Cerrahpaşa Med J 2024; 48(1): 74-80

ORIGINAL ARTICLE

Microvascular Outlook on the Peripapillary Area of the Unilateral Pseudoexfoliation Syndrome and Pseudoexfoliation Glaucoma: An Optical Coherence Tomography Angiography Study

Cansu Yüksel Elgin

Department of Ophthalmology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye

Cite this article as: Yüksel Elgin C. Microvascular outlook on the peripapillary area of the unilateral pseudoexfoliation syndrome and pseudoexfoliation glaucoma: An optical coherence tomography angiography study. *Cerrahpaşa Med J.* 2024;48(1):74-80.

Abstract

Objective: The main purpose of this study was to understand the vascular changes in the presence of the visible pseudoexfoliation material (XFM) and the fellow eye of the participants in the non-glaucomatous and glaucomatous processes.

Methods: This is study included 72 eyes of 36 patients with unilateral pseudoexfoliation syndrome (XFS) and 68 eyes of 34 patients with unilateral pseudoexfoliation glaucoma (XFG). Different indicators of the XFM positive and negative eyes in each group is evaluated using standard mean comparison *t*-tests. The XFM positive and negative eyes in both groups were also compared against each other using the Kruskal–Wallis test.

Results: For retinal nerve fiber layer (RNFL) thickness (μm), in average, all quadrants, both superior and inferior hemifields, the comparison of the paired-eyes of the participants in unilateral XFS does not show any significant difference but in the unilateral XFG group all measurements were significantly different due to the glaucomatous degeneration. Similar results were obtained with radial peripapillary capillary (RPC) vessel density (vd) (%). When correlations are calculated to examine the relationship between RNFL thickness and RPC vd, significantly positive correlations were observed generally for most of the points.

Conclusion: In glaucoma cases controlled with medical treatment, a decrease in the density of the RPC, correlated with RNFL thinning has been demonstrated. However, this vascular decrease could not be shown as an early sign in the presence of XFM, which is a major risk factor for glaucoma.

Keywords: Glaucoma, pseudoexfoliation, radial peripapillary capillary, vessel density

Introduction

Glaucoma is a multifactorial progressive optic neuropathy with the characteristic loss of retina ganglion cells and atrophy of the optic nerve.[1] Although elevated intraocular pressure (IOP) is widely accepted as a major risk factor, many proven and ongoing studies have also addressed the vascular and ischemic components of glaucomatous damage.[2,3] Even though the glaucoma pathogenesis is indisputably related to vascular dysfunction, sensitive and noninvasive measurement of the optic disc circulation was not feasible under in vivo conditions until the development of optical coherence tomography angiography (OCT-A). OCT-A is a recently developed noninvasive imaging modality that allows the measurement of red blood cell velocity. By this way, OCT-A allows worthy information about the retinal and choroidal microvascular structures and optic disc microcirculation.[4,5] Also, OCT-A holds a lot of promise for the clarification of the potential links between optic nerve head (ONH), retina, choroid, and eventually vascular pathophysiology of glaucoma.

Received: April 10, 2023 **Revision Requested:** July 9, 2023
Last Revision Received: October 2, 2023 **Accepted:** October 4, 2023
Publication Date: April 26, 2024
Corresponding author: Cansu Yüksel Elgin, Department of Ophthalmology, İstanbul University-Cerrahpaşa, İstanbul, Türkiye
e-mail: cansu.elgin@iuc.edu.tr
DOI: 10.5152/cjm.2023.23040

With the purpose of finding out clues for vascular factors in glaucoma, pseudoexfoliation material (XFM) could be a major determinant to reveal some points. It is easily detectable, can show unilateral presentation, and has a vascular affinity.[6,7] The present study suggests that ONH vascular changes could be investigated in unilateral conditions in 2 groups: one with nonglaucomatous findings, pseudoexfoliation syndrome (XFS), and the other group with glaucomatous damage, pseudoexfoliation glaucoma (XFG).

The main purpose of this study is to understand the vascular changes in the presence of visible XFM and the fellow eye of the participants in the nonglaucomatous and glaucomatous processes. I believe that understanding early alterations in the beginning and progression of the XFG cascade is crucial to diagnose and manage the glaucomatous processes.

Methods

This cross-sectional study was performed according to the tenets of the Declaration of Helsinki and was approved by the local ethics committee of Sisli Hamidiye Etfal Research and Training Hospital (Approval No: 4291, Date: April 5, 2021). Informed consent was obtained from all the enrolled patients. All participants were selected from a single tertiary eye care center. All study procedures and clinical evaluations were carried out by the same physician (the author herself). After completing ophthalmic examination, including best corrected visual acuity and refraction assessments using a Snellen chart, a biomicroscopic evaluation of the anterior

segment, gonioscopy with a Goldmann 3-mirror lens (in selected patients), and a dilated fundus examination using a +90 D lens; the participants underwent central corneal thickness (CCT) measurement, Humphrey visual field testing, and OCT-A scanning. Goldmann applanation tonometry was performed by the same physician after CCT measurement during the same period of the day (between 10 and 12 AM).

Patients with the following conditions were excluded from this study: any type of glaucoma other than XFG; bilateral XFG and/or XFS; a history of ocular trauma; any previous ocular surgery other than phacoemulsification; substantial media opacity; history of any types of optic neuropathies (ischemic or nonischemic); optic disc anomalies, such as coloboma, tilted disc, and optic disc drusen; retinal vascular diseases, including diabetic retinopathy, hypertensive retinopathy, and vascular occlusion; uveitis; vitreoretinal interface disorders; a spherical and/or cylindrical refractive error >3 diopters (D); any systemic disorders that might have caused vascular dysfunction.

All OCT-A measurements and imaging procedures were performed with the pupil dilated, using an AngioRTVue XR (Optovue Inc., Freemont, CA) with version 2015.1.1.98 software, by a qualified technician trained in using the equipment. Quantitative optic disc perfusion values were measured automatically by the device software. The device automatically determined peripapillary vascular density (%) in 10 segments and retinal nerve fiber layer (RNFL) measurements (μm). Total radial peripapillary capillary (RPC) flow density (4.5 × 4.5 mm) was measured at different levels of segmentation. Qualitative peripapillary perfusion was evaluated by comparing choroidal, retinal, and en face angiogram images. Optic nerve head and peripapillary measurements were determined for the vitreous/retinal layer over the outer plexiform layer, the RPC layer between the inner limiting membrane and the RNFL, and the choroidal layer under the retinal pigment epithelium, which were automatically segmented by the software.[8,9] Figures 1 and 2 demonstrate the segmentation and sectorial division of the layers. All images were reviewed in terms of their image quality. Patients with poor image features, such as a low signal strength index (SSI) of less than 7/10, poor clarity, blink artifacts, poor fixation causing residual motion or doubling artifacts, and segmentation errors, were re-scanned. Images with SSIs ≥7/10 were used for the quantitative assessment.

After the baseline examination and screenings, the subjects with unilateral XFM were divided into 2 groups based on the presence of the glaucomatous findings.

Group 1: 36 patients (21 females and 15 men) with a mean age of 64.00 ± 5.06. These patients have unilateral XFM (in 1 eye) and do not exhibit any glaucomatous findings (healthy optic disc, IOP <21mm Hg, symmetric RNFL measurements and a normal visual field test) in both eyes. This group is the group of patients with unilateral XFS.

Group 2: 34 patients (20 females and 14 men) with a mean age of 68.25 ± 7.24. These patients have unilateral XFM (in 1 eye) with glaucomatous findings (optic nerve glaucomatous cupping, recorded IOP ≥21 mm Hg at some point in history, asymmetric RNFL measurements, and visual field loss in accordance with glaucoma). The other eye of these patients is totally within normal limits. This group is made up of patients with unilateral XFG. In this group, all glaucomatous eyes were under control with topical anti-glaucomatous treatment.

The eyes were evaluated under 2 categories in 2 groups, as XFM positive without glaucomatous damage (XFS) and the fellow eye

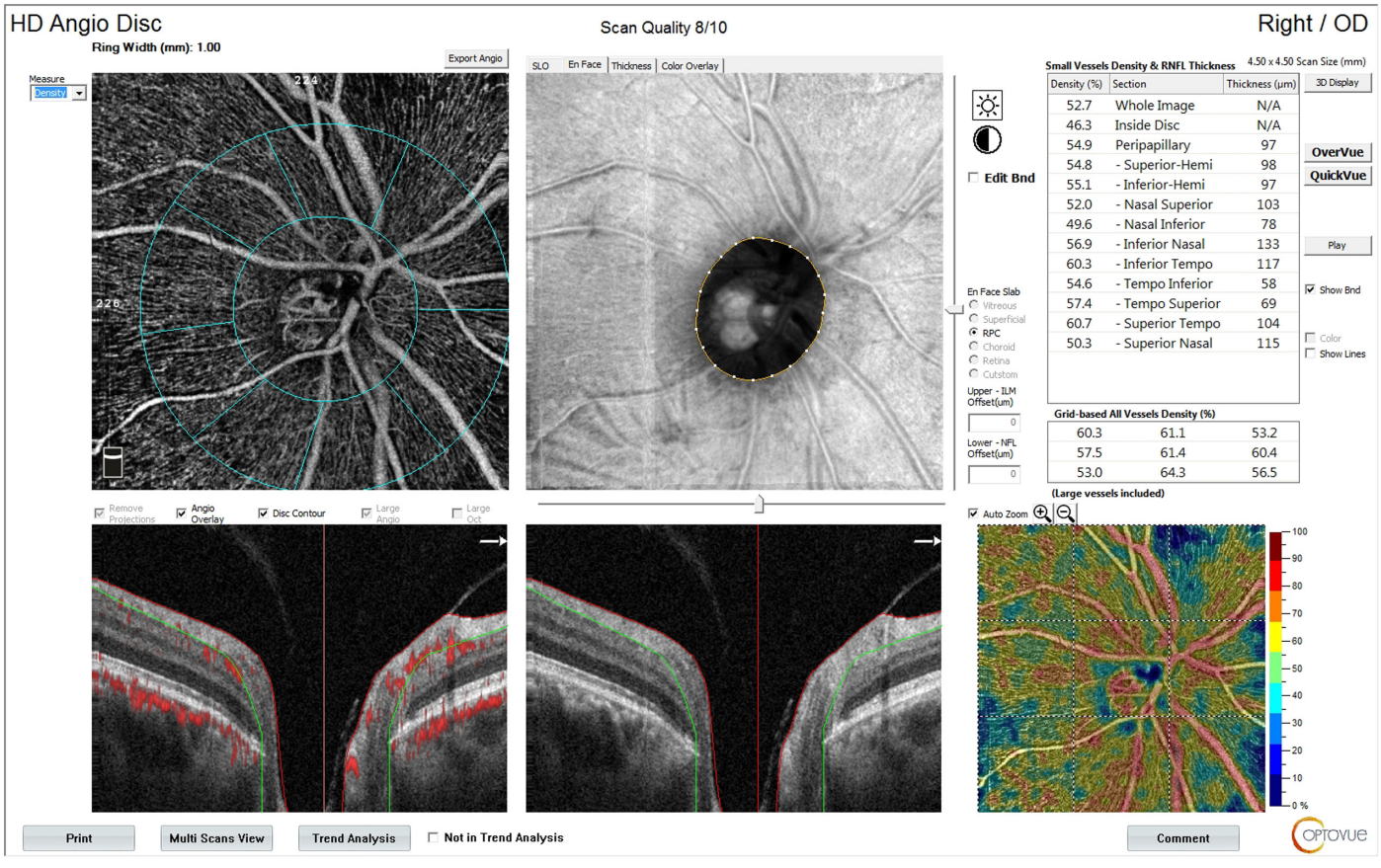

Figure 1. Retinal peripapillary capillaries for the optic nerve head.

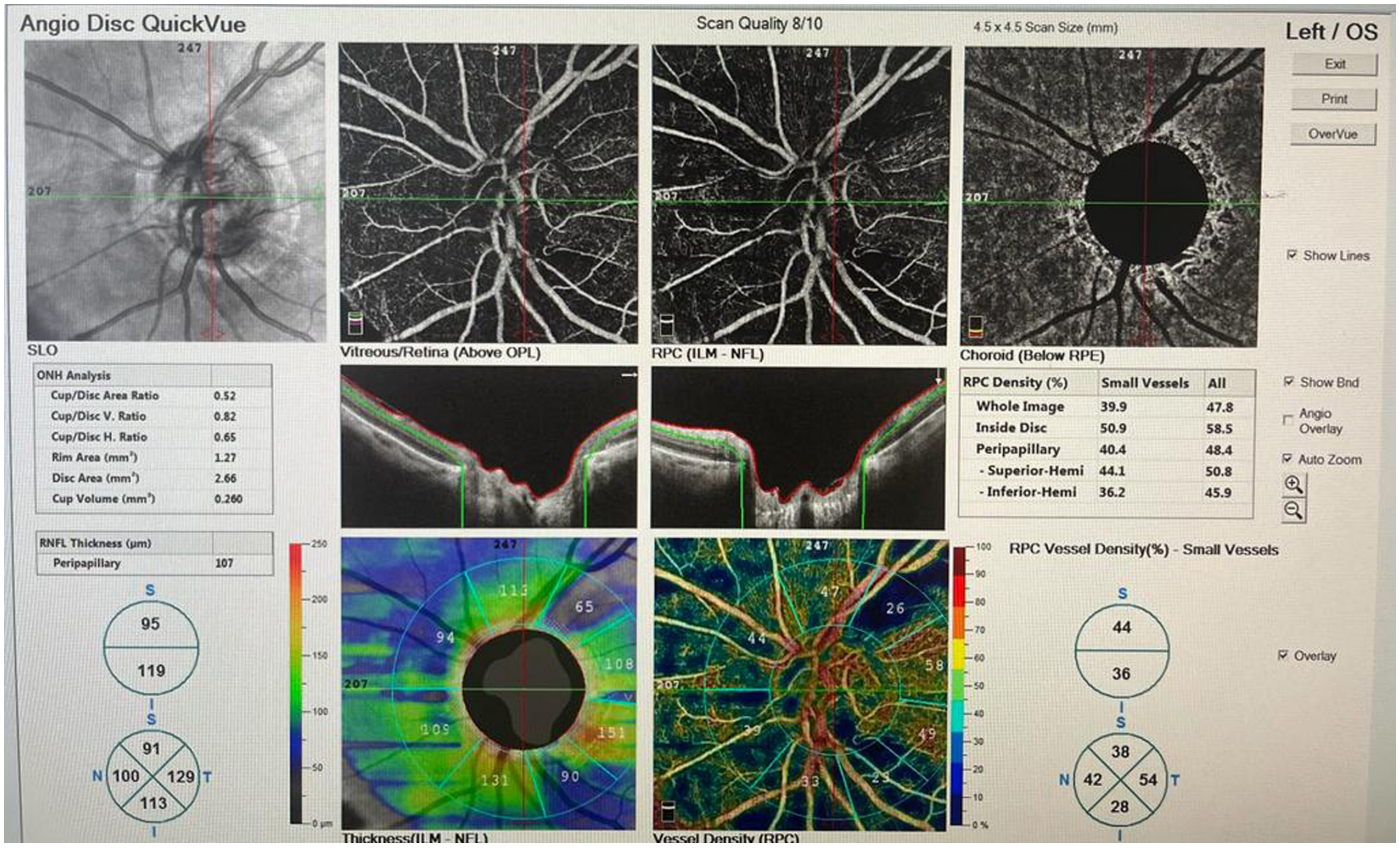

Figure 2. Retinal nerve fiber layer thickness for the peripapillary area.

(group 1), XFM positive with glaucomatous damage (XFG) and the fellow eye (group 2).

In both groups, the second eyes of the patients are XFM negative and also healthy in other aspects, and their indicators are within normal limits.

Different indicators of the XFM positive and negative eyes in each group are evaluated using standard mean comparison *t*-tests. The XFM positive and negative eyes in both groups were also compared against each other using the Kruskal–Wallis test. Moreover, Kruskal–Wallis comparison tests were also used for 3 groups consisting of unilateral XFS's in both eyes (XFM+ and XFM −). and unilateral XFG group's XFM− eye, as well as for all 4 groups consisting of unilateral XFS's and XFG's both eyes (XFM+ and XFM−).

For all the statistical analysis, calculations were made using the version 17 of the STATA software.

Results

This comparative study with prospective enrollment was conducted between June 2021 and February 2022 in a single tertiary eye care center. This study included 72 eyes of 36 patients with unilateral XFS (group 1) and 68 eyes of 34 patients with unilateral XFG (group 2). There was no significant difference between the 2 groups with respect to age (66.12 ± 5.06. vs. 68.25 ± 7.24, respectively; $P = .16$) and distribution of gender (15/36 males vs. 14/34 males, respectively; $P = .97$).

The demographic and clinical characteristics of the study participants are shown in Table 1. As also illustrated by the table, there were no statistically significant differences between the groups in terms of age, gender distribution, CCT, and IOPs ($P > .05$ for all).

Table 2, shows the comparisons of the RNFL thickness (µm) in average, all quadrants, both superior and inferior hemifields. The comparison of eyes in participants with unilateral XFS does not show any significant difference. However, in the unilateral XFG group, all measurements were significantly different due to the glaucomatous degeneration. Comparison of the 3 groups of non-glaucomatous eyes (even those with XFM) shows some significant differences only in the inferior ($P = .027$) and nasal quadrants ($P = .025$). But if the glaucomatous group was added to the comparison and it was made between 4 groups, highly significant differences appeared at all points.

From the RPC vessel density (vd) (%) point of view, the results were similar to those with RNFL thickness (Table 3). There were not any significant differences between the pairs of paired eyes of the participants with unilateral XFS, but all the comparisons (except the temporal quadrant, where the *P*-value is .91) were significant in the paired eyes of participants with unilateral XFG's paired eyes. The comparison of the nonglaucomatous groups showed significance only at the temporal quadrant ($P = .02$). However, when XFG was added to this comparison, the differences became highly significant at all points.

At the next step, correlations are calculated to examine the relationship between RNFL thickness and RPC vd (%) (Table 4). Significantly positive correlations were generally observed for most of the points.

Table 5 exhibits RPC vd (%) in overall parameters in the 4.5 x 4.5 scan-sized peripapillary area similar to Table 3, but it presents statistics in a more detailed way. Here, the same values were compared in a more detailed manner, dividing them into 10 parts to discover any specific point. The comparison of 3 groups with nonglaucomatous eyes indicates a significant difference only at

Table 1. Clinical Characteristics of the Participants

	Unilateral XFS (n = 36)			Unilateral XFG (n = 34)		
	XFM+	**XFM–**	***P***	**XFM +**	**XFM –**	***P***
IOP (mm Hg)	16.32 ± 2.33	15,63±2.09	.33	16.76 ± 4.70	15.71 ± 2.49	.38
CCT (μm)	542.21 ± 36.15	529.11 ± 37.11		514.99 ± 33.45	522.21 ± 33.12	
BCVA (decimal)	0.85 ± 0.21	0.90 ± 0.13	.37	0.74 ± 0.24	0.88 ± 0.17	.04
Topical medication (n)	0	0		1.71 ± 1.10	0	
Lens status (n)						
Phakic (%)	(28) 77.78%	(21) 58.33%	.15	(11) 32.53%	(18) 52.94%	.70
Pseudophakic (%)	(8) 22.22%	(15) 41.67%	.36	(23) 67.65%	(16) 47.06%	.20
VFMD (dB)	−0.62 ± 0.12	−1.12 ± 0.84	.0007	−6.70±8.76	−2.13 ± 1.28	**<.0001**
PSD (dB)	1.01 ± 0.6	1.21 ± 1.0	.31	5.06 ± 3.49	2.01 ± 1.70	**<.0001**
Age	64.00 ± 5.06	64.00 ± 5.06		68.25 ± 7.24	68.25 ± 7.24	
Gender (females/males)	21/15	21/15		20/14	20/14	

Values in bold indicate statistical significance.
IIEF, International Index of Erectile Function; IPSS, International Prostate Scoring System; NR, not recorded; PVR, post-void residual; Qmax, maximal flow rate; QoLs, quality of life scores.

Table 2. Retinal Nerve Fiber Layer Thickness Differences Between the Participants with Unilateral Pseudoexfoliation syndrome and Pseudoexfoliation glaucoma

	Unilateral XFS			Unilateral XFG			Kruskal–Wallis Comparison	
	XFM (+)	**XFM (–)**	***P***	**XFM (+)**	**XFM (–)**	***P***	**3 Groups**	**4 Groups**
RNFL avg (μm)	104.88 ± 10.53	107.44 ± 10.08	.38	70.79 ± 16.30	101.79 ± 16.32	**<.0001**	.126	**.0001**
sup (μm)	119.92 ± 13.27	121.42 ± 13.45	.7	78.58 ± 23.99	118.42 ± 23.78	**<.0001**	.7044	**.0001**
inf (μm)	140.42 ± 24.00	144.25 ± 22.44	.57	78.53 ± 25.19	128.26 ± 19.70	**<.0001**	**.0277**	**.0001**
temp (μm)	70.33 ± 10.33	68.46 ± 9.37	.51	59.68 ± 13.79	74.05 ± 14.62	**.004**	.3335	**.0101**
nasal (μm)	93.38 ± 10.36	98.58 ± 10.35	.09	67.32 ± 13.40	89.95 ± 16.24	**<.0001**	**.0259**	**.0001**
sup hemifield (μm)	102.17 ± 10.47	104.29 ± 10.17	.48	72.00 ± 17.17	102.11 ± 18.14	**<.0001**	.6861	**.0001**
inf hemifield (μm)	108.21 ± 13.53	110.71 ± 12.61	.51	69.63 ± 17.00	101.58 ± 14.95	**<.0001**	**.0324**	**.0001**

The Kruskal–Wallis comparison for 3 groups consists of unilateral XFS's both eyes (XFM+ and XFM–) and unilateral XFG group's XFM– eye. The Kruskal–Wallis comparison for 4 groups consists of unilateral XFS's and XFG's both eyes (XFM+ and XFM–). Values in bold indicate statistical significance.
inf, inferior; inf hemifield, inferior hemifield; RNFL, retinal nerve fiber layer; sup, superior; sup-hemifield, superior hemifield; temp, temporal; XFG, pseudoexfoliation glaucoma; XFM, pseudoexfoliation material; XFS, pseudoexfoliation syndrome.

the nasal region (P = .02). Again, when the eyes with glaucoma are added to this comparison, more significant differences appear in all the regions.

Discussion

Radial peripapillary capillaries (RPC) are essential for nourishing and supporting the nerve fiber layer due to their proximity. Investigation of the vascular plexus is critical in both the vascular and mechanical theories of glaucoma.[10] XFM has been shown to have an occlusive effect on the trabecular meshwork during the glaucomatous process and may also play a role in ischemic events in the peripapillary area, especially in the endothelium of small vessels.[11] With this in mind, the current study aimed to observe the vascular differences at the distinguishable point of XFM in glaucomatous and nonglaucomatous eyes unilaterally. I evaluated the quantitative characteristics of the RPC using OCT-A.

In the context of XFG pathogenesis, although the clogged outflow of trabecular meshwork and elevated IOP dominate its pathophysiology, there are important studies indicating the involvement of other mechanisms. Several studies that also control for the effect of the IOP (e.g., including normotensive eyes in the study) have shown that the presence of XFM is associated with higher rates of glaucoma conversion[12,13] and progression.[14] Based on these studies, I can assert that XFM is an independent risk factor for the prevalence of glaucomatous neuropathy at all IOP levels, and different associations that may contribute to the XFG process should

Table 3. Radial peripapillary capillary Vessel Density (%) Differences Between the Participants with Unilateral Pseudoexfoliation Syndrome and Pseudoexfoliation glaucoma

	Unilateral XFS			Unilateral XFG			Kruskal–Wallis Comparison	
	XFM (+) Eyes	XFM (–) Eyes	*P*	XFM (+) Eyes	XFM (–)	*P*	3 Groups	4 Groups
RPC vessel density sup (%)	50.33 ± 5.46	52.46 ± 3.73	.12	37.58 ± 11.02	50.05 ± 6.06	**.0001**	.19	**.0001**
inf (%)	52.96 ± 3.98	52.92 ± 5.62	.98	37.63 ± 11.58	50.68 ± 5.51	**.0001**	.1273	**.0001**
temp (%)	51.13 ± 4.98	50.21 ± 4.11	.49	45.47 ± 7.89	45.74 ± 6.44	.911	**.02**	**.0072**
nasal (%)	51.71 ± 7.18	54.33 ± 5.80	.17	38.26 ± 11.58	54.42 ± 7.99	**<.0001**	.7	**.0004**
sup hemifield (%)	51.58 ± 3.12	51.50 ± 3.56	.93	39.63 ± 8.73	50.32 ± 5.39	**.0001**	.7491	**.0001**
inf hemifield (%)	51.79 ± 3.50	52.17 ± 2.87	.69	39.00 ± 8.52	49.74 ± 4.49	**<.0001**	.0649	**.0001**

The Kruskal–Wallis comparison for 3 groups consists of unilateral XFS's both eyes (XFM+ and XFM–) and unilateral XFG group's XFM– eye.
The Kruskal–Wallis comparison for 4 groups consists of unilateral XFS's and XFG's both eyes (XFM+ and XFM–). Values in bold indicate statistical significance.
inf, inferior quadrant; inf hemifield, inferior hemifield; I, sup-hemifield, superior hemifield; RPC, radial peripapillary capillary; sup, superior quadrant; temp, temporal quadrant; XFG, pseudoexfoliation glaucoma; XFM, pseudoexfoliation material; XFS, pseudoexfoliation syndrome.

Table 4. Retinal Nerve Fiber Layer Thickness (µm) and Radial Peripapillary Capillary Vessel Density(%) Correlations

	Unilateral XFS				Unilateral XFG			
	Correlation for XFM+	*P*	Correlation for XFM–	*P*	Correlation for XFM+	*P*	Correlation for XFM–	*P*
Superior- quadrant	0.911896206	**<.0001**	0.919005005	**<.0001**	0.943515818	**<.0001**	0.978430987	**<.0001**
Inferior quadrant	0.293848736	.13	0.548777257	**.003**	0.787228712	**<.0001**	0.659885825	**.0002**
Temporal quadrant	0.331777696	.09	0.396071778	**.0409**	0.861316313	**<.0001**	0.461661103	**.0153**
Nasal quadrant	0.153821737	.45	0.386195252	**.0467**	0.394121348	**.042**	-0.040519072	.841
Superior hemisphere	0.367162574	**.05**	0.028483643	.8882	0.527168007	**.0047**	0.494490739	**.0087**
Inferior hemisphere	0.465269453	**.0145**	0.68598406	**.0001**	0.795977789	**<.0001**	0.685279381	**.0001**

Values in bold indicate statistical significance.
XFG, pseudoexfoliation glaucoma; XFM, pseudoexfoliation material; XFS, pseudoexfoliation syndrome.

be analyzed thoroughly from different perspectives. One such perspective is the detection of vascular involvement of the eyes with XFM using OCT-A.[11,15-19]

When I compared the sector-wise retinal nerve fiber layer thickness between the paired eyes of the unilateral exfoliation syndrome (XFS) group, I did not find any significant differences. However, when I compared the 3 nonglaucomatous eyes using the Kruskal–Wallis test, I found some differences that were affected by the presence of XFG in the fellow eye (as shown in Table 2). It has been demonstrated that RNFL thickness is a strong indicator for detecting glaucoma.[20] As expected, the eyes diagnosed as nonglaucomatous even with XFM were mostly similar in RNFL thickness, while glaucomatous eyes were significantly different from them (as shown in Table 2). I also examined the RPC vd in the same groups and anatomic locations to identify any vascular dropout, in line with the thinning of the RNFL. However, I did not find any significant differences in the RPC vd measurements, except for the temporal quadrant, in non-glaucomatous eyes (as shown in Table 3).

Previous studies have suggested that a decrease in vd is an early event in glaucomatous damage before detectable visual field loss.[21,22] Therefore, I hypothesized that if vasculature dropout occurs early in glaucoma, XFM, which has vascular affinity and is a major risk factor for glaucoma, could be an indicator of vascular pathogenesis. However, I did not find any significant evidence of RPC vd changes in nonglaucomatous eyes, even with XFM. I then compared RPC vd in 10 divided parts to identify any specific changes and found that eyes with XFG had significantly decreased vd. Among non-glaucomatous eyes, differences were observed only in the nasal inferior region.

Multiple studies have suggested that vascular dysfunction plays a role in the pathogenesis of glaucoma, and previous research has shown that XFM accumulates in vascular endothelial cells, smooth muscle cells, and pericytes, leading to microcirculation impairment.[23] However, the present study did not provide strong evidence in this context, leading one to consider the possibility that XFM may have greater affinity for larger vessels than peripapillary capillaries. Supporting this, Suwan et al[24] observed a progressive decrease in perfused capillary density from controls to XFS to XFG, while Simsek et al[15] found differences in choroidal vascularity index between XFM-positive and negative eyes in a study of unilateral XFS patients. Dikmetaş et al[16] conducted a study similar to the current paper, but with a different device, and found a significantly lower flow index in the nasal region of eyes with XFS compared

Table 5. Radial Papillary Capillary Vessel Density (%) Differences between the Participants with Unilateral Pseudoexfoliation Syndrome and Pseudoexfoliation Glaucoma in Ten Segments

	Unilateral XFS			Unilateral XFG				
	XFM (+)	XFM (–)	*P*	XFM+	XFM–	*P*	3 Groups	4 Groups
Whole image	48.88 ± 2.37	49.80 ± 2.40	.18	38.76 ± 6.10	47.09 ± 3.94	**<.0001**	.19	**0.0001**
Inside disc	47.88 ± 4.89	50.06 ± 3.72	.09	45.83 ± 5.67	45.58 ± 4.97	.88	0.27	**0.01**
Peripapillary	51.69 ± 3.04	51.79 ± 3.02	.91	39.39 ± 8.32	50.03 ± 4.80	**<.0001**	0.32	**0.0001**
Superior hemi	51.55 ± 3.21	51.47 ± 3.51	.93	39.78 ± 8.75	50.31 ± 5.34	**.0001**	0.82	**0.0001**
Inferior hemi	51.75 ± 3.53	52.12 ± 2.87	.69	38.99 ± 8.55	49.71 ± 4.47	**<.0001**	0.05	**0.0001**
Nasal sup	48.48 ± 4.84	49.18 ± 4.52	.61	35.92 ± 8.77	48.78 ± 4.42	**<.0001**	0.77	**0.0001**
Nasal inf	48.23 ± 3.45	48.27 ± 2.67	.96	36.00 ± 8.88	43.22 ± 5.21	**.0042**	**0.02**	**0.0001**
inf nasal	51.02 ± 5.81	52.62 ± 3.91	.27	34.41 ± 13.03	50.15 ± 6.40	**<.0001**	0.17	**0.0001**
inf temp	57.28 ± 5.76	58.34 ± 5.47	.52	40.63 ± 13.15	57.38 ± 5.49	**<.0001**	0.74	**0.0001**
Temp inf	51.93 ± 4.24	50.95 ± 4.70	.45	46.06 ± 6.37	50.36 ± 5.59	**.0334**	0.71	**0.005**
Temp sup	54.97 ± 3.45	54.80 ± 3.80	.87	48.70 ± 8.25	52.75 ± 6.08	.0938	0.33	**0.0229**
sup temp	54.77 ± 4.12	54.32 ± 5.29	.75	40.06 ± 12.82	52.53 ± 8.61	**.0012**	0.88	**0.0001**
sup nasal	49.08 ± 4.25	48.28 ± 4.70	.54	35.06 ± 11.18	47.74 ± 6.93	**.0002**	0.77	**0.0001**

The Kruskal–Wallis comparison for 3 groups consists of: unilateral XFS's both eyes (XFM+ and XFM–) and unilateral XFG group's XFM-eye.
The Kruskal–Wallis comparison for 4 groups consists of unilateral XFS's and XFG's both eyes (XFM+ and XFM–). Values in bold indicate statistical significance.
inf, inferior quadrant; inf hemifield, inferior hemifield; I, sup-hemifield, superior hemifield; RPC, radial peripapillary capillary; sup, superior quadrant; temp, temporal quadrant; XFG, pseudoexfoliation glaucoma; XFM, pseudoexfoliation material; XFS, pseudoexfoliation syndrome.

to fellow XFM-free eyes. Finally, Göker et al[18] also observed lower RPC vd in XFM-positive eyes compared to fellow eyes in a study of unilateral XFS.

There may be several reasons for the conflicting results in the literature. Firstly, the use of different imaging tools and demographic differences in the patient population may have influenced the findings. For instance, Rebolleda et al[25] showed that AngioVue provided better performance in measuring vascular variables compared to AngioPlex. In this study, I used AngioVue for measurements, which is a strength of the present study. Secondly, bias in the categorization of XFS in different studies could also play a role. Studies similar to the current study have reported differences in both vascular density and RNFL thickness between eyes in unilateral XFS conditions.[15-18] However, in the present study, I did not find any significant differences between the paired eyes of participants with unilateral XFS. This discrepancy may be related to the gray zone of the glaucomatous process in the pre-perimetric stage. In the present study, I excluded participants in the gray zone if there was RNFL or optic disc asymmetry between the eyes. In my opinion, the co-occurrence of RNFL and vascular density decline supports the possibility of glaucomatous damage. However, at this point, the sequence of RNFL damage and vascular dropout remains unexplainable. Based on the results reported in the current paper, I did not find evidence of peripapillary microvascular changes in the presence of XFM in the absence of glaucomatous processes.

This study has several limitations. First, the relatively small number of participants and the cross-sectional design of the study may have limited the power of the findings. Secondly, the high proportion of elderly participants may have restricted my ability to adjust for the effects of aging. Thirdly, although I only recruited participants with a limited range of refractive errors, I did not measure axial length, and some participants were pseudophakic. Axial elongation is known to stretch the retina and may result in changes in microvascular density.[26] Fourth, the use of medications for glaucoma control can also affect some of our results. Lastly, the cross-sectional design of this study prevented us from following participants over time, which limited my ability to detect progressive changes over time.

Conclusion

In conclusion, the aim of this study was to investigate the impact of visible XFM on the RPC vd. However, the current study did not provide strong evidence of causality between vd and XFM. Therefore, there is a need for prospective studies to determine the potential of OCT-A as a diagnostic parameter for predicting glaucomatous progression.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of the Şişli Hamidiye Etfal Research and Training Hospital (Approval No: 4291, Date: April 5, 2021).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Declaration of Interests: The author has no conflicts of interest to declare.

Funding: The author declared that this study received no financial support.

Data Access Statement: The data are available upon request from the author.

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