The Egyptian Journal of Hospital Medicine (July 2023) Vol. 92, Page 6527- 6534

Assessment of Macular & Peripapillary Microvasculature Using Optical Coherence Tomography-Angiography in Primary Open-Angle Glaucoma Patients

Omar Mohamed Sharaf, Mohamed Al-Sebaey Shahin, Mohamed Mounir Mohamed
Department of Ophthalmology, Faculty of Medicine, Suez Canal University, Egypt
***Corresponding author:** Omar M. Sharaf, **Mobile:** (+20) 01069933688, **E-Mail:** docomarsharaf@gmail.com

ABSTRACT

Background: Glaucoma pathogenesis is related to vascular affection. Optical coherence tomography-angiography (OCT-A) is the latest noninvasive imaging techniques for studying the retinal vasculature, optic nerve, and peripapillary region. Glaucoma is related to the reduction of ocular blood flow.

Objective: Assessment of the retinal microvasculature changes including the vascular density of macular and radial peripapillary capillary (RPC) in eyes with primary open-angle glaucoma (POAG) using OCT-A.

Subjects and Methods: The study included 44 eyes that were divided into two groups. **Group 1** included 22 eyes healthy subjects as control group and **group 2** that contained 22 eyes of POAG patients. All were subjected to history, complete ophthalmological examination including refraction, BCVA, slit-lamp, indirect ophthalmoscopy, gonioscopy, applanation tonometry. Investigations were applied; Visual Field (Carl Zeiss Humphrey A3), OCT, retinal nerve fiber layer thinning (RNFLT) & ganglion cell complex (GCC) thickness. (Triton, Topcon) and study tool Swept-Source OCT-A. (Triton, Topcon). Quantitative analysis software; GNU Image Manipulation Program (GIMP). Program V.2.10.8 software.

Results: The results showed a statistically significant decrease in vessel density (VD) in the peripapillary region ($P<0.001$) and both, superficial ($P<0.001$) and deep ($P=0.001$) macular regions in POAG subjects. So, the functional damage (VD) was associated with more pronounced structural damage (RNFLT, GCC).

Conclusion: The peripapillary and superficial macular VD outperformed the deep macular VD, as a diagnostic test differentiating between POAG and healthy eyes. The present study found the OCT-A assessment of peripapillary, and macular VD have a good value in monitoring of microcirculation changes in POAG & explaining the relationship between ocular microcirculation and glaucoma pathophysiology.

Keywords: Primary open angle glaucoma, Optical coherence tomography-angiography.

INTRODUCTION

Primary open-angle glaucoma (POAG) is a chronic progressive optic neuropathy characterized by elevated intraocular pressure (IOP) with development of retinal ganglion cells (RGC) damage, leading to retinal nerve fiber layer (RNFL) thinning and visual field (VF) defects at normal wide anterior chamber angles in both eyes [(1)].

Despite glaucoma is the leading cause of irreversible global blindness affect more than 110 million people by 2040 worldwide, its etiology is not fully explained. The population-based survey and published tables reported that the prevalence of documented glaucoma patients in Egypt was 2% in urban and 9% in rural population. POAG is the most common form of glaucoma accounting for 90% of all glaucoma cases [(2)].

It has been recognized that elevated IOP exerts direct mechanical damage to the optic nerve head (ONH). However, among glaucoma patients, only one-third to half have elevated IOP at the initial stages. In some, VF loss continues despite adequate IOP control to normal levels [(3)].

The 'vascular theory' of glaucoma hypothesizes RGC loss due to insufficient blood supply, increasing evidence that glaucoma pathogenesis can be partly vascular dysfunction of the ONH and peripapillary retina [(4)].

The radial peripapillary capillary (RPC) layer is a distinct capillary network within the RNFL, supplying the axons of RGCs. The macula contains more than 30% of total RGCs. High metabolic requirements of these RGCs depend on the macular capillary vasculature. So, assessment of RPC and macular vessel density has a role in early detection of glaucomatous damage [(5)].

Recently optical coherence tomography angiography (OCT-A) has been used to quantify the affection of macular and peripapillary microvasculature in eyes in POAG with excellent repeatability and reproducibility by rapid and noninvasive technique, which satisfy metabolic and nutritional demands of RGC and RNFL [(6-7)].

So, the gap of knowledge that were conduct in this study was related to assess RPC and macular VD in POAG patients at Suez Canal university hospitals by OCT-A.

The aim of the present study was to assess retinal microvasculature changes including macular and RPC VD in eyes with POAG using OCT-A.

PATIENTS AND METHODS

This study was carried out as a comparative case-control study design. The study was conducted at Suez Canal University Hospitals and was investigated under supervision of the co-directors. Full counseling of all participants in this study and informed consent was obtained. The privacy of patients and confidentiality of data were preserved.

Received: 06/03/2023
Accepted: 03/05/2023

Inclusion criteria: • Older than 20 y old and less than 70 y. • Open angles on gonioscopy. • Best-corrected visual acuity (BCVA) of 1/60 or better.
Control criteria: (1) IOP < 20 mm Hg without any topical medications, no family history of glaucoma in a first degree of relative, with no history of elevated IOP. (2) Normal appearing optic disc with no abnormal cup disc ratio (C/D R.) < 0.5, and no cup to disc asymmetry greater than 0.15, intact neuro-retinal rim, and normal RNFL and GCC on structural OCT. (3) One reliable within normal VF, as a mean deviation (MD) and pattern standard deviation (PSD) within 95% confidence limits with a glaucoma Hemi-field test (GHT) result within normal limits.

Patients' criteria

The second group for glaucomatous eyes were diagnosed as POAG with ONH changes, bilateral glaucomatous pattern of VF, GHT result outside limits, corresponding RNFL defects and GCC thinning, positive history of IOP lowering medications, and normal wide opened anterior chamber angle in both eyes.

Exclusion criteria:

Errors of refraction more than -6.00 D or +3.00 D, or astigmatic > 3D. Previous ocular intervention, laser and inflammation, or trauma. Topical or systemic steroids treatment. Previous history of ocular or systemic diseases affect the optic nerve. Presence of any retinal pathology. Eyes with media opacity, preventing high-quality imaging. Secondary glaucomatous eye or closure angle glaucoma. Subjects having unreliable VF, poor quality OCTA, or ONH OCT scans.

The study included 44 eyes, divided into 2 groups:
Group 1: 22 eyes of sex and age-matched, healthy persons (control group).
Group 2: 22 eyes of POAG patients.

Methodology:

Clinical data were collected from the two groups. All eyes included in both groups of this study underwent a complete eye examination as:

1. **History taking:**

- Personal data: name, age, sex, address, occupation, and number.
- Family and social history.
- Ocular history: History of previous ocular trauma surgery, medications before examination & history of presenting complaint.

2. **Ophthalmic Examination:**

- Unaided and best corrected visual acuity (BCVA) using Landolt C chart.
- External eye examination, ocular motility & pupil reaction.
- Refraction using autorefractor/keratometry.
- Slit lamp (SL-D7 slit-lamp Topcon Co, Tokyo, Japan) examination to assess the anterior segment by anterior chamber (AC) depth measurement using Van-Herick technique and exclude any media opacity.
- Slit lamp Gonioscopy was carried out using a Goldman three mirror contact lens (Volk Optical, Inc., Mentor, OH) to assess AC angle.
- IOP measurement using Haag Astrid applanation tonometry was taken after instillation of topical anesthetic eye drops; Benoxinate hydrochloride 0.4% solution (Benox, property of EIPICO 2005. Egypt).
- Fundus examination using binocular indirect ophthalmoscope (Model AAIO-7 Appasamy associates 2014, India) and Volk double aspheric +20.00D lens (**Volk optical, Ohio 1988)** after instillation of cyclopenolate 1.0%, two times with 10 minutes' interval, 30 minutes before examination.

3. **Ocular Investigations:**

(A) Visual field test; Central 24-2 full threshold automated static perimetry using ZEISS Humphrey Field Analyzer 3 (HFA3) (Carl Zeiss Meditec AG, Jena, Germany), depended on reliability indices evaluation. Fixation losses, negative errors and false positive (<33%) indices were included.

(B) Structural swept-source- oct (SS-OCT) (Triton, Topcon Co, Tokyo, Japan)
- Vertical C/D Ratio - RNFL thickness
- GCC thickness

(C) Functional SS-OCT-Angiography of peri-papillary and macula

OCT-A is done by Topcon® DRI Triton Plus (Topcon Co, Tokyo, Japan), being a swept source OCT device, it can utilize the signal decorrelation concept to detect the retinal vasculature at a range of retinal thickness.

All subjects underwent a single imaging session with OCT angiography. Measurements were conducted with 6 × 6 mm size centered at the fovea & ONH. Automatic retinal layer segmentation was performed by the software helped to generate a picture of the vascular plexus into superficial and deep vascular plexus (SVP, DVP) through en-face slabs. Superficial VD in the macula was imaged from 3 μm beneath the internal limiting membrane to 15 μm beneath the interface of the inner plexiform layer and inner nuclear layer (IPL/INL) and deep VD was generated from 15 μm to 70 μm beneath IPL/INL.

Technique of OCT angiography scanning was done as follows:
- When dilated, pupil is dilated 20 minutes prior to retinal imaging using Mydriacyl® eye drops (Alcon, Texas, USA) 1-2 drop repeated after five minutes.

- Patient is asked to fixate at the device target and maintain his head and chin resting upon the device head frame.
- Patient would be alerted that the imaging scan taking about 20-30 seconds was be started to attain gaze fixation.
- Cases of poor vision with difficult fixation, an external fixation target was used, OCTA examination was performed by selecting angiography mode from the main menu of the instrument for macular and ONH regions centered 6×6 mm cube, by the same technique as before the patient was asked to fixate the new target then start scanning and we chose the good quality images with high resolution.

Measurements taken by OCT-A device to estimate percentage of:

OCTA scans were centered on the optic disc for RPC VD, represented as a computer-generated map, and measured by percentage in the peripapillary area, then were centered on the macula for SRL & DRL VD and expressed by percentage into different regions (foveal, temporal, superior, nasal, and inferior).

Quantitative Measurements:

Superficial and deep macular and RPC VD were assessed by assessing the VD, which is represented by the ratio of the areas by areas full by vasculature and the results were calculated by The GNU Image Manipulation Program V.2.10.8 (GIMP) software [(8)].

The public available GNU Image Manipulation Program (GIMP) 2.10.8 (http://gimp.org) is a free and open-source raster graphics editor, used to perform quantitative analysis of average pixel density that was determined from the vessels after background subtraction (Photoshop). Briefly, the color threshold was changed to detect the entire vascular network in the scan area. To perform quantitative analysis of the VD, the enface images were "binarized" and vessels were defined as pixels having decor relation values above the threshold level [(9)].

Ethical approval: Faculty of Medicine, Suez Canal University Medical Ethics Committee gave its approval to this study. All participants gave written consents after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

The collected data were revised, coded, tabulated, and analyzed using Statistical Package for Social Science (IBM Corp., Armonk, NY, USA), version 28. Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Mean ± Standard deviation and range for numerical data. Frequency and percentage of non-numerical data. The Chi Square statistic was used for testing relationships between categorical variables such as age and gender of study groups. The independent t-test was used to determine whether there is a statistically significant difference between the means in two unrelated groups (controls and patients' groups). A receiver operating characteristic curve, or ROC curve was used to show connection between clinical sensitivity and specificity for every possible cut-off for the test (peripapillary and macular VDs). In addition, the area under the ROC curve gives an idea about their diagnostic accuracies. P value ≤ 0.05 was considered significant.

RESULTS

The study included 44 eyes of 25 subjects with sex and age-matched and were divided into: Group 1 (22 eyes of 12 healthy controls) and group 2 (22 eyes of 13 cases with POAG).

The mean age of group 1 and 2 was (47.86 ± 12.08 & 51.59 ± 12. 32 years) respectively, with no statistically significant difference (P=0.3). The mean IOP in the diseased eyes was 13.48 ± 2.18 vs.16 ± 3.18 mmHg in the controls (P=0.011). The mean vertical C/D R. was increased in cases group [(0.77 ± 0.12 vs. 0.33 ± 0.1 in the healthy group (P < 0.001)]. We found significant difference in BCVA between normal and POAG group. (P<0.001) with mean BCVA (0.86 ± 0.11 vs 0.4 ± 0.25 respectively)**.** About the mean of whole image of macular VD as shown in table (1), there is a statistically significant difference at superficial (P<0.001) & deep (P=0.001) between controls (group1) and POAG (group2) respectively & in all macular different regions.

Table (1): Superficial & deep macular VD (%) distribution of different segments in study group

	Control				Cases					
	Mean	**SD**	**Minimum**	**Maximum**	**Mean**	**SD**	**Minimum**	**Maximum**	**t value**	**P value**
Whole image Superficial MAC VD	47.56	2.60	40.20	51.30	41.56	1.60	40.70	44.47	10.869	< 0.001
Superior Superficial MAC VD	50.66	2.34	46.40	54.90	44.25	1.86	40.40	46.90	14.211	< 0.001
Inferior Superficial MAC VD	50.24	2.76	45.20	54.60	41.53	2.16	37.90	45.80	16.458	< 0.001
Nasal Superficial MAC VD	44.17	1.99	43.00	51.00	42.82	1.69	39.70	46.10	3.434	0.001
Temporal Superficial MAC VD	44.45	2.29	43.00	51.10	43.13	2.17	39.80	47.10	2.787	0.007
Fovea Superficial MAC VD	12.57	2.19	12.00	26.80	9.80	4.09	4.10	18.20	3.571	0.004
Whole image deep MAC VD	46.76	4.14	40.20	55.97	39.89	2.27	35.23	44.30	13.860	0.001
Superior deep MAC VD	49.82	3.79	43.70	57.10	39.64	2.40	34.70	44.10	17.995	< 0.001
Inferior deep MAC VD	48.02	4.46	42.50	56.80	39.38	2.75	34.70	44.60	14.739	< 0.001
Nasal deep MAC VD	42.30	3.34	40.55	49.80	39.37	2.62	34.70	45.10	3.007	0.003
Temporal deep MAC VD	42.42	4.70	40.00	54.40	39.65	2.37	35.80	45.10	3.486	0.009
Fovea deep MAC VD	20.45	5.10	14.00	30.20	17.21	5.44	10.20	24.10	3.447	0.007

In all eyes of POAG group included in this study, univariate regression analysis showed that the whole image of RPC, macular either superficial or deep had a strong positive correlation with the MD, RNFLT and GCC and detected significant negative correlation with vertical C/D R., as summarized in table (2). The mean of whole image of RPC VD has a severe reduction in cases group vs. controls, with high statistically significant (P < 0.001), as presented in (figure 1).

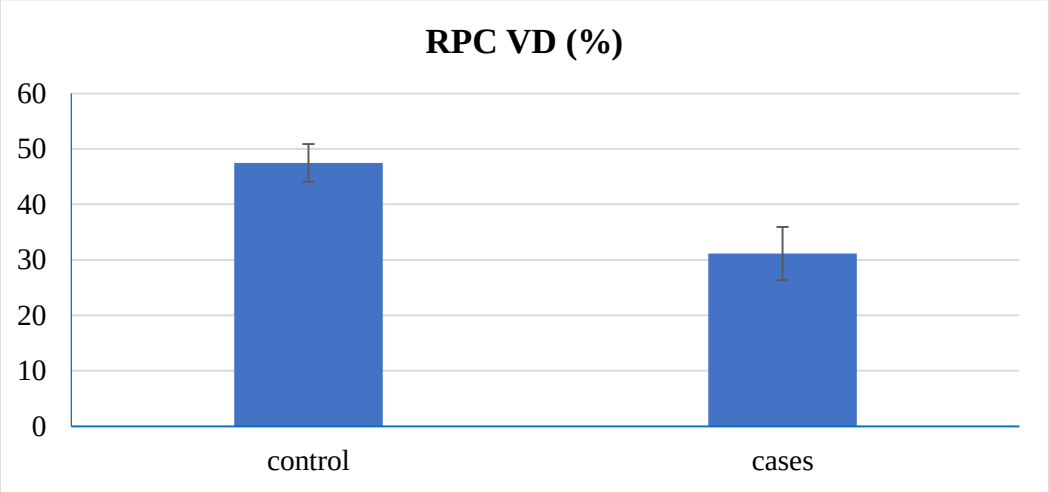

Figure (1): Comparison of study groups according to RPC VD (%).

Table (2): Correlation between superficial macular, deep macular & RPC VD according to VCDR, VFMD, RNFLT & GCCT in POAG cases group

	Whole image of Superficial MAC VD (%)		Whole image of Deep MAC VD (%)		RPC VD (%)	
	R	**P value**	**R**	**P value**	**R**	**P value**
Vertical C/D R.	-0.871	<0.001	-0.815	<0.001	-0.887	< 0.001
MD of VF (dB)	0.897	<0.001	0.878	<0.001	0.915	< 0.001
RNFL (µm)	0.838	<0.001	0.817	<0.001	0.890	< 0.001
GCC (µm)	0.821	<0.001	0.807	<0.001	0.885	< 0.001

The diagnostic values of the mean whole image of RPC VD, superficial & deep macular VD were compared with ROC curves as shown in (figure 2) and table (3). AUC for whole image peripapillary VD, superficial & deep macular VD were (0.995, 0.959 & 0.932) respectively. Further analysis was performed to determine the cut-off value with sensitivity & specificity of the VD for both peripapillary region and macula (SRL, DRL), as expressed with details in table (3).

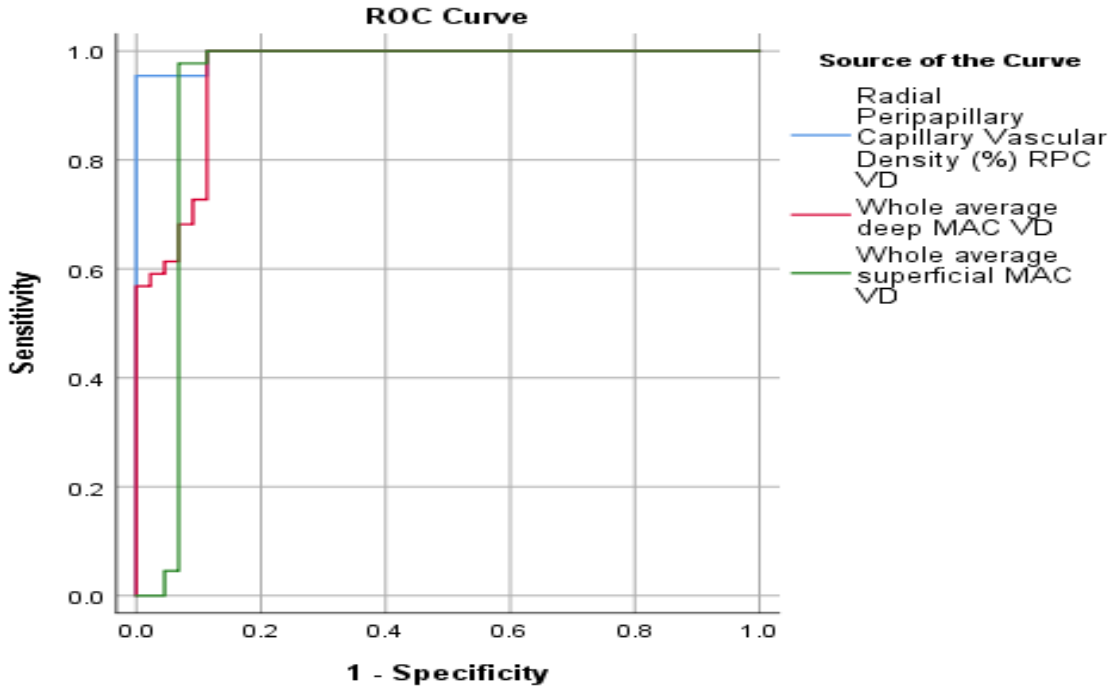

Figure (2): ROC curve for case group POAG prediction using Superficial, Deep Macular VD & RPC VD.

Table (3): Analysis of diff. VDs ROC curves in POAG cases group.

	Area Under the Curve	**P value**	**95% Confidence Interval**		**Cut off**	**Sensitivity %**	**Specificity %**
			Lower Bound	**Upper Bound**			
Whole image of superficial MAC VD	0.959	<0.001	0.920	0.997	46.1167	94.7	93.2
Whole image of deep MAC VD	0.932	0.001	0.858	1.005	45.2158	93.1	88.6
RPC VD	0.995	<0.001	0.986	1.004	39.75	95.5	100

DISCUSSION

Glaucoma is a major disease with leading cause of irreversible blindness worldwide. POAG affects over 52 million people in 2020 [10]. Traditionally, the pathophysiology of POAG was related to IOP increase, structural ONH loss, and perimetric defects. There is a growing evidence suggesting that POAG pathogenesis is related to vascular dysfunction with microvascular changes of macular and peripapillary capillary networks that may be due to blood flow disturbance [11]. However, vascular etiology of POAG can explain progressive glaucomatous damage despite of well controlled IOP and in normotensive glaucoma. Hence, recent studies discuss the ONH blood flow in POAG. OCT can give an estimation of retinal thickness, and usually utilized for monitoring glaucomatous progression [12]. We used OCT-Angio enhanced microvascular imaging system aiming to quantify and compare microvasculature changes in macula and peripapillary region between healthy and POAG eyes.

Elevated IOP is considered the main cause of optic nerve damage in glaucoma. Despite medical treatment, the present study found that the IOP of case group was higher than the control group with considered statistically difference (P=0.011), which is consistent with **Gazzard *et al.*** [13] who revealed in their study that the mean IOP in the primary angle closure glaucoma group was 37.0 mm Hg, higher than the POAG, higher than control group. Our results disagree with **Zhang *et al.*** [14] who found that there was no significant difference between the control and glaucoma groups for IOP. In this regard, the discordance could be due to well controlled IOP of cases group by medical treatment in their studies.

The current study had a significant decrease in the C/D R. (P<0.001). Our results are consistent with **Hasegawa *et al.*** [15]. There results attributed to glaucomatous structural pattern of ONH damage, leading to loss of the neuro retinal rim especially its inferior and superior rim, subsequently the vertical C/D R. increased.

By using OCT-A has exhibited the ability to evaluate macular and disc microvasculature accurately and quickly. In our study, OCTA utilized to assess the vascular plexus in POAG and control subjects [16]. **Lommatzsch *et al.*** [17], showed that the affection of RNFL and GCC thickness in POAG, correlated significantly with affection of macular and disc microvascular density, demonstrated that all were decreased in POAG eyes compared to normal eyes (P<0.05). So, suggesting that both macular microvascular densities are involved in the etiology and progression of glaucoma, and may be a reliable indicator of early glaucoma. Current results are in concurrence with **Kurysheva *et al.*** [18] that reported reduced macular microvasculature of SRL and DRL in POAG eyes compared to controls (P < 0.001). Although, the mechanism remains unclear, but they had a positive correlation between VF defect extent and hemodynamics dropout in macular plexuses. These results support microvascular dysfunction as was a POAG pathogenesis, which related to with structural damage and elevated IOP.

While SVP contains arterioles, venules, and capillaries, while the DVP consists predominantly of capillary-sized vessels. So, SVP are more affected than deep that agrees with **Moghimi *et al.*** [19], study. Our results showed that peripapillary VD were lower in glaucomatous eyes compared to normal eyes (P<0.001).

Current study confirmed the finding of several other studies and techniques that reported a significantly reduced ONH perfusion in glaucoma. Before the advent of OCTA, studies used laser Doppler flowmetry for analysis of full-field perfusion of scanning images. These previous studies demonstrated that, glaucomatous eyes had significantly lower blood flow in the ONH compared to healthy subjects [20]. **Dastiridou *et al.*** [21], concluded that the peripapillary VD had statistically significant decrease in glaucomatous compared to healthy eyes (P<0.001). These investigations presented that the peripapillary VD decreased according to POAG severity. These results suggest that OCTA measurements reflect tissue damage relevant to POAG pathophysiology.

Present study is in concurrence with **Alnawaiseh *et al.*** [22], which detected significant negative correlations in POAG at MD, RNFLT, GCC and RPC VD compared to control eyes. So, POAG is associated with structural and functional damage. Current study is in agreement with the study of **Yarmohammadi *et al.*** [23] who reported that VD in both peripapillary and macular regions in the intact hemiretina of POAG eyes were higher than in the affected hemiretina (P < 0.001), but lower than in healthy eyes (P < 0.001). Moreover, the correlations in the intact hemifields between MD with RPC VD and MAC VD were higher (r=0.450 and 0.403) than the correlations between MD and RNFLT and GCC thickness measurements (r=0.340 and 0.290; P values<0.05 for all) [23]. In contrast to present study, investigation of **Triolo *et al.*** [24] concluded that diagnostic abilities of POAG are excellent for structural variables (P < 0.01), less so but still good for peripapillary VD, and poor for macular VD (P>0.05). In this regard, the discordance between microvascular and structural damage could be due to presence of primary neurodegeneration, and capillary dropout that may be secondary to RNFL loss and the discrepancy between studies could be related to difference in study design, OCTA technical aspects, and in POAG severity.

As glaucoma pathology can be best visualized in the RNFL then GCC. So, glaucomatous damage can be best visualized by using OCT-A primarily in the VD of SVC and RPC slabs more than DVC, then the DVC

affection progresses in moderate and severe stages. This conclusion is in concurrence with **Wu Dunn *et al.* [25]**.

Our study also demonstrated that, the diagnostic accuracies of POAG, as measured by AUROC, were about 0.995 for peripapillary VD as a test, compared to 0.959 in the superficial macular VD and 0.932 in the deep macular VD. By AUROC both peripapillary and superficial macular VDs were considered higher than deep macular VDs. Our findings are consistent with **Yarmohammadi *et al.* [23]** study. The present study is mostly consistent with **Akil *et al.* [9]**, who showed that the AUC for VD was 0. 982 at SRL and was 0.976 at DRL, with cut-off point by ROC curve for VD was 0.411 at SRL 92.5% sensitivity and 95% specificity and 0.383 at DRL 90%sensitivity and 95% specificity between POAG and control subjects. This result is in accordance with our study that showed the superior and inferior macular VD to be more affected. Our current study is consistent with **Mohammed *et al.* [26]**, who demonstrated that there was a statistically significant positive correlation between structural decrease of RNFL and GCC thickness with superior and inferior superficial macular VD ($P < 0.05$).

Thus, OCTA has the potential to improve the staging and monitoring of glaucoma progression in these later stages. Large longitudinal clinical studies are needed to demonstrate the practical value of this potential application.

Our study hypothesised that OCT-A can be considered as a good investigation for assessment of retinal microvascular density to diagnose POAG, as well as, explaining the relation between POAG pathophysiology and retinal capillary perfusion. That is in accordance with **Fard *et al.* [27]** study.

Pairwise comparisons showed that the diagnostic accuracies among peripapillary VD, superficial & deep macular VD were similar ($P \leq 0.001$ for all) for differentiating between glaucomatous and healthy eyes. However, further analysis showed that the VD of RPCs and macular VDs had high values of both sensitivity and specificity, which agree in these results with **Al-Nashar *et al.* [28]** study.

Our study showed that OCTA assessment of MAC and RPC vascular density had a good value in POAG diagnosis and monitoring, as well as, supporting the relation between POAG pathophysiology and ocular microvasculature. That is consistent with **Hormel *et al.* [29]**, who reported that SS-OCTA is a good investigation for monitoring of retinal microcirculation changes.

Finally, OCTA provides a good method for diagnosis and staging of POAG by plexus-specific examination. POAG affects the VD of RPC and macular SVP more than macular DVP, then the vascular affection reaches deeper in more advanced stages.

Limitations: Our study had some limitations. First, the small sample size in this study limited the further subgroup analysis of glaucoma patients with different disease stages. Further studies are needed with more participants to evaluate whether OCT-A has a sufficient dynamic range, and to provide clinically relevant information across the full spectrum of glaucoma severity. Second, because of the case-control nature of our study, we were unable to determine the cause-effect relationship between reduction of microvascular density and glaucoma. Third, we could not precisely assess the perfusion by measuring the functional blood flow, due to SS-OCTA software limitation, so we specified to assess retinal VD.

More prospective studies are recommended for explaining the faster rate of microvascular affection before structural damage in progression of POAG at severity. After that, we can be able to guarantee OCTA reproducibility and reliability in POAG. Further longitudinal studies to investigate this relationship and as well as the impact of glaucoma control on microvascular density would be useful in understanding and managing the disease process.

CONCLUSION

Assessment appeared to have less pronounced floor effect compared to thickness parameters and hence better biomarkers in monitoring eyes with advanced stage. Quantitative parameters of OCTA have a good value in POAG diagnosis and monitoring as well as explaining the relationship between ocular capillary perfusion and vascular pathophysiology of POAG.

Sponsoring financially: Nil.
Competing interests: Nil.

REFERENCES

1. **Prum B, Rosenberg L, Gedde S *et al.* (2016):** POAG Preferred Practice Pattern Guidelines. Ophthalmology, 123 (1): 41-111.
2. **Tham Y, Cheng C (2017):** Associations between chronic systemic diseases and POAG: an epidemiological perspective. Clin Exp Ophthalmology, 45: 24–32.
3. **Huang D, Liu L, You Q (2018):** OCTA: a new tool for glaucoma evaluation. Ophthalmology Manage, 22: 22–24.
4. **Hou H, Moghimi S, Zangwill L *et al.* (2019):** Macula VD and thickness in early POAG. Am J Ophthalmology, 199: 120–132.
5. **Takusagawa H, Liu L, Ma K *et al.* (2017):** Projection-Resolved OCTA of Macular Retinal Circulation in Glaucoma. Ophthalmology, 124 (11): 1589–1599.
6. **Ang M, Tan A, Cheung C *et al.* (2018):** OCTA: a review of current and future clinical applications. Graefes Arch Clin Exp Ophthalmology, 256 (2): 237-245.
7. **Mansoori T, Sivaswamy J, Gamalapati J (2017):** RPCVD measurement using OCTA in early glaucoma. J Glaucoma, 26: 438–443.
8. **Almbsut M, Abdelhameed A, Sabry D *et al.* (2020):** Ghanem Evaluation of Macular VD Changes in Patients with POAG by SS-OCTA. ARC Journal of Ophthalmology, 5 (1): 6-13.

9. **Akil H, Chopra V, Al-Sheikh M *et al.* (2018):** SS-OCTA imaging of the macular capillary network in glaucoma. Br J Ophthalmology, 102: 515–519.
10. **Lee E (2021):** OCT-Angiography. In OCT Imaging in Glaucoma. Springer, Singapore. Pp: 71-88. https://link.springer.com/book/10.1007/978-981-16-1178-0
11. **Hwang J, Konduru R, Zhang X *et al.* (2012):** Relationship among VF, blood flow, and neural structure measurements in glaucoma. Invest Ophthalmology Vis Sci., 53 (6): 3020-6.
12. **Na J, Sung K, Lee J *et al.* (2013):** Detection of glaucomatous progression by SD-OCTA. Ophthalmology, 120 (7): 1388-95.
13. **Gazzard G, Foster P, Devereux J *et al.* (2003):** IOP and VF loss in ACG and POAG. British Journal of Ophthalmology, 87 (6): 720-5.
14. **Zhang S, Wu C, Liu L *et al.* (2017):** OCTA of the peripapillary retina in POAG. American Journal of Ophthalmology, 182: 194-200.
15. **Hasegawa T, Akagi T, Yoshikawa M *et al.* (2015):** Microcystic INL Changes and RNFL Defects in Eyes with Glaucoma. PLoS One, 10 (6): e0130175. https://doi.org/10.1371 /journal. pone.0130175
16. **Jia Y, Wei E, Wang X *et al.* (2014):** OCTA of optic disc perfusion in glaucoma. Ophthalmology, 121 (7): 1322-32.
17. **Lommatzsch C, Rothaus K, Koch J *et al.* (2018):** VD in OCTA permits differentiation between normal and glaucomatous ONH. Int J Ophthalmol., 11 (5): 835-843.
18. **Kurysheva N, Maslova E, Trubilina A *et al.* (2017):** Macular blood flow in glaucoma. Vestn Oftalmol., 133 (2): 29-38.
19. **Moghimi S, Bowd C, Zangwill L *et al.* (2019):** Measurement Floors and Dynamic Ranges of OCT and OCTA in Glaucoma. Ophthalmology, 126: 980–988.
20. **Hafez A, Lesk M (2015):** Role of ocular blood flow in the pathogenesis of glaucoma. In Glaucoma WB Saunders, Pp: 88-97. DOI:10.1016/B978-0-7020-5193-7.00009-1
21. **Dastiridou A, Chopra V (2018):** Potential applications of OCTA in glaucoma. Curr Opin Ophthalmology, 29 (3): 226-233.
22. **Alnawaiseh M, Lahme L, Müller V *et al.* (2018):** Correlation of flow density, as measured using OCTA, with structural and functional parameters in glaucoma patients. Graefes Arch Clin Exp Ophthalmology, 256 (3): 589-597.
23. **Yarmohammadi A, Zangwill L, Manalastas P *et al.* (2017):** Peripapillary and Macular VD in Patients with POAG and Unilateral Visual Field Loss. Ophthalmology, 125: 578–587.
24. **Triolo G, Rabiolo A, Shemonski N *et al.* (2017):** OCTA Macular and Peripapillary VD in Healthy Subjects, Glaucoma Suspects, and Glaucoma Patients. Invest Ophthalmol Vis Sci., 58 (13): 5713-5722.
25. **WuDunn D, Takusagawa H, Sit A *et al.* (2021):** OCT Angiography for the Diagnosis of Glaucoma: A Report by the American Academy of Ophthalmology. Ophthalmology, 128 (8): 1222-1235.
26. **Mohammed N (2021):** Changes of Macular VD in POAG. The Egyptian Journal of Hospital Medicine, 83: 1129-1133.
27. **Fard M, Ritch R (2020):** OCT-A in glaucoma. Ann Transl Med., 8 (18): 1204. doi: 10.21037/ atm-20-2828.
28. **Al-Nashar H, El-Haig W, Al-Naimy M (2020):** Assessment of RPC and macular VD in POAG. J Egypt Ophthalmology Soc., 113: 46-53.
29. **Hormel T, Hwang T, Bailey S *et al.* (2021):** Artificial intelligence in OCT-A. Prog Retin Eye Res., 85: 100965. doi: 10.1016/j.preteyeres.2021.100965.