Original Article

Taiwan J Ophthalmol 2019;10:184-188

Access this article online

Quick Response Code:

Website:
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DOI:
10.4103/tjo.tjo_67_18

Peripapillary and macular choroidal thickness in both eyes of patients with acute unilateral retrobulbar optic neuritis

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Abstract:

PURPOSE: The purpose of this study was to examine macular and peripapillary choroidal thickness (CT) in patients with acute unilateral retrobulbar optic neuritis.

MATERIALS AND METHODS: In this cross-sectional study, 19 patients with acute unilateral retrobulbar optic neuritis were examined. A control group was matched with patients for sex and age. Enhanced depth imaging optical coherence tomography in macula and peripapillary areas in both eyes was performed for evaluation of CT. The CT was measured in subfoveal and other six points of macula and four points of peripapillary areas with a 3.4-mm scan circle centered on the optic nerve head.

RESULTS: The mean subfoveal CT was 384.7 ± 101.6 μm, 380.5 ± 109 μm, and 401.2 ± 84.6 μm for affected eye, unaffected fellow eye, and healthy control, respectively. All measurements of macular CT were thinner in the patient group compared with healthy controls. Global peripapillary CT in affected eyes, unaffected fellow eyes, and healthy controls were 202 ± 43.3, 195.1 ± 42.9, and 234 ± 71.2, respectively. The difference between the three groups was statistically significant in the nasal point of peripapillary area ($P = 0.023$). No correlation was seen between CT and initial visual acuity or duration from symptom onset to medical survey in acute phase of retrobulbar optic neuritis.

CONCLUSION: Patients with acute retrobulbar optic neuritis showed no significantly thinner macular and peripapillary CT in both eyes compared with healthy controls.

Keywords:

Macular choroidal thickness, optic neuritis, optical coherence tomography, peripapillary choroidal thickness

Introduction

Optic neuritis is an inflammatory condition of optic nerves and is a main cause of acute unilateral vision loss in young-to-middle-aged adults. The most important association of this condition is multiple sclerosis (MS), which leads to neurologic impairment with severe important socioeconomic effects.[1,2] In 25% of MS cases, optic neuritis is a presenting symptom.[3,4]

Inflammatory diseases usually can alter vascular changes. In the eye, the choroid is the vascular layer and thus can be changed with inflammatory disorders.[5] For evaluation of the retinal and choroidal changes has several methods, including fundus fluorescein angiography, indocyanine green angiography, ultrasound, and optical coherence tomography (OCT). Of these methods, only OCT can provide any quantitative analysis of the retinal and choroidal layers.

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Submission: 14-07-2018
Accepted: 20-12-2018
Published: 18-02-2019

How to cite this article: Dehghani A, Ghanbari H, Akhlaghi M, Kianersi F, Alemzadeh-Ansari MH. Peripapillary and macular choroidal thickness in both eyes of patients with acute unilateral retrobulbar optic neuritis. Taiwan J Ophthalmol 2020;10:184-8.

OCT depends on interferometry of near-infrared light to illustrate high-resolution, three-dimensional anatomical information and cross-sectional images of any layers of the retinal.[6,7] Recently, for evaluation of the choroidal layer was introduced enhanced depth imaging OCT (EDI-OCT) by Spaide *et al*.[8] EDI-OCT technology can provide more accurate qualitative and quantitative data about choroidal layer.[9] EDI-OCT can measure choroidal thickness (CT) at any area of the fundus. In the previous studies, CT was indirectly indicative of ocular perfusion status. Therefore, CT was presumed as a parameter for quantitative analysis of the choroidal layer.[10,11] The most two areas where CT was measured, included: peripapillary and macula areas.[7,12]

Some reports described the patients with MS after optic neuritis as having decreased subfoveal CT.[13,14] However, to the best of our research, there has been no report, thus far about macular CT of the optic neuritis at acute-phase disease. In the current study, we evaluated the macular and peripapillary CT in patients with acute unilateral retrobulbar optic neuritis with EDI-OCT to access potential effects of this disease on choroidal layer as vascular layer of the eye. Hence, we measure the CT of affected and unaffected eyes with optic neuritis and compare them with CT of healthy controls.

Materials and Methods

This observational cross-sectional study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethical Committee of the Isfahan University of medical science, Iran. Between October 2016 and September 2017, consecutive patients, aged 18–40 years, with acute unilateral retrobulbar optic neuritis were enrolled in this study. The diagnosis of acute retrobulbar optic neuritis was based on eye movement pain, no optic disc swelling, and optic nerve dysfunction, including decreased visual acuity, dyschromatopsia, or relative afferent papillary defect presented in <7 days of initial symptoms. Inclusion criteria were included no history of corticosteroid use, no history of any chronic drug use, no history of previous optic neuritis, no known MS or systemic disease, no optic atrophy, lack of smoking, and refractive errors (spherical equivalent) <3 diopters.[7,9,13] Furthermore, ocular pathologies, such as central serous chorioretinopathy, age-related macular degeneration, retinal dystrophies, uveitis, or glaucoma, were ruled out.[7] The age- and sex-matched control group of healthy individuals had all inclusion criteria. This matching was performed for controlling better-unwanted bias affecting CT.[9] All participants filled the written informed consent to the study procedures.

Demographic features of all participants were documented. All participants underwent comprehensive neuro-ophthalmic examination by an ophthalmologist (A.R.D, H.A, and F.K.). The examination included autorefractometry (Topcon RM-800, USA), best-corrected visual acuity (BCVA) converted to logarithm of minimum angle of resolution (logMAR), intraocular pressure measurement by Goldmann applanation tonometry, slit-lamp examination of the anterior segment, and dilated fundus examination. CT was measured using Spectralis HRA + OCT (Heidelberg Engineering, Heidelberg, Germany). To avoid diurnal variation of CT,[15-17] all imaging of EDI-OCT were performed between 9:00 and 11:00 am.

To access a high resolution of choroidal section, spectral-domain OCT with EDI-OCT mode (wavelength: 870 nm) was done. The one-line raster imaging mode was applied along 6-mm (mm) line passing through the central part of the fovea. The choroidal layer was defined between the hyperreflective line corresponding to the Bruch's membrane and the innermost choroid-sclera boundary. CT was measured perpendicularly at the subfoveal and other six points, located at 0.5-mm intervals, up to 1.5 mm temporal and nasal to the fovea (there were expressed as follows: N500 = CT 500 μm nasal to the fovea; N1000 = CT 1000 μm nasal to the fovea; N1500 = CT 1500 μm nasal to the fovea; T500 = CT 500 μm temporal to the fovea; T1000 = CT 1000 μm temporal to the fovea; and T1500 = CT 1500 μm temporal to the fovea) [Figure 1]. Furthermore, for the measurement of the peripapillary CT was used the spectral-domain OCT with EDI-OCT mode. For this purpose, a 360°, 3.4-mm diameter peripapillary circle scan (including 100 averaged scans with centered on the optic disc) was done. The images were exported, and CT (vertical distance between the Bruch's membrane and the innermost choroid-sclera boundary) was measured at four points (nasal, superior, temporal, and inferior) that each equidistant (90° intervals) to the next point [Figure 2]. Furthermore, all measurements of CT in macula and peripapillary were averaged as global macular CT and global peripapillary CT, respectively. In the study group, both eyes (affected and contralateral unaffected eyes) were included, whereas in the control group, one eye were randomly selected.

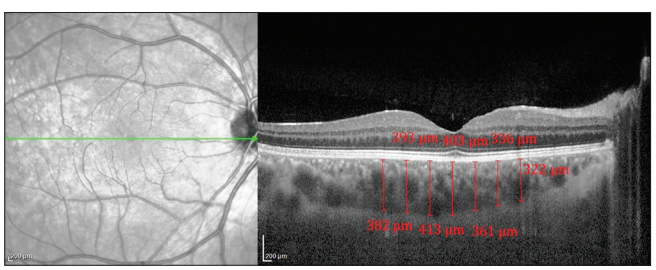

Figure 1: Measurement of choroidal thickness perpendicularly to the subfoveal and six other points, with three points located on each side of a center at 0.5-mm intervals, making for a 1.5-mm distance from each side (temporal and nasal) of the fovea

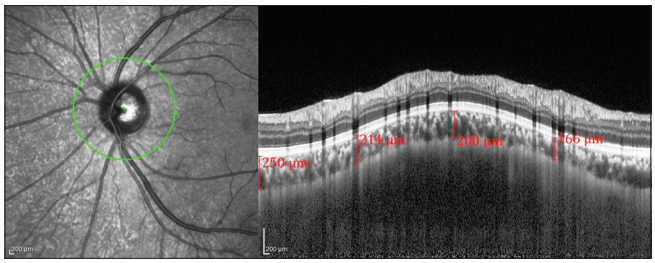

Figure 2: Measurement of peripapillary choroidal thickness perpendicularly at four equidistant (90°) points

All measurements were done by two masked ophthalmologists (M.R.A and M.H.A.A) in the high-quality image (quality >20) with manual caliper tool of the OCT software. The mean values were recorded for analysis. The interobserver reproducibility of the CT measurements was analyzed by measuring the intraclass correlation coefficient (ICC).

All data analyses were performed using SPSS 18 software for Windows (SPSS, Inc., Chicago, IL, USA). Continuous data were expressed as mean ± standard deviation and for categorical data as numbers and percentages. The normal distribution of CT in the all categories was confirmed with the Kolmogorov–Smirnov test and P-P plots. Due to all the analysis of the Kolmogorov–Smirnov test was nonsignificant, we used parametric test for analyzing. One-way ANOVA and *post hoc* Tukey's tests were used for comparing CT of three groups. Correlation was evaluated the association between CT and other parameters. In all analyses, the statistically significant level was considered values of <0.05 based on two-sided tests.

Results

Nineteen patients (14 female) with acute unilateral retrobulbar optic neuritis were enrolled in this study. In the control group, 19 healthy people (14 females) were enrolled. Mean age was 27.4 ± 5.9 years (range: 18–39 years) for patients group and 25.2 ± 2.1 years (range: 23–30 years) for control group. The difference age between the groups was not statistically significant (P = 0.144). The mean duration between the starting of initial symptom to taking EDI-OCT was 4.05 ± 2.5 days (range: 1–7 days). The mean logMAR BCVA for affected eye was 1.61 (0.40–3.00). For other two groups, the mean logMAR BCVA was zero. The interobserver ICC for all measurement was >0.90 (95% confidence interval 0.902–0.971).

The mean subfoveal CT was 384.7 ± 101.6 µm, 380.5 ± 109 µm, and 401.2 ± 84.6 µm for affected eye, unaffected fellow eye, and healthy control, respectively. On the other hand, macular CT was thinner in the patient group (affected and unaffected fellow eyes) compared with healthy control group [Figure 3]. ANOVA and *post hoc* Tukey's tests were done for

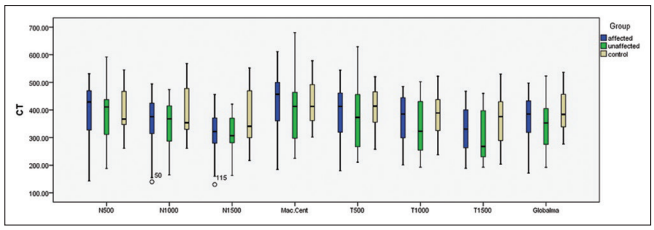

Figure 3: Comparison of macular choroidal thickness between three groups

comparing macular CT in the three groups and were not seen significant difference between groups for all measurements [Table 1].

Global peripapillary CT in affected eyes, unaffected fellow eyes, and healthy controls were 202 ± 43.3, 195.1 ± 42.9, and 234 ± 71.2, respectively. Similar to macular CT, peripapillary CT in all points was thinner in the patient group compared with control group [Figure 4]. Difference between three groups was statistically significant in the nasal point (P = 0.023), and in the *post hoc* Tukey test, the difference was seen between control and unaffected fellow eyes in this point (P = 0.024). In the patient group, peripapillary CT was thicker in the affected compared with unaffected fellow eyes but not statistically significant [Table 2].

In the affected eyes of patients, no correlation was found between any CT measurement and initial BCVA or duration from symptom onset to medical survey in acute phase of retrobulbar optic neuritis.

Discussion

Acute optic neuritis is the inflammatory condition that is similar to other inflammation, alter the vascular regulation.[18] The choroid being the highly vascular layer of the eye can easily be affected by inflammation. One of the popular methods of choroid evaluation is measurement of CT with EDI-OCT. In this study, we evaluated macular and peripapillary CT in the patients with acute unilateral retrobulbar optic neuritis and compared with healthy controls.

In the optic neuritis, female preponderance is revealed in all studies.[2] In this study, the ratio of male to female in patient group was 1:2.8.

In some studies, the reduction of ocular blood flow had shown in MS patients using color Doppler imaging. Higher resistivity indices in the main ocular arteries in MS patients with optic neuritis history compared with healthy controls reported by Akarsu *et al*.[19] Disturbances of ocular blood flow in the main arteries in the MS patients with past retrobulbar optic neuritis showed by Modrzejewska *et al*.[20] This finding confirmed that in patients with a history of optic neuritis, ocular blood

Table 1: Comparing of choroidal thickness in macula region in the three groups

CT	Affected eye	Unaffected eye	Healthy control eye	*P**			ANOVA between three groups
				Affected versus unaffected	Affected versus control	Unaffected versus control	
Subfoveal	384.7±101.6	380.5±109	401.2±84.6	0.990	0.865	0.795	0.793
N500	358.9±107.4	369.2±102.1	376.6±86.9	0.946	0.847	0.971	0.859
N1000	334.2±94	334.8±89.8	370.4±85.8	1.00	0.439	0.447	0.372
N1500	300.2±76.4	301.8±74.3	353.1±90.2	0.998	0.116	0.132	0.080
T500	353.1±94.4	356.4±109.3	380.4±75.1	0.994	0.645	0.713	0.623
T1000	340.6±79.7	331.1±100.5	359.3±77	0.938	0.784	0.575	0.594
T1500	306.1±74.9	298.8±85.6	348.6±83	0.959	0.249	0.152	0.135
Global macular	339.7±80.9	338.9±88.4	369.9±71.8	1.00	0.485	0.467	0.407

**Post hoc* Tukey's test was done. CT=Choroidal thickness

Table 2: Comparing of choroidal thickness in peripapillary region in the three groups

CT	Affected eye	Unaffected eye	Healthy control eye	*P**			ANOVA
				Affected versus unaffected	Affected versus control	Unaffected versus control	
Superior	208.8±45.9	199.9±48.1	237.9±65.8	0.869	0.228	0.086	0.085
Inferior	168.7±45.7	168.4±41.2	202.5±76.5	1.00	0.167	0.162	0.113
Temporal	227.5±57.7	220.6±56.4	254.8±89.7	0.951	0.453	0.294	0.287
Nasal	203.1±47.2	191.8±43	240.6±71.9	0.807	0.102	0.024	0.023
Global peripapillary	202±43.3	195.1±42.9	234±71.2	0.920	0.172	0.079	0.071

**Post hoc* Tukey's test was done. CT=Choroidal thickness

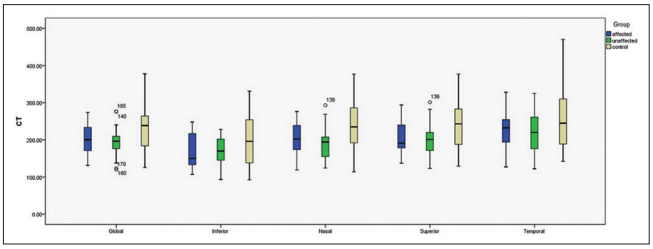

Figure 4: Comparison of peripapillary choroidal thickness between three groups

flow had been altered. Hence, changes in the thickness of choroid layer as globe vascular layer is expected.

In multiple studies, CT was measured in the MS with a history of optic neuritis using EDI-OCT. In the study done by Esen *et al*. showed that macular CT was significantly thinner in the MS patients compared with healthy controls. Furthermore, a significant correlation was shown between subfoveal CT and disease duration ($r = -0.28$) in MS patients.[13] Omer *et al*. demonstrated that macular CT was thinner in MS patients compared with control.[14] In this study, macular CT in the subfovea, other six points of extrafovea, and global macular CT were thinner in the patients compared with healthy controls, but these differences were not statistically significant. We found no correlation between the duration from symptom onset to medical survey and any CT measurement.

A study done by Chen *et al*. showed that peripapillary CT was thicker in eyes affected acute retrobulbar optic neuritis compared with fellow eyes.[21] Similar to this report, we had found thicker peripapillary CT in the affected eyes compared with unaffected fellow eyes and both were also found to be thinner than the peripapillary CT of healthy eyes.

Furthermore, Chen *et al*. reported the correlation between initial BCVA and peripapillary CT in the papillitis type of acute optic neuritis, but this correlation was not seen in the acute retrobulbar optic neuritis.[21] Similarly, we found no correlation between initial BCVA and macular and peripapillary CT.

There are several potential limitations in this study. First, the number of patients enrolled was not large. This limitation causes inadequate statistical power to detect difference in macular and peripapillary CT between groups. Second, follow-up was not long enough to examine that differences in CT are statistically significant between affected eyes and healthy controls. Third, we only measured the total CT and did not examine the choroidal blood flow. Fourth, the patient group was only retrobulbar optic neuritis and was compared them with controls; therefore, we are not able to state on CT in patients with papillitis optic neuritis.

Nevertheless, our study has some strengths. First, to the best of our knowledge, this is the first report about macular CT in acute retrobulbar optic neuritis. Second, using strict inclusion criteria for recruitment, many confounding factors can be affected CT was minimized, and the effect of optic neuritis disease on CT was evaluated. Third, the previous studies demonstrated a

circadian rhythm of CT.[15-17] In this study, for removing this diurnal fluctuation in CT measurement, all precipitations were taken EDI-OCT in the same time period (between 9:00 and 11:00 am).

Conclusion

Patients with acute retrobulbar optic neuritis showed no significant thinner macular and peripapillary CT in both the eyes compared with healthy controls. In optic neuritis, thinning of CT occurs, and it seems that this thinning will increase over time as long as this difference is statistically significant as compared with normal individuals.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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