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Original Article

Evaluation of Choroidal Structures in Children with Newly Diagnosed Type-1 Diabetes Mellitus

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Abstract

Objectives: The objective of this study was to evaluate the subfoveal choroidal thickness (SFCT) and choroidal vascularity index (CVI) in children with newly diagnosed type 1 diabetes mellitus (T1DM).

Methods: A total of 80 children (40 with T1DM and 40 healthy controls) were included in this cross-sectional study. Enhanced depth imaging optical coherence tomography (EDI-OCT) images of all participants were analyzed. The SFCT, total choroidal area (TCA), luminal area (LA), stromal area (SA), and CVI measurements were obtained from EDI-OCT images and compared between groups. The effects of HbA1c, fasting plasma glucose, and axial length measurements on choroidal measurements were investigated.

Results: There was no significant difference between the groups according to TCA (0.84 [0.57–1.26] vs. 0.88 [0.65–1.16] mm^2, p=0.745), LA (0.55 [0.41–0.79] vs. 0.59 [0.43–0.74] mm^2, p=0.745), SA (0.27 [0.15–0.47] vs. 0.28 [0.15–0.47] mm^2, p=0.935), and CVI (68.03 [66.5–70.5] vs. 67.75 [66.2–69.5] %, p=0.794), respectively. However, T1DM patients had thinner SFCT compared to control subjects (309.0 [327–489] and 398.5 [219–491], p<0.044). No correlation was found between HbA1c, fasting plasma glucose, axial length measurements, and SFCT, TCA, LA, SA, or CVI.

Conclusion: Children with newly diagnosed T1DM have thinner SCFT in comparison to healthy children, however, no significant difference in CVI was observed between the groups. Long-term follow-up should be used to confirm the impact of the DM duration on CVI.

Keywords: Choroidal vascularity index, optical coherence tomography, subfoveal choroidal thickness, type 1 diabetes mellitus

Introduction

Type 1 diabetes mellitus (T1DM) is one of the most prevalent chronic autoimmune disorders in childhood, with a worldwide incidence of 3% (1). Due to microvascular complications, patients with T1DM have the risk of vision impairment throughout their lives (2). However, early diagnosis and appropriate management of the disease decrease that risk (3). Choroidal circulation is the major blood supply of the outer retina; therefore, the evaluation of choroidal vasculature is a potential research subject in studies related to diabetic retinopathy (DR) (4-7).

The advancement of enhanced depth imaging optical coherence tomography (EDI-OCT) allows for improved in vivo observation of the choroidal vasculature, particularly those localized in the layers of Sattler and Haller (8). Further anal-

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ysis of the EDI-OCT images with the binarization method provided a better assessment of the choroidal vascular structure and enabled to quantification of the total choroidal area (TCA), luminal area (LA), and stromal area (SA) of the choroid (9,10). Choroidal vascularity index (CVI), the proportion of LA to TCA, has been widely used for assessment of the choroidal vasculature in many ocular diseases (10-13). Unlike subfoveal choroidal thickness (SFCT), which can be influenced by factors such as age and refractive error, CVI offers a stable and consistent parameter for assessing the vascular status of the choroid, making it a superior indicator for clinical evaluations and research (13,14).

The knowledge about choroidal vasculature changes in T1DM patients without DR is limited (6,7,15,16). Nevertheless, information regarding the choroidal structure of children recently diagnosed with T1DM has not yet been evaluated. Due to the clinical importance of early detection of choroidal microvascular alterations in these patients, in the present study, assessment of the SFCT and CVI of pediatric T1DM patients was aimed.

Methods

This cross-sectional study was conducted at the Pediatric Endocrinology and Ophthalmology Departments of Zonguldak Bülent Ecevit University. The study was conducted in accordance with the tenets of the Declaration of Helsinki and with the approval of the Ethics Committee of Zonguldak Bülent Ecevit University (2023/18-11). Informed consent and oral assent were obtained from all participants and their legal guardians.

Patient Selection and Data Collection Criteria

The children recently diagnosed with T1DM and healthy controls were referred to the ophthalmology department. All participants underwent a complete ophthalmic examination between 9 and 11 am by the same ophthalmologist (TG), including autorefractometry, best corrected visual acuity (BCVA) with Snellen Chart, biomicroscopic examination, dilated fundus examination, axial length measurement with optical biometer (Optical Biometer AL-Scan, Nidek Co., Japan), and EDI-OCT imaging (Spectralis, Heidelberg Engineering, Heidelberg, Germany).

Subjects with a history of significant ocular disease (congenital or juvenile cataract or glaucoma, hereditary retinal diseases, DR and other retinal vascular diseases), BCVA worse than 20/20, amblyopia, more than 2 diopters (D) of cylindrical and/or 4 D spherical error, poor image quality, and children who were too young to cooperate for OCT were excluded from the study.

Image Processing and Calculation of Choroidal Parameters

SFCT was measured perpendicular to the retinal pigment epithelium (RPE), from the lower edge of the RPE to the choroid-scleral junction at the subfoveal section manually by the EDI-OCT device. EDI-OCT image binarization was made according to the method reported by Agrawal et al. (17) Single horizontal EDI-OCT images passing through the fovea were imported into ImageJ 1.51 software (National Institutes of Health, Bethesda, MD, USA) for analysis. A 3000 µm wide region was chosen, with 1500 µm for the nasal and 1500 µm for the temporal boundaries from the fovea. The ImageJ ROI Manager was used to manually establish the boundaries of the choroidal area. The selected area represents the TCA. The Niblack auto-local threshold was utilized to modify the image (Fig. 1). Then, the image was converted back to red, green, and blue. Demarcation of the black pixels was made by the color threshold tool to determine the luminal (vascular) area (LA). The SA which is represented with white pixels was calculated by subtraction of LA from TCA. The ratio of LA to TCA gave us the CVI.

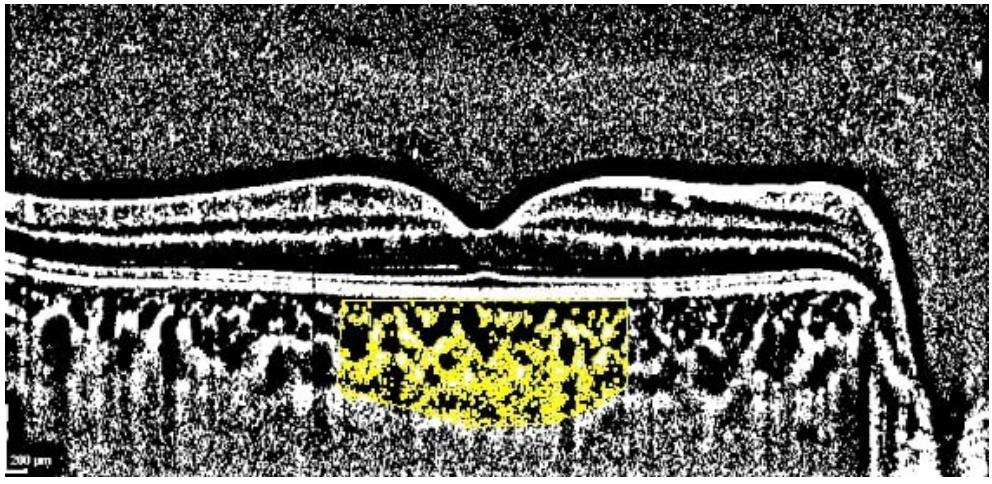

Figure 1. Binarization of optical coherence tomography image.

Statistical Analysis

Data analysis was performed with SPSS 20.0 software (IBM SPSS, IBM, New York, USA). The normality of data was determined with Shapiro-Wilk test. Because the variables' normal distribution is rarely encountered, non-parametric tests were conducted. The Mann–Whitney U test was used to compare the variables between the T1DM and the control group. Correlations between HbA1c, fasting plasma glucose, axial length measurements, and SFCT, TCA, LA, SA, and CVI were evaluated with Spearman's rho analysis. P<0.05 was considered statistically significant.

Results

In the present study, the data of 40 children (26 girls and 14 boys) with T1DM and 40 healthy children (16 girls and 24 boys) were analyzed. The demographic and clinical characteristics of both groups are presented in Table 1. The mean age of the T1DM group was 11.70±2.92 years, and the mean age of the control group was 10.50±3.15 years. There was no significant difference between the groups in terms of age and gender (p=0.161 and p=0.113, respectively).

Data regarding SFCT, TCA, LA, SA, and CVI values are shown in Table 2. The medians (min-max) of SFCT in T1DM and the control group were 309.0 (327–489) and 398.5 (219–491), respectively. The T1DM group had thinner SFCT than the control group (p=0.044). There were no statistically significant differences between T1DM and control groups in terms of the medians (min-max) of TCA (0.84 [0.57–1.26] vs. 0.88 [0.65–1.16] mm^2, p=0.745), LA (0.55 [0.41–0.79] vs. 0.59 [0.43–0.74] mm^2, p=0.745), SA (0.27 [0.15–0.47] vs. 0.28 [0.15–0.47] mm^2, p=0.935), and CVI (68.03 [66.5–70.5] vs. 67.75 [66.2–69.5] %, p=0.794), respectively.

Table 1. Demographic and clinical characteristics of participants

	T1DM Group (n=40)	Control Group (n=40)	p
Age, years	11.70±2.92	10.50±3.15	0.161†
Gender			
Female	26	16	0.113*
Male	14	24	
BCVA, LogMAR	0	0	1.0†
Axial length, mm	23.49±1.14	22.96±0.78	0.176†
HbA1c, %	9.81±2.93	n/a	-
FBG	272.65±140.03	n/a	-

T1DM: Type 1 diabetes mellitus; BCVA: Best-corrected visual acuity; BCVA: Best corrected visual acuity; FBG: Fasting blood glucose; MBP: Mean arterial pressure; AL: Axial Length; †: Kruskall-Wallis*: Pearson Chi-square.

To evaluate the impact of HbA1c, FPG, and AL on SFCT, TCA, LA, SA, and CVI, correlation analysis was also performed. However, no association was found between any of the parameters (Table 3).

Discussion

The risk of developing DR in DM cases increases with the duration of the disease. T1DM patients are diagnosed at an earlier age and have a longer life expectancy, so their lifetime risk of developing DR is significantly higher (2,18). However, the most effective way to prevent vision loss due to DR is early diagnosis and appropriate treatment (3). Protecting visual function in pediatric T1DM patients requires early detection of vascular alterations that precede the onset of DR symptoms. Studies assessing choroidal vasculature in T1DM patients are extremely rare (6,7,16). To the best of our knowledge, however, this study is the first to evaluate

Table 2. Comparison of choroidal structural parameters between the groups

	T1DM Group (n=40)	Control Group (n=40)	p*
SFCT, µm	309.0 (327–489)	398.5 (219–491)	0.044
CVI (%)	68.03 (66.5–70.5)	67.75 (66.2–69.5)	0.794
TCA, mm^2	0.84 (0.57–1.26)	0.88 (0.65–1.16)	0.745
LA, mm^2	0.55 (0.41–0.79)	0.59 (0.43–0.74)	0.745
SA, mm^2	0.27 (0.15–0.47)	0.28 (0.14–0.41)	0.935

SFCT: Subfoveal choroidal thickness; CVI: Choroidal vascularity index; TCA: Total choroidal area; LA: Luminal area; SA: Stromal area; *: Mann-Whitney U test.

Table 3. Correlations between clinical characteristics and choroidal structures

	HbA1c	FBG	AL
SFCT	r: –0.157	r: 0.101	r: –0.006
	p=0.510	p=0.672	p=0.972
CVI	r: 0.012	r: 0.032	r: –0.093
	p= 0.960	p=0.895	p=0.566
TCA	r: 0.074	r: 0.335	r: –0.034
	p=0.757	p=0.148	p=0.836
LA	r: 0.108	r: 0.337	r: –0.012
	p=0.649	p=0.146	p=0.940
SA	r: 0.047	r: 0.224	r: –0.082
	p=0.845	p=0.342	p=0.615

SFCT: Subfoveal choroidal thickness; CVI: Choroidal vascularity index; TCA: Total choroidal area; LA: Luminal area; SA: Stromal area; HbA1c: Hemoglobin A1c; FBG: Fasting blood glucose; AL: Axial Length. Spearman's rho analysis.

the choroidal vascular alterations in the pediatric group with recently diagnosed T1DM.

In the present study, SFCT and CVI of the newly diagnosed T1DM children were analyzed and compared to those of healthy children. It has found that children with T1DM have thinner SCFT than healthy children, however, no significant difference was observed in CVI between the groups.

Aksoy et al. evaluated the CVI in young adults with T1DM (the mean disease duration: 6.2±0.7 years) and revealed a statistically significant decrease which they related to disease duration (6). Duran et al. conducted a similar study in a pediatric T1DM group with a mean disease duration of about 4 years and they also revealed a decreased CVI that could not reach the statistical significance level (16). They have also found a negative correlation between disease duration and CVI readings. The present study included recently diagnosed pediatric cases with T1DM, this may be the reason that no significant change in CVI. The absence of the CVI difference at the time of diagnosis period supports the relation between DM duration and CVI. It should be mentioned that cross-sectional analyses were used to draw these conclusions. Hence, the effect of the DM duration on CVI should be validated using serial OCT images that would be obtained from a long-term follow-up.

Histopathologic examinations in diabetes patients revealed choroidal neovascularization, vascular dropout, and regions of vascular nonperfusion (5). It is also stated in postmortem examinations that more focal choriocapillaris degeneration areas were observed in diabetic subjects in comparison to nondiabetic subjects (19). Choroidal blood flow may be impacted by structural alterations in choroid vessels. The foveal region of individuals with DME had markedly reduced choriocapillaris blood flow, as measured by laser Doppler flowmetry and OCT angiography (20,21). The intermediate-large blood vessels in the Sattler's and Haller's layers have been shown to exhibit tortuosity and loss using EDI-OCT (22). Recent studies revealed that a disease duration-related decrease in CVI was observed in T1DM patients which was assumed as a result of choroidal hypoxia-related vascular narrowing (6,16). However, our cohort is composed of children with newly diagnosed T1DM, which is the probable reason for the observation of no change in CVI.

The results in the literature regarding SFCT in T1DM patients are controversial. Esmaeelpour et al. found decreased SFCT in T1DM cases independent of the retinopathy presence or disease duration (23). Aksoy Aydemir et al. also revealed that children with T1DM have thinner SFCT (24). Findings of the current study, having thinner SFCT in newly diagnosed T1DM children, also support that decreased SFCT in those patients is independent of the disease duration. In addition, some studies regarding SFCT in children with T1DM found no differences while some even found an increased SFCT in comparison to healthy children (25-27). The reason behind that inconsistency between studies may be the vulnerability of SFCT to many factors such as age, systolic blood pressure, axial length, and intraocular pressure; whereas CVI was unaffected by those factors (10).

The present study has certain limitations. The foremost is the relatively small number of participants. Second, it is possible that one single horizontal scan was insufficient to reflect the entire choroid for detecting variations in SFCT and CVI measurements. Finally, the lack of histopathological studies to confirm the binarization technique representing choroidal vasculature and stromal regions may induce errors and restrictions to our conclusion.

Conclusion

The present study showed that children with T1DM have thinner SCFT than healthy children, however, no significant difference was observed in CVI between the groups. Therefore, subsequent OCT sections that would be obtained during a long-term follow-up should be used to confirm the impact of the DM duration on CVI.

Disclosures

Ethics Committee Approval: The study was conducted in accordance with the tenets of the Declaration of Helsinki and with the approval of the Ethics Committee of Zonguldak Bülent Ecevit University (2023/18-11).

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