Original Article

Evaluation of Posterior Ocular Structures in Patients with Isolated Iris Coloboma

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Abstract

Objectives: To measure lamina cribrosa thickness (LCT), lamina cribrosa depth (LCD) and subfoveal choroidal thickness (SFCT) by imaging posterior ocular structures in pediatric cases with isolated unilateral iris coloboma and to investigate the differences as compared with healthy contralateral eyes of these cases (fellow eyes) and healthy control eyes.

Methods: This cross-sectional, comparative prospective study included seven children (age range, 9-17 years) with unilateral isolated iris coloboma. The healthy contralateral eyes of these cases formed the fellow group. An age-matched (age range 8-17 years) control group (n=9), including children with both eyes having either normal or corrected-to-normal visual acuity, was formed. A detailed ophthalmic examination was performed. The posterior ocular segments were evaluated using spectral domain-optical coherence tomography (SD-OCT) with enhanced depth imaging (EDI) technique.

Results: The SFCT was 372.0±48.8 μm, 375.3±44.0 μm, and 386.5±71.8 μm, respectively, and the LCD was 362.4±68.3 μm, 354.4±47.1 μm, and 350.7±38.1 μm, respectively, in the coloboma, fellow, and control eyes. There was no difference between the groups regarding SFCT and LCD. The mean LCT was significantly thinner in the coloboma eyes (200.2±9.5 μm) than in the fellow (238.8±26.7 μm; p=0.023) and control eyes (240.0±12.9 μm; p<0.001). The LCT showed no significant correlation with age, axial length or spherical equivalent.

Conclusion: Better visual prognosis is expected in isolated iris coloboma. However, detailed examinations using new technologies, such as SD-OCT, may reveal some structural changes. Longitudinal studies are required to understand if a thinner LCT in coloboma eyes is associated with any future problems.

Keywords: Coloboma of iris, choroid, lamina cribrosa, optical coherence tomography

Introduction

Coloboma is a congenital anomaly characterized by missing pieces of tissue in the ocular structures. The estimated incidence is estimated to range from two to 14 per 100.000 births (1). During the intrauterine development process, a partial tissue defect occurs in any of the cornea, iris, ciliary body, lens, retina, choroid, and optic nerve tissues due to aberrant closure of the choroid fissure in the 5th-7th week of the fetal life (2). The anomaly presents itself within a wide spectrum from iris coloboma to clinical anophthalmia. It has heterogeneous etiology and may be genetically inherited; it can be seen together with chromosomal anomalies or some syndromes or may be isolated in individuals who are otherwise healthy (1,3). Ocular coloboma may be unilateral or bilateral. Visual prognosis depends on location and other accompanying conditions (2). While colobomas involving the retina or optic nerve resulting in loss of vision, iris coloboma usually does not cause loss of vision. Thus, it is considered underdiagnosed (https://ghr.nlm.nih.gov/condition/coloboma). However, iris coloboma is the most common type of colobomas (4,5). A typical iris coloboma extends inferonasally and creates a characteristic keyhole-

shaped pupil. Iris coloboma may either be isolated or involve other ocular tissues (6). Surgical techniques can be used for functional and cosmetic repair in iris coloboma (7).

In the literature, only a single study evaluating other ocular structures in patients with isolated iris coloboma was encountered, which was conducted by Karatepe Haşhaş et al. (8) in which the cornea was evaluated. To our knowledge, to date, there has been no study investigating the posterior segment structures in the eyes with isolated unilateral coloboma. Accordingly, the present study aimed to measure lamina cribrosa thickness (LCT), lamina cribrosa depth (LCD), and subfoveal choroidal thickness (SFCT) by imaging posterior ocular structures in pediatric cases with isolated iris coloboma and to investigate the differences as compared with healthy contralateral eyes of these cases (fellow eyes) and healthy control eyes. To our knowledge, this study is the first study to investigate posterior segment structures (LCT, LCD, and SFCT) in the eyes with isolated unilateral iris coloboma.

Methods

Patients

A detailed ophthalmic examination was performed in children who were admitted to the ophthalmology clinic due to unilateral isolated iris coloboma. Patients who had strabismus, cataract, glaucoma or other retinal disorders, patients with organic ophthalmic disorders, patients with a history of intraocular surgery, patients previously underwent laser therapy, patients who would not able to cooperate on ophthalmic examination or optical coherence tomography (OCT) were excluded from this study. Accordingly, seven children (age range, 9-17 years) with unilateral isolated iris coloboma were enrolled in this study. Healthy contralateral eyes of these children formed the fellow group. An age-matched (age range 8-17 years) control group was also formed from children (n=9) who were admitted to the hospital for ophthalmic examination and in whom both eyes had normal or corrected-to-normal visual acuity (VA) (that is, the logarithm of the minimum angle of resolution [logMAR] of 0 units or better).

The present study was approved by the local ethics committee and informed consent was obtained from all participants or their parents or legal representatives. This study was conducted in accordance with the Declaration of Helsinki.

Procedures

All participants underwent detailed ophthalmic examination and the following parameters were measured: VA, spherical equivalent (SE), intraocular pressure (IOP), axial length (AL), central corneal thickness (CCT), LCT, LCD, and SFCT.

A standard Snellen chart was used to measure VA and decimal VA was converted into logMAR units. To assess the refractive status, five sequential readings were performed using a tonometer (TonoRef II; Nidek Co., Ltd; Aichi, Japan) 45 minutes after administration of an ophthalmic solution containing 1% cyclopentolate for three times with 5-minute intervals. All readings were required to be within 0.25 diopter (D) of each other. SE was calculated as the sum of spherical error and half of a cylindrical error. CCT was measured using a Scheimpflug camera (Pentacam HR; Oculus GmbH, Wetzlar, Germany). AL was measured using an IOL Master (Carl Zeiss Meditec Inc., Dublin, CA, USA). LCT and SFCT measurements were performed using spectral domain (SD)-OCT device.

Spectral-Domain Optical Coherence Tomography Measurements

In all patients and controls, an SD-OCT device (Heidelberg Engineering, Heidelberg, Germany) with an enhanced depth imaging (EDI) program (HEYEX software 6.0) was used for the measurement of LCT after pupillary dilation (9) and also for the measurement of SFCT according to the procedure previously described by Spaide et al. (10). Scans with a quality score of <20 or poor-quality scans (those with unclear fundus images or unclear LCT borders) were excluded from the analysis both for the LCT and SFCT measurements.

To obtain the enhanced depth imaging of the optic nerve head (ONH), the SD-OCT device was arranged in a way to form a rectangular image of 15°×10° centered on the optic disc. This rectangular field was then divided into nearly 65 sections, each having an average of 100 OCT frames. On these horizontal B scans, three frames passing through the center, mid-upper and mid-lower aspects of the ONH were selected and the parameters were measured on each of these frames. The center of the lamina cribrosa plate was used for the LCT measurements. Figure 1 depicts the lamina cribrosa borders in an ONH OCT image.

The line combining the two ends of the Bruch's membrane was defined as the Bruch's membrane opening (BMO). All distances were measured on the line perpendicular to the reference line and the parameters were measured as closer as possible to the vertical center of the ONH. In case a vessel precluded a measurement, the measurements were performed in the temporal region. In the horizontal SD-OCT sections, the anterior and posterior borders of the highly reflective area in the vertical center of the ONH were defined as the borders of lamina cribrosa and the distance between these two borders was defined as the LCT. Contrast adjustments helped with the identification of images that most clearly illustrate the lamina cribrosa. The LCD was defined as the distance between the BMO and the anterior border of the lamina cribrosa.
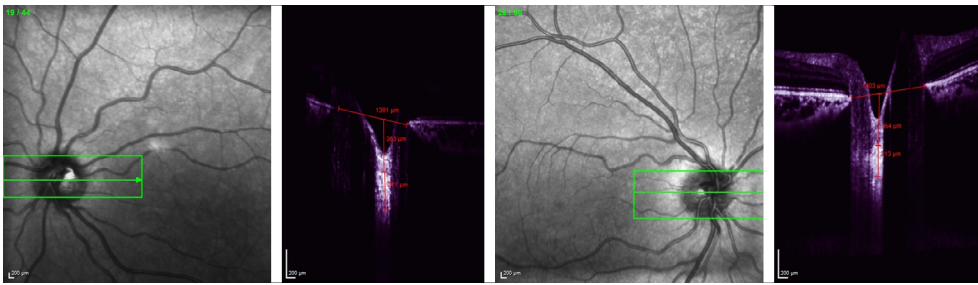
Figure 1. Optical coherence tomographic images of an 11-year-old patient with unilateral isolated iris coloboma. Horizontal scans. (Left) Fellow eye of the patient with isolated iris coloboma. The thickness of the lamina cribrosa was 271 μm. (Right) Coloboma eye of the patient with isolated iris coloboma. The thickness of the lamina cribrosa was 213 μm.

The SCFT measurements were performed using the EDI-OCT technique, where the SD-OCT device is pushed close to the eye to gather an inverse image. To adjust the signal-to-noise ratio, seven sections, each containing 100 scans, on average were obtained within a 5°×30° rectangular area comprising the macula and the optic nerve. The horizontal section passing directly through the foveal center was used to measure the choroidal thickness. The choroid was measured from the outer edge of the hyperreflective line, which corresponds to the retinal pigment epithelium to the internal scleral edge. Macular choroidal thickness was measured in the subfoveal region.

Statistical Analysis

Data analyses were performed using the IBM SPSS Statistics for Windows, version 21.0 (IBM Corp. Armonk, NY, USA). The pretest statistical power was 90%. Descriptive statistics were expressed as mean±standard deviation (SD) for numerical variables. Multiple group comparisons of normally distributed numerical variables were performed using the Analysis of Variance (ANOVA) test. The Tukey test was used for post-hoc comparisons.

Pearson's correlation coefficient was used to determine the relationship between numerical variables. The level of statistical significance was set at a p-value of <0.05.

Results

In this study, seven eyes with isolated iris coloboma and their fellow eyes and 9 control eyes were included in the analysis. The mean age of the patient group (5 females and 2 males) was 13.14±3.93 years and the mean age of the control group (7 females and 2 males) was 13.11±3.95 years. The patient and control groups did not differ concerning distributions of age and sex (p=0.98 and p=0.77). The coloboma, fellow, and control eye groups did not differ concerning their ocular characteristics (IOP, VA, SE, AL, and CCT) (Table 1).

Evaluation of the posterior ocular regions of the eyes revealed that the coloboma eyes did not differ from the fellow and control eyes in terms of the mean SFCT and LCD. On the other hand, the mean LCT was significantly thinner in the coloboma eyes (200.2±9.5 μm) as compared with the fellow (238.8±26.7 μm) and control (240.0±12.9 μm) eyes (p=0.023 and p<0.001, respectively; Table 2).

The correlation analysis performed to evaluate the relationship of LCT with age, AL, and SE revealed that the LCT was not significantly correlated with age, AL or SE in the coloboma, fellow, and control eyes (Table 3).

Table 1. Results of comparison of ocular characteristics of coloboma, fellow and control eyes

	Coloboma eyes (n=7)	Fellow eyes (n=7)	Control eyes (n=9)	p1	p2	p3
IOP, mmHg	13.0±1.0	13.5±2.2	13.8±2.0	0.83	0.62	0.94
VA, logMAR	0.02±0.04	-0.01±0.03	-0.02±0.04	0.18	0.07	0.93
SE, D	0.81±0.64	0.66±0.28	0.24±0.46	0.83	0.07	0.22
AL, mm	22.29±0.52	22.57±0.76	22.64±0.53	0.69	0.52	0.97
CCT, μm	559.00±27.86	543.80±25.87	544.44±27.32	0.65	0.61	0.99

IOP, intraocular pressure; VA: visual acuity; logMAR: the logarithm of the minimum angle of resolution; D: diopter; SE: spherical equivalent; AL: axial length; CCT: central corneal thickness. p1: Coloboma vs. fellow eyes, p2: Coloboma vs. control eyes, p3: Fellow vs. control eyes.

Table 2. Results of measurements of subfoveal choroidal thickness, lamina cribrosa thickness, and lamina cribrosa depth in coloboma, fellow and control eyes

	Coloboma eyes (n=7)	Fellow eyes (n=7)	Control eyes (n=9)	p1	p2	p3
SFCT, μm	372.0±48.8	375.3±44.0	386.5±71.8	0.99	0.88	0.93
LCT, μm	200.2±9.5	238.8±26.7	240.0±12.9	0.023	<0.001	0.99
LCD, μm	362.4±68.3	354.4±47.1	350.7±38.1	0.95	0.89	0.98

SFCT: subfoveal choroidal thickness; LCT: lamina cribrosa thickness; LCD: lamina cribrosa depth; p1: Coloboma eyes vs. fellow eyes, p2: Coloboma vs. control eyes, p3: Fellow vs. control eyes.

Table 3. Correlation of LC thickness values with the age, axial length, and SE in coloboma, fellow and control eyes

	LCT					
	Coloboma eyes		Fellow eyes		Control eyes	
	r	p	r	p	r	p
Age	-0.60	0.15	-0.14	0.76	-0.53	0.14
AL	0.58	0.22	-0.71	0.11	0.12	0.74
SE	-0.15	0.74	0.66	0.10	-0.35	0.34

LCT: Lamina cribrosa thickness; AL: axial length; SE: spherical equivalent.

Discussion

In children with coloboma, the prognosis is affected by the eye sections involved. Poorer prognosis has been reported for colobomas accompanied by microcornea, microphthalmia, cysts, and other abnormalities, whereas simple coloboma has been reported to have the best prognosis (11). Studies evaluating other structures of the eye in patients with isolated iris coloboma are quite limited in number. In their study, Karatepe Haşhaş et al. (8) evaluated the cornea in patients (n=9) with isolated iris coloboma and reported differences in several parameters, including lower keratometry values, increased corneal thickness, reduced anterior chamber depth, greater pupil diameter, and smaller horizontal corneal diameter in the eyes with coloboma as compared with completely normal contralateral (fellow) eyes. In the present study, although the CCT tended to be higher in the eyes with unilateral iris coloboma as compared with their contralateral (fellow) eyes, this difference failed to reach the level of statistical significance.

In the present study, the mean LCT among the posterior segment parameters was significantly thinner in the eyes with isolated iris coloboma as compared with the fellow and healthy control eyes. Although the mean LCD was higher in the eyes with coloboma as compared with the fellow and control eyes, the difference did not reach the level of statistical significance. The mean SFCT was also lower in the coloboma eyes as compared with the fellow and control eyes; however, the difference was not statistically significant.

Lamina cribrosa is the region at which the optic nerve fibers exit the eye through a hole in the posterior sclera and through which central retinal vessels pass (11). Until recently, data on the structural and histological features of lamina cribrosa have been based on the information obtained from animal studies, cadavers, and enucleated eyes and there was no opportunity to conduct a prospective examination in particular. The opportunity for in vivo investigation of ocular structures has been provided along with the introduction of OCT (11,12). The sensitivity of imaging the deep ocular layers has been enhanced with the use of the EDI feature of the SD-OCT. Thus, better visualization of the posterior segments and lamina cribrosa has become possible (11,13,14). In the EDI-OCT technique, the OCT device is pushed towards the eye close enough and detailed cross-sectional images of the lamina cribrosa, including the anterior laminar surface, the laminar pores, and the neuroretinal rim, are obtained (11).

Structural and histological changes in the lamina cribrosa are investigated in ocular diseases and in some systemic diseases with ocular involvement (15–22). Particularly, based on the consideration that it plays a role in the pathogenesis

in patients with glaucoma, changes in the lamina cribrosa are investigated (15,16). It has been suggested that quantitative changes determined by OCT can be used as biomarkers in predicting glaucoma-related injury (17). Early detection of changes in the lamina cribrosa would enable the early diagnosis of glaucoma (18). Increased severity of glaucoma was associated with increased LCD and decreased LCT (19). LCT was low and LCD was high in migraine patients either with or without aura and these findings suggested to indicate that migraine patients are at risk of developing glaucoma (20). LCT was lower in patients with retinal vein occlusion as compared with healthy individuals (21). In a study evaluating the lamina cribrosa using OCT, a thicker and more anteriorly positioned lamina cribrosa was demonstrated in patients with diabetes mellitus as compared with healthy controls (22).

A study conducted in healthy adults (≥18 years old) reported a positive correlation between LCT and age (23). In the present study, no correlation was determined between age and LCT either in the coloboma cases or in the controls. This might have resulted from the study participants' consisting of pediatric cases within a limited age range. I think that repeating the measurements in adults and within a wider age range would be beneficial. Moreover, in the present study, the LCT was not found to be correlated with AL or SE. In their study conducted in healthy adults, Xio et al. (23) found no correlation between LCT and AL. Likewise, Lee et al. (24) found that the LCT was not correlated with CCT or AL.

In brief, the present study found that the mean LCT was significantly lower in coloboma eyes of patients with isolated iris coloboma as compared with their fellow eyes and healthy control eyes. The above-mentioned studies have suggested that there is a relationship between LCT and ophthalmic or certain systemic diseases. Based on this suggestion, I could speculatively propose that some other pathologies associated with low LCT may occur in this cases in the future. Longitudinal studies, including larger populations, are required to confirm this relationship.

Limited patient number can be considered a limitation of the present study; however, isolated unilateral iris coloboma is already a rare condition. Nevertheless, the pretest statistical power of the present study is 90% and this is adequate for the present study to be worthy of note.

Conclusion

A better visual prognosis is expected for patients with isolated iris coloboma. However, detailed examinations performed using new technologies, such as SD-OCT may reveal some structural changes, that have not yet caused clinical problems. In the present study, the LCT was lower in the coloboma eyes as compared with the fellow and control eyes. Longitudinal studies, including larger populations, are

required to understand whether this is associated with some other future problems.

Disclosures

Ethics Committee Approval: The present study was approved by the local ethics committee and informed consent was obtained from all participants or their parents or legal representatives. This study was conducted in accordance with the Declaration of Helsinki.

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Conflict of Interest: None declared.

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