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Assessment of Optic Disc Perfusion in Open Angle Glaucoma (OAG) Using Optical Coherence Tomography Angiography (OCTA)

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ABSTRACT

Background: glaucoma is a major disease that potentially results in irreversible blindness, some prospective studies demonstrated that in primary open-angle glaucoma (POAG), blood flow is diminished in the ophthalmic, retinal, choroid and retro-bulbar circulations. **Aim of the Work:** this study aimed to compare Optic disc perfusion in normal healthy persons with that of Open Angle Glaucoma (OAG) patients by using Optical Coherence Tomography Angiography (OCTA) and to see if a correlation exists between optic disc perfusion, visual field changes and retinal nerve fiber layer thickness in normal healthy persons and in OAG patients. **Patients and Methods:** we did an analysis of optic disc perfusion in two groups of normal healthy persons and primary open angle glaucoma patients who were previously diagnosed and attended follow up in outpatient clinic in Sayed Galal University Hospital located in Cairo. In our study we included 22 eyes of 12 people, (10 normal eyes and 12 Open angle glaucoma patients eyes) aged between 20 and 78 years old.

Results: there was a statistically significant relationship between optic disc perfusion and glaucoma group in comparison with normal group, thus in normal group the optic disc perfusion indicated good optic disc perfusion which was significantly lower in glaucoma group. Also we discovered that there was a statistically significant correlation between optic disc perfusion with (Visual field changes and RNFL thickness).

Conclusion: optic disc perfusion assessment by using OCT angiography could be beneficial in evaluation of glaucoma and assessment of disease progression and it's follow up together with Visual Field assessment and clinical examination.

Keywords: optic disc perfusion, open angle glaucoma, optical coherence tomography angiography.

INTRODUCTION

Glaucoma is a major disease that potentially results in irreversible blindness. It is the second leading cause of induced vision loss worldwide. For a long period of time, elevated intraocular pressure (IOP) was recognized as the only cause of neural tissue loss at the optic nerve head (ONH), subsequently resulting in visual field loss [(1)].A prospective study demonstrated that in primary open-angle glaucoma (POAG), blood flow was diminished in the ophthalmic, retinal, choroidal, and retrobulbar circulations [(2)].

Recently, a newly developed OCT angiography using split- spectrum amplitude-decorrelation angiography (SSADA) has demonstrated the ability to quantify retinal and disc blood flow rapidly and accurately [(3)].

Optical coherence tomography angiography (OCTA) is a new non-invasive imaging technique that employs motion contrast imaging to high-resolution volumetric blood flow information generating angiographic images in a matter of seconds [(4)]. Both the retinal and the choroidal microvasculature can be visualized by using OCT angiography while, fluorescein angiography (FA) is used for seeing the retinal vessels and Indocyanine green angiography (ICGA) is more ideal for imaging the choroid [(5)].OCTA is a useful tool for evaluating optic disc perfusion in glaucomatous eyes. The normally dense peripapillary microvascular network is attenuated in both the superficial disc vasculature and the deeper lamina cribosa [(6)].

Measurements of optic nerve head microcirculation with OCT angiography revealed a significant reduction of blood flow in glaucomatous eyes and these measurements were also well correlated with visual field function [(7)].There is a general consensus that ocular blood flow is reduced in glaucoma and that vascular factors might be more prominent in open-angle glaucoma (OAG). Despite this, the study of disc perfusion in patients with OAG has been rare. Additionally, the relationship between the severity of damage of optic disc perfusion and the functional and anatomical changes of glaucoma has not been established. To explore the possible correlation between disc perfusion and visual field loss in OAG patients, this study will be performed using OCT angiography [(3)].

AIM OF THE WORK

The aim of this study was to compare optic disc perfusion in normal healthy persons with that of Open Angle Glaucoma (OAG) patients using Optical Coherence Tomography Angiography (OCTA) and to see if a correlation exists between optic disc perfusion, visual field changes and retinal nerve fiber layer thickness in normal healthy persons and in OAG patients.

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PATIENTS AND METHODS

In this study, we did an analysis of optic disc perfusion in two groups of normal healthy persons and primary open angle glaucoma patients who were previously diagnosed and attending follow up in outpatient clinic in Sayed Galal University Hospital located in Cairo. In our study we included 22 eyes of 12 people, (10 Normal eyes and 12 Open Angle Glaucoma Patients eyes) aged between 20 and 78 years old.

The study was approved by the Ethics Board of Al-Azhar University.

Inclusion criteria in the study:

1) Glaucomatous patients when diagnosis is established.
2) Able to give informed consent before enrollment in the study.

Exclusion criteria in the study:

- Presence of other diseases affecting optic disc perfusion, eg: Diabetic retinopathy, retinal vein occlusion, etc.

Patient evaluation:

All patients were submitted to:

- **Complete ophthalmic examination in the form of:**

1. Auto-refraction assessment.
2. Anterior segment examination by slit lamp examination.
3. Intra-Ocular Pressure assessment using applanation tonometer to know whether the disease status is controlled or not.
4. Fundus examination using direct ophthalmoscope and +90 D lens to evaluate optic nerve head changes after pupillary dilatation with tropicamide 1% and 2.5% phenylephrine eye drops.
5. Assessment of Anterior Chamber Angle using goniolens.
6. Full history taking including previous and present anti-Glaucomatous treatment.

- **All subjects were investigated as follows:**

- Optical Coherence Tomography Angiography.
- Visual Field Assessment.

❖ **Evaluation of Optical Coherence Tomography Angiography**:

Optical Coherence Tomography Angiography was performed for all subjects included by a swept source based OCT angiography instrument to obtain images for quantification of optic disc perfusion and to assess retinal nerve fiber layer thickness.

The following parameters were provided:

- Optic Disc Perfusion: measured as Radial Peripapillary Capillaries Vessel Density (RPC Density).
- Retinal Nerve Fiber Layer (RNFL) Thickness.

Optic nerve head (ONH) Analysis.

Statistical analysis

Data were processed and analyzed by using the appropriate statistical tests as the computerized 10^{th} version of Statistical Package for Social Sciences (SPSS). P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS).

RESULTS

Table 1: showing data analysis of age and sex in both the normal and glaucoma groups

		Normal group	Glaucoma group	Test value	P-value	Sig.
		No. = 10	No. = 12			
Age (Year)	Mean±SD Range	43.70 ± 15.11 20 – 62	62.50 ± 12.92 41 – 78	-3.148•	0.005	HS
Gender	Male Female	3 (30.0%) 7 (70.0%)	6 (50.0%) 6 (50.0%)	0.903*	0.342	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*:Chi-square test; •: Independent t-test

In normal group, ages of normal eyes ranged from 20 to 62 years old with a mean value of 43.70 ± 15.11 years old. In glaucomatous group, ages of glaucomatous eyes ranged from 41 to 78 years old with a mean value of 62.50 ± 12.92 years old. The study included 3 eyes of male persons (30.0%) of whole eyes in normal group and 7 eyes of female persons (70.0%) of whole eyes in normal group. Also the study included 3 eyes of male patients (50%) of whole glaucoma group and 3 eyes of female patients (50%) of whole glaucoma group.

Table 2: showing data analysis of Whole image, Sup hemi, Inf hemi and Peri-papillary density percentage in both the normal and glaucoma groups

		Normal group	Glaucoma group	Test value•	P-value	Sig.
		No. = 10	No. = 12			
Whole Image (%)	Mean±SD Range	51.80 ± 1.55 49 – 54	34.67 ± 8.92 25 – 48	5.977	0.000	HS
Superior hemi density (%)	Mean±SD Range	55.70 ± 2.71 51 – 58	36.83 ± 11.85 20 – 53	4.908	0.000	HS
Inferior hemi density (%)	Mean±SD Range	55.20 ± 1.62 52 – 58	33.42 ± 10.94 22 – 52	6.214	0.000	HS
Peripapillary Density (%)	Mean±SD Range	55.60 ± 1.71 52 – 58	35.25 ± 11.28 22 – 53	5.627	0.000	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test

There was a highly statistically significant difference between the normal and glaucoma groups regarding whole image, superior hemi density, inferior hemi density and peripapillary density (p-value=0.000).

Table 3: showing visual field analysis in both the normal and glaucoma group

Visual Field Mean Deviation	Normal group	Glaucoma group	Test value	P-value	Sig.
	No. = 10	No. = 12			
Median (IQR)	-0.18 (-0.75 – 0.03)	-15.43 (-19.41 – -5.63)	-3.824	0.000	HS
Range	-1.3 – 0.12	-29.47 – -1.03			

P-value > 0.05: non significant; P-value < 0.05: significant; P-value < 0.01: highly significant
≠: Mann-Whitney test

There was a highly significant correlation between visual field mean deviation and glaucoma group in comparison with normal group, thus in normal group visual field was normal which was significantly affected in glaucoma group with P-value < 0.01: highly significant (HS).

Table 4: showing data analysis of RNFL thickness peripapillary, Cup/Disc V Ratio and IOP in both the normal and glaucoma groups

		Normal group	Glaucoma group	Test value•	P-value	Sig.
		No. = 10	No. = 12			
RNFL thickness Peripapillary	Mean±SD Range	113.80 ± 12.44 95 – 130	71.42 ± 20.11 45 – 111	5.791	0.000	HS
Cup Disc V Ratio	Mean±SD Range	0.59 ± 0.06 0.45 – 0.65	0.67 ± 0.20 0.31 – 0.87	-1.262	0.222	NS
IOP	Mean±SD Range	12.30 ± 1.49 10 – 15	18.58 ± 3.58 14 – 25	-5.172	0.000	HS

P-value >0.05: non significant (NS); P-value <0.05: significant (S); P-value< 0.01: highly significant (HS)
•: independent t-test

There was a highly statistically significant difference between normal group and glaucoma group regarding RNFL thickness Peripapillary and IOP (p-value=0.000) while that there was non statistical significant difference between normal group and glaucoma group regarding Cup Disc V Ratio.

Table 5: showing whole image optic disc perfusion density analysis in glaucoma group

	Superior hemi(%)		Inferior hemi(%)		Peripap-density(%)		Age	
Whole image (%)	**R**	**P-value**	**R**	**P-value**	**r**	**P-value**	**r**	**P-value**
	0.89	0.000	0.928	0.000	0.951	0.000	-0.597	0.040
	Visual field(MD)		**RNFL**		**Cup Disc V ratio**		**IOP**	
Whole image (%)	**R**	**P-value**	**R**	**P-value**	**r**	**P-value**	**r**	**P-value**
	0.819	0.001	0.634	0.027	-0.833	0.001	0.074	0.818

In this study we have done a correlation between the four main optic disc perfusion parameters and the reset of other parameters and it showed a significant correlation between each other.

Table 6: showing superior hemi optic disc perfusion density analysis in glaucoma group

	Whole image		Inferior hemi(%)		Peripap-density(%)		Age	
Superior hemi(%)	**R**	**P-value**	**R**	**P-value**	**r**	**P-value**	**r**	**P-value**
	0.896	0.000	0.813	0.001	0.981	0.000	-0.424	0.169
	Visual field(MD)		**RNFL**		**Cup Disc V ratio**		**IOP**	
Superior hemi(%)	**R**	**P-value**	**R**	**P-value**	**r**	**P-value**	**r**	**P-value**
	0.678	0.015	0.641	0.025	-0.677	0.016	0.190	0.553

There was a highly significant correlation between whole image optic disc perfusion density and sub hemi, inf hemi, peripapillary disc perfusion and visual field mean deviation with P-value < 0.01: highly significant (HS). There was non-significant correlation between whole image optic disc perfusion percentage and IOP with P-value > 0.05: no significant (NS).

Table 7: showing inferior hemi optic disc perfusion density analysis in glaucoma group

	Whole image		Superior hemi(%)		Peripap-density(%)		Age	
Inferior Hemi (%)	**R**	**P-value**	**R**	**P-value**	**r**	**P-value**	**r**	**P-value**
	0.928	0.000	0.813	0.001	0.895	0.000	-0.566	0.055
	Visual field(MD)		**RNFL**		**Cup Disc V ratio**		**IOP**	
Inferior Hemi (%)	**R**	**P-value**	**R**	**P-value**	**r**	**P-value**	**r**	**P-value**
	0.813	0.001	0.689	0.013	-0.746	0.005	0.219	0.494

There was a highly significant correlation between superior hemi optic disc perfusion percentage and whole image, inf hemi and peripapillary disc perfusion) with P-value < 0.01: highly significant (HS). There was a non-significant correlation between sub hemi optic disc perfusion percentage and age, visual field mean deviation, RNFL thickness, Cup/Disc V ratio and IOP with P-value > 0.05: no significant (NS).

Table 8: showing peri-papillary optic disc perfusion density analysis in glaucoma group

	Whole image		Superior hemi(%)		Inferior hemi(%)		Age	
Peri-papillary density (%)	**R**	**P-value**	**r**	**P-value**	**r**	**P-value**	**r**	**P-value**
	0.951	0.000	0.981	0.000	0.895	0.000	-0.481	0.113
	Visual field(MD)		**RNFL**		**Cup Disc V ratio**		**IOP**	
Peri-papillary density (%)	**R**	**P-value**	**r**	**P-value**	**r**	**P-value**	**r**	**P-value**
	0.757	0.004	0.679	0.015	-0.724	0.008	0.196	0.541

There was a highly significant correlation between inf hemi and whole image, superior hemi, peripapillary optic disc perfusion percentage, visual field mean deviation and cup/disc V ratio) with P-value < 0.01: highly significant (HS). There was a non-significant correlation between inf hemi optic disc perfusion density percentage and age, RNFL thickness and IOP) with P-value > 0.05: no significant (NS).

DISCUSSION

This study was conducted to compare optic disc perfusion in normal healthy persons with that of Open Angle Glaucoma (OAG) patients using Optical Coherence Tomography Angiography (OCTA) and to see if a correlation exists between optic disc perfusion, visual field changes and retinal nerve fiber layer thickness in normal healthy persons and in OAG patients.Our results agreed with a study done by **Jia *et al.*** [8] who studied a comparison of optic disc perfusion between normal subjects and subjects with glaucoma using optical coherence tomography angiography (OCTA) and the detection of optic disc perfusion changes in glaucoma, this study included twenty-four normal subjects and 11 patients with glaucoma, one eye of each subject was scanned by a high-speed 1050-nmewavelength swept-source OCT instrument. They showed that in normal discs, a dense microvascular network was visible on OCT angiography. This network was visibly attenuated in subjects with glaucoma. The disc flow index was reduced by 25% in the glaucoma group (P= 0.003). The flow index was highly correlated with VF pattern standard deviation (R2 = 0.752, P= 0.001). These correlations were significant even after accounting for age, C/D area ratio, NFL and rim area. Their findings came to the same conclusion we did as optical coherence tomography angiography, generated by the new SSADA, repeatabley measures optic disc perfusion and may be useful in the evaluation of glaucoma and glaucoma progression.Our results also agree with a study done by **Wang *et al.*** [3] who showed that optic disc perfusion varied in patients with open-angle glaucoma (OAG) and how this correlates with glaucoma severity. Their study included 62 eyes from 62 patients with OAG, divided into three groups according to their visual field (VF) results, and 20 eyes from 20 normal control subjects. Optic disc perfusion was studied using optical coherence tomography angiography (angio-OCT), and flow index and vessel density were determined. The VF, mean deviation (MD), pattern standard deviation (PSD), retinal nerve fiber layer (RNFL) thickness, and ganglion cell complex (GCC) thickness were also recorded. The potential associations between disc perfusion and VF defects or structural loss were analyzed. Also, their study showed that in OAG patients, the disc flow index and vessel density were significantly lower than in normal controls (all $p<0.001$) and were correlated with the severity of glaucoma. In OAG eyes, the flow index and vessel density were significantly correlated with MD, RNFL, and GCC thickness (all $p<0.01$), but were not in the normal controls. Thus the study gave a conclusion that angiograms demonstrated a reduced disc flow index and vessel density in glaucoma, and this reduction was closely related to GCC thickness. This indicated that measurement of disc perfusion by angio-OCT might be important for the monitoring of glaucoma. Our results also agree those of **Chen *et al.*** [9] who investigated the differences of perfusion in the optic nerve head (ONH) between normal and glaucomatous eyes using optical micro-angiography (OMAG) based optical coherence tomography (OCT) angiography technique. Their study involved 20 normal and 21 glaucoma subjects, their eyes were scanned with a 68 kHz Cirrus 5000 HD-OCT-based OMAG prototype system centered at the ONH (Carl Zeiss Meditec Inc, Dublin, CA, USA). Micro-vascular images were generated from the OMAG dataset by detecting the differences in OCT signal between consecutive B-scans. The pre-laminar layer (preLC) was isolated by a semi-automatic segmentation program. En face OMAG images for preLC were generated using signals with highest blood flow signal intensity. ONH perfusion was quantified as flux, vessel area density, and normalized flux within the ONH. Standard t-tests were performed to analyze the ONH perfusion differences between normal and glaucomatous eyes. Linear regression models were constructed to analyze the correlation between ONH perfusion and other clinical measurements. Their study showed that glaucomatous eyes had significantly lower ONH perfusion in preLC in all three perfusion metrics compared to normal eyes ($P\leq0.0003$). Significant correlations between ONH perfusion and disease severity as well as structural changes were detected in glaucomatous eyes ($P\leq0.012$). Their study also came to the same conclusion we did as ONH perfusion detected by OMAG showed significant differences between glaucoma and normal controls and was significantly correlated with disease severity and structural defects in glaucomatous eyes. ONH perfusion measurement using OMAG may provide useful information for detection and monitoring of glaucoma.

CONCLUSION

In this study we compared Optic Disc Perfusion in normal healthy persons with that of Open Angle Glaucoma (OAG) patients using Optical Coherence Tomography Angiography (OCTA) to see if a correlation exists between optic disc perfusion, Visual Field Changes and Retinal Nerve Fiber Layer

Thickness in normal healthy persons and in OAG patients.

We discovered that there is a statistically significant relationship between (Whole image, superior hemi, inferior hemi and peripapillary Optic disc perfusion percentage) and glaucoma group in comparison to normal group, thus in normal group the all 4 parameters were indicating good optic disc perfusion which was significantly lower in glaucoma group with P-value < 0.01: highly significant (HS) in all the 4 main parameters.Also, we discovered that there was a statistically significant correlation between (Whole image density and Peri-papillary Density) with (Visual Field changes and RNFL thickness).

These results suggest that Optic disc perfusion assessment using OCT Angiography could be beneficial in evaluation of glaucoma and assessment of disease progression and it's follow up together with Visual Field assessment and clinical examination.

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