# The Relationship Between Optic Nerve Head and Peripapillary Vascular Densities and Visual Field Analysis in Open Angle Glaucoma

*Ahmet Kaderli[1], Sinem Karabulut[2], Sema Tamer Kaderli[2], Cansu Kaya[3], Aylin Karalezli[4]*

## ABSTRACT

**Purpose:** To correlate optic nerve head and peripapillary micro-vascular changes as detected by optical coherence tomography angiography (OCT-A) with visual field (VF) deviation parameters and retinal nerve fiber layer (RNFL) thickness in open angle glaucoma.

**Materials and Methods:** Forty-eight eyes of 48 patients with primary open angle glaucoma (POAG) and 46 eyes of 46 patients with pseudoexfoliation glaucoma (PEG) were included in the study. Total, intra-disc and peripapillary (all quadrants) vascular densities (VD) were evaluated with OCT-A. All patients underwent 24-2 standard automated perimetry and mean deviation (MD) -pattern standard deviation (PSD) values were obtained. Patients with optic nerve pathologies, intraocular pressure ≥25mmHg and media opacities were excluded from the study.

**Results:** The VF MD values were negatively correlated with all OCT-A parameters in POAG and with all quadrants other than intra-disc and nasal-inferior quadrant in PEG. While there was a significant negative correlation between PSD and total image, peripapillary, nasal-inferior, inferior-nasal, inferior-temporal, temporal-inferior, temporal-superior and superior-temporal quadrants in POAG, there was no significant correlation in any parameters other than intra-disc in PEG. When RNFL and OCT-A values were considered, significant positive correlation was detected in all peripapillary micro-vascular parameters other than intra-disc capillary density in both POAG and PEG groups and the temporal-superior quadrant in POAG group.

**Conclusion:** The significant correlation between VF MD value and peripapillary and optic nerve head VD measurements detected by OCT-A value may indicate that OCT-A measurements in the most common glaucoma types may be a potential biomarker in terms of glaucomatous functional damage.

**Keywords:** Optical Coherence Tomography Angiography; Peripapillary Vascular Densities; Visual Field.

## INTRODUCTION

Glaucoma is a progressive optic neuropathy characterized by several visual field (VF) defects, which affects more than 60 million people worldwide.[1] Although various treatment modalities are used to decrease progression rate in cases with glaucoma, progression rate shows individual variations. Identification of risk factors for glaucoma progression is important for follow-up and individualization of treatment. To date, there is limited number of clinical studies linking glaucoma progression with vascular factors due to insufficiency of available methods for assessment of vascular content of glaucoma.[2 3]

Micro-vascularity can be demonstrated in both qualitative and quantitative manner by introduction of optical coherence tomography angiography (OCT-A) and perfusion state can be assessed in different retinal layers. Previous studies showed relationship of focal losses in choroidal micro-vascularity and VF defects in myopic eyes with choroidal micro-circulation defect in progressive glaucoma involving disk hemorrhage.[4,5] These results revealed clinical relevance of OCT-A in the assessment of glaucoma. In this study, it was aimed to assess relationship between VF mean deviation (MD), pattern standard deviation (PSD), retinal nerve fiber layer (RNFL) thickness

1- Assistant Prof., Muğla Sıtkı Koçman University, Ophthalmology, Muğla, Turkey
2- MD., Muğla Sıtkı Koçman University, Research and Training Hospital, Ophthalmology, Muğla, Turkey
3- MD., Muğla Sıtkı Koçman University, Ophthalmology, Muğla, Turkey
4- Prof., Muğla Sıtkı Koçman University, Ophthalmology, Muğla, Turkey

**Received:** 04.11.2020
**Accepted:** 20.03.2021

*Glo-Kat 2021; 16: 113-117*

DOİ: 10.37844/glauc.cat.2021.16.19

**Correspondence Adress:**
Ahmet Kaderli
Muğla Sıtkı Koçman University, Ophthalmology, Muğla, Turkey

**Phone:** +90 506 719 7619
**E-mail:** akaderli@hotmail.com

and optic nerve head-peripapillary vascular densities as measured by OCT-A in primary open angle glaucoma (POAG) and pseudo-exfoliation glaucoma (PEG).

## MATERIAL AND METHOD

This cross-sectional, observational study included 48 eyes of 48 patients with POAG and 46 eyes of 46 patients with PEG, who were followed at Ophthalmology Department of Research and Training Hospital, Muğla Sıtkı Koçman University between January, 2018 and May, 2020.

The study was approved by Ethics Committee of Muğla University (21.05.2020/200142) and conducted in accordance to tenets of Helsinki Declaration.

A through ophthalmological examination including best-corrected visual acuity (BCVA), slit-lamp examination, IOP measurement by Goldmann applanation tonometry, central corneal thickness measurement, gonioscopy and dilated fundus examination was performed in all patients. The VF testing was performed by Humphrey Field Analyzer (Carl Zeiss Meditec740i, Inc., Dublin, CA, USA) using SITA 24-2 algorithm. Only reliable tests (<15% of false-positive and false-negative rate; <%20 of fixation losses) were included to the study. The RNFL measurement were performed using optical coherence tomography (OCT; Zeiss Cirrus HD-OKT, Zeiss Meditec. Inc, Germany).

OCT-A images were captured by spectral domain OCT system (AngioVue Software Version 2017.1.0.134, Optovue, Fremont, USA) using angiographic platform that allows anatomic and functional analyses. By 840 nm super-luminescent diode, 70,000 A-screens per second was captured. SSADA algorithm ensured optimization of vascular data by eliminating reflectance amplitude values secondary to erythrocyte motion from consecutive B-screens. Peripapillary OCT-A screen (4.5 mm x 4.5 mm) centered over optic disc was used. Capillary density was measured from internal limiting membrane including radial branches of peripapillary vessels to posterior margin of RNFL. The software version 2017.1.0.134 created a sectoral capillary density map by placing an annular ring (750 µm in diameter) in an automated manner. The capillary density was presented as percent by calculating ratio for areas of blood vessels with blood flow. A single researcher (A.K) assessed OCT-A images for signal power, segmentation errors, fixation errors and motion artifact.

The diagnosis of POAG was made based on open angle in gonioscopy, typical glaucomatous optic disc appearance in fundus examination, glaucomatous RNFL thinning on OCT and VF findings while the diagnosis of PEG was made based on observation of exfoliation material on slit-lamp examination and gonioscopy in addition to above-mentioned findings.

The inclusion criteria were spherical refractive error between -5D and +3D and cylindrical refractive error<3DD in addition to imaging studies with reliable results. The exclusion criteria were presence of systemic diseases such as diabetes mellitus and hypertension, active smoking, history of ocular surgery other than uncomplicated cataract surgery, retinal disease, non-glaucomatous optic neuropathy, media opacities which can impair image quality and IOP>25 mmHg during measurements.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 21.0.0.0 (IBM Corporation and other(s) 1989, 2012). For continuous variables, distribution was assessed using histogram and Shapiro Wilk W normality. The PEG data with normal distribution was assessed using Pearson's correlation analysis while POAD data with skewed distribution by Spearman's correlation analysis. Demographic characteristics are presented as mean±standard deviation for continuous data whereas percent for categorical variables. Numerical demographic variables with normal distribution were assessed using Student's test while categorical variables were assessed using Chi-square test. A p value<0.05 was considered as statistically significant.

## FINDINGS

The study included 48 eyes of 48 patients in POAG group and 46 eyes of 46 patients in PEF group. Mean age was 65.42±8.29 years in POAG group whereas 67.59±6.70 in PEG group. No significant differences were detected in age, gender, laterality, BCVA, number of medications and IOP between POAG and PEG groups (Table 1).

**Table 1:** *Demographic characteristics of participants.*

| | POAG (n=48) | PEG (n=46) | p |
|---|---|---|---|
| Age (years) | 65.42±8.29 | 67.59±6.7 | 0.167 |
| Gender (F/M) | 26/22 | 25/21 | 0.575 |
| Laterality (right/left) | 24/24 | 24/22 | 0.498 |
| BCVA (logmar) | 0.09±0.32 | 0.11±0.28 | 0.744 |
| Number of Agents Used | 2.35±1 | 2.20±0.9 | 0.429 |
| IOP | 15.38±3.9 | 16±2.1 | 0.349 |

POAG: Primary Open Angle Glaucoma, PEG: Pseudo-exfoliation, BCVA: Best-corrected visual acuity, IOP: Intraocular pressure, Age, BCVA, number of agents used and IOP are presented as mean±standard deviation

When all optical nerve head and peripapillary vessel densities as measured by OCT-A were considered, no significant difference was detected between POAG and PEG. Mean RNFL and VF MD values were comparable between groups while PSD was significantly higher in POAG group than PEG group (Table 2).

In the POAG group, all optic nerve head and peripapillary vessel densities showed significant negative correlation with VF MD value. Again, RNFL value showed a significant positive correlation in all parameters other than intra-disc and superior quadrant while VF PSD showed significant negative correlation in total image, peripapillary, nasal-inferior, inferior-nasal, inferior-temporal, temporal-inferior, temporal-superior and superior-temporal quadrants in the POAG group (Table 3).

In the PEG group, VF-MD showed significant correlation with OCT-A parameters other than intra-disc and nasal-inferior quadrant vessel density while RNFL showed a significant correlation with OCT-A parameters other than intra-disc vessel density. No significant correlation was detected between VF PSD parameter and OCT-A parameters other than intra-disc vessel density (Table 4).

**Table 2:** *Comparison of mean OCT-A, visual field and OCT between glaucoma groups.*

| | Mean±standard deviation | | |
|---|---|---|---|
| | **POAG** | **PEG** | **p value** |
| Total image (%) | 44.4±6.9 | 43.7±6.0 | 0.639 |
| Intra-disc (%) | 50.0±8.1 | 49.9±5.0 | 0.921 |
| Peripapillary (%) | 45.6±8.1 | 44.5±7.6 | 0.515 |
| Superior hernia (%) | 46.1±10.1 | 44.9±8.2 | 0.538 |
| Inferior hernia (%) | 44.2±8.9 | 44.1±7.2 | 0.968 |
| Nasal-superior (%) | 44.3±8.9 | 42.1±7.9 | 0.216 |
| Nasal-inferior (%) | 41.4±8.4 | 41.9±6.7 | 0.780 |
| Inferior-nasal (%) | 41.1±12.7 | 41.7±9.9 | 0.785 |
| Inferior-temporal (%) | 46.7±13.2 | 47.8±12.5 | 0.698 |
| Temporal-inferior (%) | 48.6±7.3 | 46.4±7.8 | 0.169 |
| Temporal-superior (%) | 52.6±6.3 | 49.8±7.2 | 0.055 |
| Superior-temporal (%) | 48.1±10.1 | 47.4±10 | 0.741 |
| Superior-nasal (%) | 43.1±11.9 | 41.1±10.5 | 0.388 |
| Mean deviation (dB) | 8.0±6.5 | 7.2±7.2 | 0.603 |
| Pattern Standard Deviation (dB) | 6.4±3.8 | 3.9±2.4 | 0.000 |
| Mean RNFL (µm) | 85.5±15.6 | 86.7±16.9 | 0.741 |

POAG: Primary open angle glaucoma, PEG: Pseudo-exfoliation glaucoma, dB: Decibel. dB: RNFL: retinal nerve fibre layer

**Table 3:** *Correlation of OCT-A vascular densities with visual field and RNFL in POAG.*

| | | Total image | Intra-disc | Peri-papillary | sup. hernia | inf. hernai | nasal. sup | nasal. inf | inf. nasal | inf. temp | temp. inf | temp. sup | sup. tempo | sup. nasal |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean Deviation** | Spearman's rho correlation | -.501 | -.399 | -.485 | -.383 | -.487 | -.289 | -.394 | -.404 | -.484 | -.459 | -.412 | -.451 | -.344 |
| | p | **.000** | **.005** | **.000** | **.007** | **.000** | **.046** | **.006** | **.004** | **.000** | **.001** | **.004** | **.001** | **.017** |
| **Pattern standard deviation** | Spearman's rho correlation | -.428 | -.278 | -.388 | -.262 | -.423 | -.174 | -.406 | -.393 | -.385 | -.336 | -.335 | -.400 | -.257 |
| | p | **.002** | .056 | **.006** | .072 | **.003** | .237 | **.004** | **.006** | **.007** | **.019** | **.020** | **.005** | .078 |
| **RNFL** | Spearman's rho correlation | .627 | .182 | .597 | .582 | .590 | .649 | .594 | .592 | .376 | .405 | .198 | .538 | .614 |
| | p | **.000** | .215 | **.000** | **.000** | **.000** | **.000** | **.000** | **.000** | **.008** | **.004** | .177 | **.000** | **.000** |

*Significant values are marked as bold, POAG: Primary open angle glaucoma, RNFL: Retinal Nerve Fiber Layer, OCT-A: Optical coherence tomography angiography.

**Table 4:** *Correlation of OCT-A vascular densities with visual field and RNFL in PEG.*

| | | Total image | Intra-disc | peri-papiller | sup. hernia | inf. hernia | nasal. sup | nasal. inf | inf. nasal | inf. temp | temp. inf | temp. sup | sup. tempo | sup. nasal |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean Deviation** | Pearson Correlation (r) | -.615 | -.286 | -.621 | -.630 | -.580 | -.567 | -.244 | -.490 | -.588 | -.468 | -.582 | -.634 | -.554 |
| | p | **.000** | .054 | **.000** | **.000** | **.000** | **.000** | .102 | **.001** | **.000** | **.001** | **.000** | **.000** | **.000** |
| **Pattern Standard Deviation** | Pearson Correlation (r) | -.114 | -.492 | -.051 | -.071 | -.028 | -.012 | .230 | .019 | -.330 | .103 | -.034 | -.142 | -.075 |
| | p | .449 | **.001** | .736 | .641 | .852 | .936 | .125 | .901 | .025 | .497 | .823 | .346 | .622 |
| **RNFL** | Pearson Correlation (r) | .881 | .232 | .867 | .837 | .866 | .832 | .732 | .764 | .698 | .520 | .725 | .752 | .787 |
| | p | **.000** | .120 | **.000** | **.000** | **.000** | **.000** | **.000** | **.000** | **.000** | **.000** | **.000** | **.000** | **.000** |

*Significant values are marked as bold, PEG: Pseudo-exfoliation glaucoma, RNFL: Retinal Nerve Fiber Layer

## DISCUSSION

Recent studies have shown that there is more structural and micro-vascular damage in POAG when compared to health eyes and those with suspected glaucoma.[6, 7] Yarmohammadi et al.[6] suggested that there is a strong correlation between decreased peripapillary vascular density and global VF damage and that the correlation is stronger than relationship between RNFL and VF. In a study by Shin et al.[8] it was found that there was a significant, strong correlation between moderate-to-severe peripapillary vascular density and visual field sensitivity in glaucoma regardless of subtype. In early stage, the correlation was found to be significant in only superotemporal and inferotemporal quadrants which are more sensitive to glaucomatous injury. However, the vascular-functional relationship hasn't been studied in pseudo-exfoliation glaucoma in detail. In our study, as similar to PAOG, it was found that there was a significant correlation between VF MD and peripapillary vascular density in almost all quadrants in PEG. This shows that OCT-A parameters may be a novel alternative that demonstrate global damage in glaucoma. Again, lack of significant correlation between PSD and vascular density suggests that, in detection of localized defects, OCT-A may not be as successful as detecting global damage.

In our study, the relationship between structural state and vascular density was also assessed. Mean RNFL value was showed a significant correlation with all optic nerve head and peripapillary vascular densities. Similarly, in a study by Enders et al.[9] it was shown that conventional morphometric parameters had significant, positive correlation with peripapillary vascular density (p=0.013) Again, in the study by Shin et al.[8] a significant, positive correlation was found between vascular densities and RNFL values; however, unlike our study, the correlation was found to be stronger between global vascular density and VF values. It is well-known that circumpapillary RNFL thickness showed a base effect by disease progression to advanced glaucomatous damage. As a result, it becomes more challenging to detect in morphometric manner when reached to glaucoma progression reached base value.[10-11] In such case, visual field testing are preferred to OCT in advanced glaucoma.[12] However, visual field tests may show broad range of fluctuations in patients with advanced glaucoma, making it difficult to detect true glaucomatous change.[13] Thus, positive correlation detected between RNFL and vascular densities shows that OCT-A vascular density parameters may be one of the variables to monitor progression in glaucoma.

## LIMITATIONS

This study has some limitation including retrospective design and addressing visual field output and OCT-A images in a generalized manner rather than sectoral assessment by Garway-Heath map.[14] In addition, due to significant variations, comparability and reproducibility are still limited in OCT-A studies.[15] Moreover, it is highly important which retinal layers are considered while determining vascular density. Addressing these approaches will ensure standardization of outcomes by decreasing potential projection artifacts and facilitating segmentation of retinal layers.

## CONCLUSION

In conclusion, optic nerve head and peripapillary vascular densities as assessed by OCTA-A showed negative correlation in VF MDA in most common subtypes of open angle glaucoma. The OCT-A should be considered as a tool that may help clinician for monitoring progression in generalized, glaucomatous damage.

## REFERENCES


1. Leske MC. Open-angle glaucoma -- an epidemiologic overview. Ophthalmic Epidemiol 2007; 14:166-72.
2. Sung KR, Cho JW, Lee S, et al. Characteristics of visual field progression in medically treated normal-tension glaucoma patients with unstable ocular perfusion pressure. Invest Ophthalmol Vis Sci 2011; 52:737-43.
3. Ahrlich KG, De Moraes CG, Teng CC, et al. Visual field progression differences between normal-tension and exfoliative high-tension glaucoma. Invest Ophthalmol Vis Sci 2010; 51:1458-63.
4. Park HL, Kim JW and Park CK. Choroidal Microvasculature Dropout Is Associated with Progressive Retinal Nerve Fiber Layer Thinning in Glaucoma with Disc Hemorrhage. Ophthalmology 2018; 125:1003-13.
5. Park HL, Jeon SJ and Park CK. Features of the Choroidal Microvasculature in Peripapillary Atrophy Are Associated With Visual Field Damage in Myopic Patients. Am J Ophthalmol 2018; 192:206-16.
6. Yarmohammadi A, Zangwill LM, Diniz-Filho A, et al. Optical Coherence Tomography Angiography Vessel Density in Healthy, Glaucoma Suspect, and Glaucoma Eyes. Invest Ophthalmol Vis Sci 2016; 57:OCT451-459.
7. Triolo G, Rabiolo A, Shemonski ND, et al. Optical Coherence Tomography Angiography Macular and Peripapillary Vessel Perfusion Density in Healthy Subjects, Glaucoma Suspects, and Glaucoma Patients. Invest Ophthalmol Vis Sci 2017; 58:5713-22.
8. Shin JW, Lee J, Kwon J, et al. Regional vascular density-visual field sensitivity relationship in glaucoma according to disease severity. Br J Ophthalmol 2017; 101:1666-72.
9. Enders P, Longo V, Adler W, et al. Analysis of peripapillary vessel density and Bruch's membrane opening-based neuroretinal rim parameters in glaucoma using OCT and OCT-angiography. Eye (Lond) 2019.
10. Asrani S, Essaid L, Alder BD, et al. Artifacts in spectral-domain optical coherence tomography measurements in glaucoma. JAMA Ophthalmol 2014; 132:396-402.
11. Bayer A and Akman A. Artifacts and Anatomic Variations in Optical Coherence Tomography. Turk J Ophthalmol 2020; 50:99-106.
12. Leite MT, Zangwill LM, Weinreb RN, et al. Structure-function relationships using the Cirrus spectral domain optical coherence tomograph and standard automated perimetry. J Glaucoma 2012; 21:49-54.
13. Rao HL, Senthil S, Choudhari NS, et al. Behavior of visual field index in advanced glaucoma. Invest Ophthalmol Vis Sci 2013; 54:307-12.
14. Garway-Heath DF, Poinoosawmy D, Fitzke FW, et al. Mapping the visual field to the optic disc in normal tension glaucoma eyes. Ophthalmology 2000; 107:1809-15.
15. Allegrini D, Montesano G, Fogagnolo P, et al. The volume of peripapillary vessels within the retinal nerve fibre layer: an optical coherence tomography angiography study of normal subjects. Br J Ophthalmol 2018; 102:611-21.