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Original article

Characteristics of Peripapillary Changes in High Myopia Detected by Using Optical Coherence Tomography-Angiography

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Abstract

Background: Optical Coherence Tomography Angiography (OCTA) is a new, non-invasive imaging technique that generates angiography images in a matter of seconds and can detect posterior segment complications of high myopia. **Objectives:** Assessment of peripapillary changes in high myopia and to quantify vasculature parameters using Optical Coherence Tomography Angiography (OCTA) to determine the relation between retinal vasculature and peripapillary parameters in highly myopic eyes. **Methods:** This study is an observational cross- sectional study for high myopic patients, Study will include 130 eyes of 70 patients included 2 groups;group (A) of high myopic (N=100 eyes of 55 patients), group (B) (N=30 healthy eyes of 15 populations) of emmetropia. All patients were subjected to full ophthalmologic evaluation, AL measurement, OCTA and Fundus photo. **Results**: The results of the study revealed a statistically significant difference in the RNFL thickness (average, superior, inferior and nasal) (p value<0.001) in all but there was no statistically significant difference in temporal RNFL (p value=0.056). There was significant difference in (whole image, peripapillary, superior-hemi and inferior-hemi disc vessel density) between the cases of 2 study groups (P<0.001 in all), there was no significant correlation between superficial macular density and disc density (p=0.781), on the other hand; there was significant positive correlation between deep macular density and disc density (P=0.006) **Conclusion:** Eyes with high myopia have decrease macular and peripapillary perfusion in comparison with emmetropic eye. These vascular findings may raise the vulnerability to vascular associated eye disorders.

Keywords: OCTA; High Myopia; RNFL; Vessel Density.

Introduction

Myopia is a refractive error in which distant light entering a non-accommodating eye is focused in front of, rather than, on the retina. Myopia is categorised as refractive or axial myopia. Axial myopia is more common and results from an elongated eyeball; the onset and progression of axial myopia occur during childhood and adolescence. Conversely, refractive myopia is relatively uncommon, and involves the refractive elements of the eye; for example: curvature myopia in patients with abnormal corneal curvature (1).

High myopia is defined as the presence of a high negative refractive error (>−6) diopters in the context of eye elongation (>26 mm), the two factors driving the development of pathologic myopia are: 1) elongation of the axial length and 2) posterior staphyloma. The presence of posterior staphyloma is the key differentiating factor between these two terms, high and pathologic myopia. The occurrence of staphyloma will lead to other conditions such as atrophic traction or neovascular maculopathy (2).

The newly developed Optical Coherence Tomography Angiography (OCTA) could cover most of deficiencies of FFA through its noninvasive and very rapid process. OCTA provides the imaging of en-face retinal and choroidal vasculature by detecting erythrocytes flowing in blood vessels with time (3).

Aim of the work

Assessment of peripapillary changes in high myopia and to quantify vasculature parameters using Optical Coherence Tomography Angiography (OCTA) to determine the relation between retinal vasculature and peripapillary parameters in highly myopic eyes.

Patients and methods

This research was carried out at the Benha University's department of ophthalmology in Benha, Egypt. The study was done from October 2020 to January 2022.

Study design: This study is an observational cross- sectional study for high myopic patients study. Study will include 130 eyes of 70 patients included 2 groups;group (A) of high myopic (N=100 eyes of 55 patients ;one eye included in 10 patients and both eyes included in 45 patients), in addition to, group (B) (N=30 healthy eyes of 15 populations) of emmetropia.

Inclusion criteria

1) Age is between 20 to 50 years old.
2) Myopia of ≥ (-6.00) diopters.
3) No history of trauma, eye surgery and systemic diseases affecting optic disc or macula.
4) Non- glaucoma patients.

Exclusion criteria

1) Myopia of less than (- 6, 00) diopters.
2) History of ocular surgery or ocular trauma.
3) Media opacity that does not permit optical coherence tomography acquisition with good signal strength.
4) Patients with history of neurologic, metabolic or other systemic diseases (diabetes mellitus or hypertension).

5) Ocular diseases, including glaucoma.

Examination

All of the cases were put through general examination and a comprehensive history taking process after receiving a permission of the Benha Faculty of Medicine's institutional review board (MS/17.03.91) and obtaining an informed written consent from the participants who were included in the study. For each and every one of the cases, a comprehensive ophthalmic examination was performed, which included a Landolt's VA chart was used to assess the patients' visual acuity (VA). This data was then transformed for statistical analysis into logarithms of the minimal angle of resolution units. Slit lamp biomicroscopy was utilised in order to evaluate the corneal clarity, the depth and regularity of the anterior chamber, the shape, size, regularity, and reactivity of the pupil, as well as the state of the lens. An examination of the fundus was carried out using a +90 D volk lens. Axial length was measured by IOL master (Zeiss IOL master 500 Jena Germany). All the included subjects underwent assessment by **OCT angiography** (Angio Vue; optivue Inc, Fremont, (California, USA) machine in Benha Diagnostic Eye Center) and fundus photography by fundus camera (Topcon 3D-OCT 2000) in Benha Diagnostic Eye Center).

Patient preparation

All patients were examined with mydriatic eye drop. Patient was asked to put his chin in chin rest of machine, look at the center of internal fixation target that was central in position during macular scanning and nasal during optic disc scanning.

The scan protocol examined a 3.0×3.0 mm^2 area focused on the macula and a 4.5×4.5 mm^2 area focused on the optic disc to obtain the superficial and deep inner retinal vascular plexuses. We choose from option list HD Angio retina 3x3 and HD Angio disc 4.5x4.5.

The retinal nerve fiber layer (RNFL) thickness and OCT scan of optic disc. We choose ONH from option list.

Approval number: MS/17.03.91

Statistical analysis

The clinical data were recorded on a report form. These data were tabulated and analyzed using the computer program SPSS ((IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.): Descriptive statistics were calculated for the data in the form of Mean and standard deviation for quantitative data. Frequency and distribution for qualitative data. Student's *t*-test: - Used to compare mean of two groups of quantitative data. Inter-group comparison of categorical data was performed by using chi square test (X^2-value). A *P* value <0.05 was considered statistically significant (*) while >0.05 statistically insignificant P value <0.01 was considered highly significant (**) in all analyses.

Results

Our study included 28 males (40%) and 42 female (60%). Age had a mean ± SD of (35.82 ±7.07) years in group A and (37.80±10.15) years in group B. **Table 1**

There is a statistically highly significant difference in the MSE, IOP and axial

length among the cases within the 2 study groups (p value <0.001) in all. There was a statistically highly significant difference in the RNFL thickness (average, superior, inferior and nasal) (p value<0.001) in all but there is no statistically significant difference in temporal RNFL (p value=0.056) between the cases within the 2 study groups. The was a high significant difference in (whole image, peripapillary, superior-hemi and inferior-hemi disc vessel density) between the cases of 2 study groups (P<0.001 in all). **Table 2**

Figure 1 revealed that there is a statistically highly significant difference in the superficial whole image macular vessel density (P<0.001) but there is no significant difference in superficial foveal vessel density (P=0.29) among the cases within the 2 study groups. There is a statistically significant difference in the deep whole image macular vessel density (P=0.003) but there is no significant difference in deep foveal vessel density (p=0.82) between the cases of the 2 study groups. **Table 3**

Correlation between mean spherical equivalent with different parameters: There is significant positive correlation between MSE with (superficial macular density%, deep macular density%, optic disc density% and average RNFL thickness μm) (r=0. 448, r=0. 426, r=0.391, r=0.246, respectively) (P<0.001) in all, but there is weak correlation between MSE and disc area mm2 (P=0.511) and cup volume mm3 (P=0.265). **Table 4**

Correlation between axial length with different parameters: There is significant negative correlation between AL with superficial macular vessel density%, optic disc vessel density% and average RNFL thickness, but there is weak correlation between AL with deep macular vessel density% (P=0.086), disc area mm^2 (p=0.533) and cup volume mm^3 (P=0.462). **Table 5**

Correlation between macular vessel density (superficial and deep) with different parameters: There is significant negative correlation between superficial macular density and macular thickness, but there is weak correlation between it and both disc density (p=0.781) and macular volume (P=0.054) on the other hand; there is significant positive correlation between deep macular density and disc density, but there is significant negative correlation between deep macular density and macular thickness and with macular volume. **Table 6**

Table (1): Distribution of the studied cases according to demographic data.

variable	Group A (High myopes) n= 100		Group B (Emmetropes) n= 30		Statistical test (st t)	P value
	Mean	±sd	Mean	±sd		
Age	35.82	7.07	37.80	10.15	1.21	0.23
Gender n (%)						
Male	24	43.6	4	26.7	$\chi 2$= 2.89	0.089
Female	31	56.4	11	73.3		
Eye n (%)						
OD	58	58.0	16	53.3	$\chi 2$= 0.21	0.65
OS	42	42.0	14	46.7		

p= Inter group significance SD: Standard deviation* *statistically significant if P <0.05.

Table (2): Comparison between the studied groups according to different parameters, RNFL thickness and Optic disc vessel density % in 4.5X4.5mm.

Variable	Group A (High myopes) n= 100		Group B (Emmetropes) n= 30		Statistical test (st t)	P value
	Mean	±sd	Mean	±sd		
MSE	-11.59	4.51	-0.38	0.60	13.52	**<0.001****
IOP (mmHg)	15.20	2.08	12.80	1.40	5.92	**<0.001****
Axial length (mm)	26.89	1.05	22.86	0.54	20.17	**<0.001****
RNFL thickness						
Average RNFL (µm)	91.46	13.14	105.13	5.72	5.53	**<0.001****
Superior RNFL(µm)	105.5	25.51	124.47	14.12	3.89	**<0.001****
Inferior RNFL (µm)	114.5	17.92	128.2	9.44	4.02	**<0.001****
Nasal RNFL (µm)	72.82	25.46	89.0	14.86	3.31	**0.001****
Temporal RNFL(µm)	73.48	12.03	78.0	8.01	1.93	**0.056**
Optic disc vessel density % in 4.5X4.5mm						
Whole image vessel density	51.40	4.74	57.42	1.94	6.77	**<0.001****
Peripapillary	53.45	5.10	59.39	1.81	6.26	**<0.001****
Superior-hemi	53.18	6.36	59.69	1.83	5.53	**<0.001****
Inferior-hemi	53.45	6.29	59.26	2.06	4.97	**<0.001****

P= Inter group significance, SD: Standard deviation, MSE=mean spherical equivalent, RNFL=Retinal nerve fiber layer, IOP=Intraocular pressure, **statistically highly significant if p<0.01.

Table (3): Comparison between the study groups according to deep macular vessel density %in 3.00X3.00mm scan.

Deep macular vessel Density %	Group A (High myopes) N= 100		Group B (Emmetropes) N= 30		Statistical test (st t)	P value
	Mean	±sd	Mean	±sd		
Whole macular vessel density %	48.60	8.94	53.78	3.80	3.08	**0.003****
Fovea vessel density %	35.89	9.37	35.46	8.30	0.23	0.82

p= Inter group significance, SD: Standard deviation, * *statistically highly significant if P <0.01.

Table (4): Correlation between mean spherical equivalent with different parameters.

Variable	MSE r	P
Superficial macular vessel density%	0. 448	**<0.001****
Deep macular vessel density%	0. 426	**<0.001****
Optic disc vessel density%	0.391	**<0.001****
Average RNFL thickness(µm)	0.246	**<0.001****
Disc area mm^2	-0.067	0.511
Cup volume mm^3	-0.113	0.265

r: spearman's correlation, P: probability, MSE=mean spherical equivalent, **statistically highly significant if P <0.01, RNFL=Retinal nerve fiber layer

Table (5): Correlation between axial length with other parameters.

Variable	AL	
	r	**P**
Superficial macular density%	-0.208	**<0.038***
Deep macular density%	-0.173	0.086
Optic disc vessel density%	-0.249	**<0.013***
Average RNFL thickness (µm)	-0.322	**<0.001****
Disc area mm^2	0.063	0.533
Cup volume mm^3	-0.074	0.462

r: spearman's correlation, P: probability, **statistically highly significant if P <0.01, AL=Axial length.

Table (6): Correlation between macular vessel density (superficial and deep) with other parameters.

	Superficial macular vessel density%		**Deep macular vessel density%**	
	r	**P value**	**r**	**P value**
Variable				
Optic disc vessel density %	0.028	0.781	0.273	**0.006****
Macular thickness(µm)	-0.198	**0.048***	-0.299	**0.002****
Macular volume mm^3	-0.193	0.054	-0.287	**0.004****

R: spearman's correlation, P: probability, * statistically significant if P<0.05, **Statistically highly significant if P <0.01

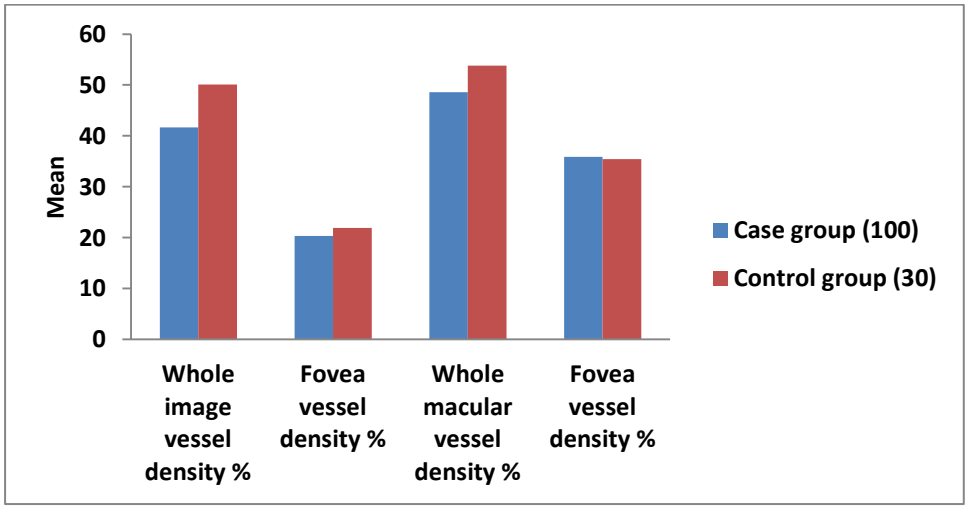

Figure 1: Comparison between the study groups according to superficial macular vessel density % in 3.00X3.00 mm

Discussion

The aim of the current study is to detect peripapillary changes in high myopia and to quantify vasculature parameters using Optical Coherence Tomography Angiography (OCTA) and to determine the relation between retinal vasculature and Peripapillary parameters in highly myopic eyes.

The study included total number 130 eyes of 70 patients; the cases were distributed into 2 study groups: Group (A) =100 eyes of 55 patients of high myopia and group (B) =30 eyes of 15 populations of emmetropia.

Regarding to RNFL thickness, our study revealed that there was a statistically highly significant difference in the RNFL thickness (average-superior-inferior-nasal) all (P<0.001) but there was no statistically difference in temporal RNFL between the cases within the 2 study groups (P=0.056).

Results of the current study matched with a study reported that there was a statistically significant decrease in average RNFL thickness (P=0.001) and also in the RNFL thickness of all the quadrants except in the temporal quadrant (P=0.862) (4).

According to optic disc vessel density, the current study reported that there was a statistically highly significant difference between A&B groups in whole image (51.40±4.74%,57.42±1.94%,resp),peripapillary(53.45±5.10%,59.39±1.81%,resp.),superiorhemi(53.18±6.36%,59.69±1.83% ,resp.) and inferior-hemi (53.45±6.2 9%, 59.26±2.06% ,resp.),highly myopic eyes have lower disc vessel density ,(P<0.001)..

A study determined the same results; the average peripapilary vessel density were significantly lower in high myopia (47.61 ± 6.58) (p<0.001) (5).

Such outcomes reported also by a study determined that highly myopic eyes have a lower peripapillary vessel density than mild myopic eyes (6).

In this study, the superficial whole macular vessel density (VD) in high myopic eyes was (41.63±7.29%), which was significantly reduced compared to (50.12± 1.35%) in the emmetropic eyes (P <0.001), but there is no statistically significant change in superficial foveal vessel density (20.30±8.05, 21.91±3.54, resp.) (P=0.29).

A study reported the same results; when the foveal superficial vessel densities were analyzed, no changes occurred in HM compared to control eyes. This indicates that the SE did not affect on the vascular density in the fovea of the eyes without pathological myopic changes. A possible reason is that the arterial blood supply is different in each part of the retina. Most of the fovea is an avascular zone characterized by active local metabolism, maintaining the blood flow in a relatively stable state (7).

Regarding deep macular vessel density, there was a statistically highly significant change in the whole image deep macular vessel density between the cases within the A &B groups (48.60±8.94, 53.78±3.80, resp.) (P<0.003), but there was no statistically significant change in deep foveal vessel density (35.89±9.37, 35.46±8.30, respectively) (P=0.82).

These results came in harmony with a study evidenced that the whole image deep vessel density was significantly lower (44.5 ± 5.4) $P < 0.001$ (8).

This may be due to marked elongation of the eyeball might induce retinal thinning, with subsequent reduction of O_2 demand and finally ends in reduction of the blood circulation. In spite of all these explanation, reduction of the blood supply in patients with high myopia still debated and under investigations.

In this study, there was positive correlation between superficial macular density and mean spherical equivalent (r=0.448, P< 0.001) and there was negative correlation between superficial macular density and axial length (r=-0.208, P<0.038).

Also, there was positive correlation between deep macular vessel density and mean spherical equivalent (r=0. 426, P<0.001) but there is weak correlation between deep macular vessel density and axial length (r=-0.173, P=0.086).

A study revealed that the superficial macular vascular density was significantly associated with AL ($P < 0.001$), spherical equivalent ($P < 0.001$). The deep vascular density was also significantly accompanied with AL ($P < 0.001$), spherical equivalent ($P = 0.001$) (9).

The current study revealed positive correlation between optic disc vessel density and mean spherical equivalent (r=0.391, P<0.001) and negative correlation between optic disc vessel density and axial length (r=-0.249, P<0.013).

These results agree with a study reported the same results; there was negative correlation between peripapillary vascular density and AL (r=-386, P<0.006), however there is a positive correlation between peripapillary vascular density and SE (r=0.408, P=0.004) (7).

Regarding correlation between average RNFL and AL, there was significant high negative correlation between them (r=-0.322, p=0.001), but, there is positive significant correlation between average RNFL thickness and MSE (r=0.246, P<0.001).

A study found the same results; A highly significant negative correlation between axial length and average RNFL thickness (r= -0.711, p<0.001) and highly positive correlation between average RNFL thickness and MSE (r=0.722, P<0.001) (10).

Elongation and thinning of the sclera and the retina, which spread the nerve fibers over a larger surface area, could be the reason for thin RNFL in myopes. It could also represent a decrease in nerve fiber number, although there is no histological basis for it yet. Thus, thin RNFL measurements in moderate to high myopes appeared to be related to axial lengthening (6).

Our study revealed that there is weak relationship between RNFL thickness and (superficial macular vessel density, deep macular vessel density and disc density) (r= -0.102, p=0.313) (r=0.148, P=0.143) (r=0.094, P=0.354, resp.).

Results of the current study matched with a study reported that the vascular density in optic disc region was not associated with RNFL thickness (r=−0.092, p>0.05) (9).

Regarding correlation between macular vessel density (superficial and deep) with optic disc density, our study revealed that there was weak correlation between superficial macular density and optic density (r= 0.028, P=0.781), but there was significant positive correlation between deep macular density and optic disc density (r= 0.273, P=0.006).

Our findings are consistent with previous studies; a study found no significant correlation between macular vessel density and peripapillary density (beta=0.109, P=0.144) average magnification-adjusted RNFL was thicker in the myopic group than in the control group, as it was (109.21 ±7.38 lm), (96.30 ±4.91 lm) respectively, (p=0.0001) (11).

There were only a few cases in this single-center, cross-sectional, monoracial study. The ocular vasculature of myopia may be better understood by a larger study.

Conclusion

Eyes with high myopia have decreased macular and peripapillary perfusion in comparison with emmetropic eye. These vascular findings may raise the vulnerability to vascular associated eye disorders. It is essential to assess the retinal perfusion in patients with myopia, as it gives baseline information on physiologic alterations between various stages of myopia, and as it is useful for initial recognition of chorio-retinal atrophy, CNV and other complications of high myopia. OCTA is a sensitive device for detection of macular and foveal changes associated with myopia.

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