVD[β]	44.12±5.75	46.93±5.46	50.39±2.63	<0.001[a,b,c]
pfVD*	43.73±4.96	43.35±5.18	46.48±4.67	0.007[b, c]
pVD[β]	46.81±7.17	50.42±6.70	54.22±2.84	<0.001 [a,b,c]
pVD-SH[β]	47.05±7.70	50.91±6.85	54.47±2.88	<0.001[a,b,c]
pVD-IH[β]	46.54±6.97	49.89±7.08	53.95±3.20	<0.00 [a,b,c]
pVD-inferior[β]	48.58±7.20	51.64±7.91	55.36±4.62	<0.001[a,b,c]
pVD-nasal[β]	46.90±10.60	50.73±10.50	54.76±6.66	0.005[b]
pVD-superior[β]	46.68±9.42	49.62±9.27	55.24±3.59	<0.001[a,b,c]
pVD-temporal[β]	45.81±8.15	48.89±8.03	52.60±4.76	0.001[a,b,c]

wpVD: Whole image peripapillary vessel density, idVD: Intradisc vessel density, pVD: Peripapillary vessel density, SH: Superior hemisphere, IH: Inferior hemisphere. Data expressed as mean ± SD (standard deviation). Pairwise comparisons were performed using *one-way ANOVA for normally distributed data and [β]Kruskal-Wallis test for non-normally distributed data. LSD or Conover-Iman test was used for multiple comparisons between groups. Statistically significant differences in [a]PEG vs. POAG, [b]PEG vs. control, [c]POAG vs. control.

Table 3. Comparison of macular vessel density values by group

	Groups			p
	PEG (n=31)	POAG (n=55)	Control Group (n=42)	
wmVD$^{\beta}$	41.35±4.78	43.59±5.22	48.33±2.88	<0.001 ^{b,c}
pfVD*	42.97±5.03	44.90±5.23	49.58±3.56	<0.001 ^{b,c}
pfVD-SH*	43.08±5.12	44.92±5.49	49.58±3.84	<0.001 ^{b,c}
pfVD-IH*	42.89±5.38	44.90±5.58	49.57±3.63	<0.001 ^{b,c}
pfVD-inferior*	43.71±5.99	45.61±6.32	50.71±4.23	<0.001 ^{b,c}
pfVD-nasal*	39.03±5.99	42.97±5.42	45.56±3.96	<0.001 ^{a,b,c}
pfVD-superior*	44.45±4.87	45.77±5.78	50.86±4.61	<0.001 ^{b,c}
pfVD-temporal$^{\beta}$	44.67±6.16	45.19±7.20	51.20±3.79	<0.001 ^{b,c}

wmVD: Whole image macular vessel density, pfVD: Parafoveal vessel density, SH: Superior hemisphere, IH: Inferior hemisphere. Note: Data expressed as mean ± SD (standard deviation). Pairwise comparisons were performed using *one-way ANOVA for normally distributed data and $^{\beta}$Kruskal-Wallis test for non-normally distributed data. LSD or Conover-Iman test was used for multiple comparisons between groups. Statistically significant differences in ^{a}PEG vs. POAG, ^{b}PEG vs. control, ^{c}POAG vs. control.

Table 4. Comparison of peripapillary and macular vessel densities in patients with mild glaucoma

	Glaucoma type		p value
	PEG (n:22)	PAAG (n:42)	
wpVD*	46.28±3.56	48.24±3.63	**0.043**
idVD*	43.10±4.85	43.27±5.28	0.902
pVD*	49.78±4.09	51.96±4.61	0.066
pVD-SH*	50.31±3.88	52.26±5.36	0.136
pVD-IH*	49.20±4.65	51.64±4.48	**0.045**
pVD-inferior*	50.00±4.88	53.36±6.16	**0.030**
pVD-nasal*	49.95±9.39	53.00±7.80	0.172
pVD-superior$^{\beta}$	50.36±6.54	51.43±7.82	0.308
pVD-temporal$^{\beta}$	48.91±5.81	49.98±7.05	0.605
wmVD$^{\beta}$	42.54±4.11	44.48±4.25	0.064
pfVD*	44.15±4.26	45.37±4.76	0.314
pfVD-SH*	44.33±4.40	45.32±5.15	0.447
pfVD-IH*	43.98±4.68	45.46±4.97	0.252
pfVD-inferior*	44.82±4.78	45.91±5.98	0.461
pfVD-nasal*	39.76±6.33	43.04±5.63	**0.038**
pfVD-superior*	45.53±4.41	46.48±5.32	0.479
pfVD-temporal*	46.43±4.67	45.95±5.69	0.735

wpVD: Whole image peripapillary vessel density, idVD: Intradisc vessel density, pVD: Peripapillary vessel density, SH: Superior hemisphere, IH: Inferior hemisphere, wmVD: Whole image macular vessel density, pfVD: Parafoveal vessel density. Data expressed in mean ± SD (standard deviation). Pairwise comparisons performed using *Student's t-test for normally distributed data and $^{\beta}$Mann-Whitney U test for non-normally distributed data

Table 5. Correlation between retinal nerve fiber layer thickness and peripapillary vessel density values in the glaucoma groups, total patient group, and control group

	PEG		POAG		PEG + POAG		Control Group	
	r	p	r	p	r	p	r	p
RNFLT/pVD	0.793	<0.001	0.786	<0.001	0.793	<0.001	0.558	<0.001
RNFLT/pVD-SH	0.790	<0.001	0.784	<0.001	0.787	<0.001	0.548	<0.001
RNFLT/pVD-IH	0.809	<0.001	0.792	<0.001	0.803	<0.001	0.486	0.001
RNFLT/pVD-Inferior	0.388	0.034	0.581	<0.001	0.545	<0.001	0.373	0.016
RNFLT/pVD-nasal	0.369	0.045	0.428	0.001	0.426	<0.001	0.077	0.631
RNFLT/pVD-superior	0.603	<0.001	0.176	0.209	0.305	0.005	0.039	0.806
RNFLT/pVD-temporal	0.272	0.145	0.327	0.017	0.317	0.003	0.039	0.811

PEG: Pseudoexfoliation glaucoma, POAG: Primary open-angle glaucoma, RNFLT: Retinal nerve fiber layer thickness, pVD: Peripapillary vessel density, SH: Superior hemisphere, IH: Inferior hemisphere. Note: Controlled for age. Partial correlation analysis was used

Table 6. Correlation of mean deviation, pattern standard deviation, and vessel density values in the glaucoma groups

		PEG		POAG	
		MD	PSD	MD	PSD
pVD	r	0.393	-0.537	0.401	-0.397
	p	0.039	0.003	0.004	0.004
wmVD	r	0.589	-0.414	0.382	-0.209
	p	0.001	0.029	0.006	0.145
pfVD	r	0.455	-0.216	0.201	-0.050
	p	0.015	0.269	0.162	0.728

PEG: Pseudoexfoliation glaucoma, POAG: Primary open-angle glaucoma, MD: Mean deviation, PSD: Pattern standard deviation, pVD: Peripapillary vessel density, wmVD: Whole image macular vessel density, pfVD: Parafoveal vessel density

Discussion

Detection of RNFL damage is important in the early diagnosis and treatment of glaucomatous optic neuropathy. This damage later leads to functional loss detected by perimetry.[27] In our study, there was a significant difference in mean RNFLT between the glaucoma groups and the control group. This result is consistent with other studies in the literature.[28,29]

Focal RNFL damage is typically observed in early-stage glaucoma. The inferotemporal quadrant is most affected, followed by the superotemporal quadrant.[30] The course of the radial peripapillary capillaries within the RNFL and parallel to the retinal nerve fibers is believed to enable supply of the retinal nerve fibers and be associated with its function.[31] In our study, we conducted separate comparisons of pVD average, superior and inferior hemisphere, and inferior, nasal, superior, and temporal quadrant values between the groups. There was a significant decrease in pVD in all quadrants except the nasal quadrant between the POAG and PEG groups. Lommatzsch et al.[32] examined pVD average and sector values (superonasal, superotemporal, nasal, inferonasal, inferotemporal, temporal) in 97 glaucoma patients (41 with POAG, 26 with PEG, 24 with normal tension glaucoma, and 6 with primary angle-closure glaucoma, and found significant reduction in pVD mean and all sector values. Clinically, typical glaucomatous damage first begins in the inferotemporal and superotemporal quadrants, and nasalization of the central vessels is observed in the advanced stage of the disease.[33] Therefore, pVD in glaucoma patients is expected to decrease most in the temporal quadrant. The literature data on this subject vary. Lommatzsch et al.[32] found that pVD was lowest in the nasal and superonasal quadrants. Jia et al.[34] found that vessel density decreased significantly in the temporal quadrant, while Rao et al.[35] found that there was no significant difference between the temporal quadrant and other quadrants. In our study, we determined the temporal quadrant to have the lowest vessel density in the glaucoma groups. The reason for this difference in the literature data is difficult to explain, and further studies on this subject are needed. Lu et al.[24] conducted a study with 44 preperimetric glaucoma (PPG), 42 early-stage glaucoma, and 41 normal eyes and found that the RNFL was significantly thinner in the inferotemporal

and superotemporal quadrants in the early glaucoma group compared to the PPG group, while pVD was significantly lower only in the inferotemporal quadrant. The authors noted that this supports observations that structural damage occurs earlier than vascular damage in glaucoma.

In our study, we examined wpVD, idVD, and pVD values, parameters related to optic disc vascularity, in all three groups and found that vessel densities in the glaucoma groups were significantly lower than those of the control group in all quadrants except the nasal quadrant. In this respect, our study is consistent with the literature. Liu et al.[20] compared 9 perimetric and 3 preperimetric POAG groups with normal eyes and found a significant decrease in pVD compared to normal eyes. Similarly, in the study of Rao et al.[35], pVD was significantly lower in the POAG group compared to the control group. There are many OCTA studies conducted with different glaucoma types in the literature. In a study by Park et al.[36] comparing PEG and POAG patients with a similar disease stage, pVD values were found to be lower in the PEG group, especially in the nasal and inferonasal quadrants. In a study by Suwan et al.[25] investigating pVD in POAG, pseudoexfoliation syndrome, PEG, and healthy individuals, it was shown that vascular density was lower in POAG and PEG patients compared to the control group. In their study, they found that among patients with similar stage POAG and PEG, vascular density was lower in the PEG group. Similarly, in our study, we compared patients in the POAG and PEG groups at similar stages and determined that peripapillary vessel densities were significantly lower in the PEG group, especially in the inferior quadrant. This is consistent with the literature data and supports that PEG is a more aggressive type of glaucoma and progresses faster and shows a poorer response to treatment than POAG. The lower mean IOP in our control group during measurement may have had an impact on the difference between the study and control groups.[20]

In this study, the average, superior and inferior hemisphere, and quadrant RNFLT and sector pVD values were investigated in all three groups. In the entire patient group (POAG + PEG), there was a significant correlation between these parameters in all quadrants. Mansoori et al.[37] examined the relationship between radial peripapillary capillary vessel density and RNFLT in 8 sectors in 24 patients with early POAG and found no significant correlation except in the superotemporal and inferotemporal sectors. Mase et al.[38] observed a stronger correlation between the superotemporal and inferotemporal quadrants than other quadrants. In their study, Triola et al.[39] found a strong correlation between superior, inferior, and average RNFLT and pVD in eyes with glaucoma. In a study by Chung et al.[40] comparing eyes with early, moderate, and advanced glaucoma and healthy eyes, there was a strong correlation between pVD and RNFLT, but no correlation was found between the temporal and inferotemporal quadrants in eyes with early glaucoma. These findings of the present study and similar studies in the literature demonstrate the significant relationship between structural and vascular parameters.

In this study, we evaluated the patients' visual field findings and their correlation with OCTA parameters. For this purpose, we analyzed whether MD and PSD were correlated with pVD, wmVD, and pfVD and found significant correlations. The strongest correlations were between MD and wmVD in the PEG group and between MD and pVD in the POAG group. Looking at the literature data on this subject, a study by Poli et al.[41] investigating the relationship between peripapillary and macular vascular densities and structural and functional tests in glaucoma patients showed that vascular density more strongly correlated with structural tests than functional tests. They also observed greater correlation with peripapillary vessel density values than macular vessel density values. The correlation of visual field findings with both peripapillary and macular vessel densities in our study and similar studies in the literature may be important in terms of the future use of OCTA in glaucoma diagnosis and follow-up.

Study Limitations

Our study has certain limitations. The rather small number of patients in the study group is an important limitation. Another limitation of our study was that patients in the PEG group were relatively older than the POAG group and those in the POAG group relatively older than the control group. This affects vascular density values but is actually an expected result due to the fact that PEG presents at a later age and has a worse prognosis. Although the average RNFLT values were lower in the eyes with PEG than those with POAG, we noted that the patients included in the study had similar glaucoma duration and glaucoma stage assessed according to visual field. Another limitation of our study is the effect of topical antiglaucoma therapy on vessel density. All of the patients in our study were receiving topical antiglaucoma treatment. Prospective studies investigating the effect of antiglaucoma agents on vascular density are needed.

Conclusion

Although there are various theories, the etiopathogenesis of glaucoma remains unclear. This study focused on changes in the vasculature of glaucomatous eyes. We found that vessel density was reduced in eyes with glaucoma compared to healthy eyes, and vessel densities significantly correlated with both visual field and RNFL analysis. It was also determined that in POAG and PEG patients at a similar stage according to visual field findings, eyes with PEG had statistically significantly lower RNFLT and vessel densities. This result shows that PEG is a more aggressive type of glaucoma and that structural and vascular damage occur earlier than functional damage. This information is consistent with the current literature data and leads to the conclusion that OCTA can be used as a reproducible and reliable examination in addition to visual field and structural tests in the diagnosis and follow-up of glaucoma. It may also be preferrable in patients who do not cooperate with visual field testing or advanced glaucoma patients who cannot be monitored for progression due to the

floor effect in structural analyses. Correlation studies between central visual field values and OCTA parameters in eyes with advanced glaucoma in particular will provide more information on this subject.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ankara Training and Research Hospital Ethics Committee (no: 102, date: 01 October 2019), and all study procedures were carried out in accordance with the Declaration of Helsinki.

Informed Consent: Prospective.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: G.D., G.Ü., M.Y., S.Ö-U., Ü.E., Concept: E.D., G.D., Design: E.D., G.D., Data Collection or Processing: E.D., Analysis or Interpretation: A.K., G.D., Literature Search: E.D., A.K., Writing: E.D., A.K.

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