Lamina Cribrosa Position in Primary Open Angle Glaucoma with Swept- Source Optical Coherence Tomography

Primer Açık Açılı Glokom Olgularında Swept-Source Optik Koherens Tomografi Cihazı ile Lamina Kribrosa Dokusunun Değerlendirilmesi

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ABSTRACT

Purpose: To compare the thickness and depth measurements of the lamina cribrosa (LC) obtained using a swept-source optical coherence tomography (SS-OCT) device in primary open angle glaucoma (POAG) patients and healthy subjects.

Materials and methods: This retrospective, cross-sectional observational study included 26 eyes with POAG and 20 control eyes. The LC measurements with serial horizontal B-scans of the optic nerve head were obtained using SS-OCT (Topcon 3D DRI OCT Triton). The anterior lamina surface (ALS) depth, posterior lamina surface (PLS) depth, and LC thickness measurements were evaluated.

Results: In patients with POAG, the mean ALS depth was 471,92±162,22 µm (236-861); the mean PLS depth was 673,19±158,24 µm (426-984); and the mean LC thickness was 201,26±53,33 µm (80-310). In the glaucoma control group, the corresponding values were 442,30±91,18 µm (200-587); 648,90±81,35 µm (483-768); and 206,60±50,41 µm (168-284), respectively (p=0,66; p=0,59; p=0,79).

Conclusions: Lamina cribrosa can be evaluated using an SS-OCT device. Lamina cribrosa were displaced posteriorly in POAG eyes compared with normal controls. Since the difference between groups was not statistically significant in our study, further prospective studies with a larger number of subjects are needed to assess the utility of the LC position as a diagnostic tool in glaucoma.

Key words: Primary open angle glaucoma,Swept-source optic coherence tomography, Lamina cribrosa.

ÖZ

Amaç: Primer açık açılı glokom (PAAG) olguları ve sağlıklı bireylerde swept-source optik koherens tomografi (SS-OKT) cihazı kullanılarak elde edilen lamina kribrosa (LK) derinlik ve kalınlık ölçümlerini karşılaştırmak.

Gereç ve yöntemler: Bu retrospektif, kesitsel ve gözlemsel çalışmaya PAAG'lu 26 göz ve 20 kontrol gözü dahil edildi. Optik sinir başı seri B yatay taramaları ile yapılan LK ölçümleri SS-OKT (Topcon 3D DRI OCT Triton) kullanılarak elde edildi. Ön lamina yüzey (ÖLY) derinliği, arka lamina yüzey (ALY) derinliği ve LK kalınlık ölçümleri değerlendirildi.

Bulgular: PAAG olgularında ortalama ÖLY derinliği 471,92±162,22 µm (236-861); ortalama ALY derinliği 673,19±158,24 µm (426-984); ve ortalama LK kalınlığı 201,26±53,33 µm (80-310) idi. Glokom kontrol grubunda karşılık gelen değerler sırasıyla 442,30±91,18 µm (200-587); 648,90±81,35µm (483-768); ve 206,60±50,41µm (168-284) idi (p=0,66; p=0,59; p=0,79).

Sonuç: Lamina kribrosa dokusu, SS-OKT cihazı kullanılarak değerlendirilebilir. Lamina kribrosa, PAAG'lu gözlerde normal kontrollere göre arkaya doğru yer değiştirmişti. Çalışmamızda gruplar arasındaki fark istatistiksel olarak anlamlı değildi. Lamina kribroza lokalizasyonunun glokomda bir teşhis aracı olarak kullanımını değerlendirmek için daha fazla olgu sayısı ile prospektif çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Primer açık açılı glokom, Swept-source optik koherens tomografi, Lamina kribroza

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INTRODUCTION

Glaucoma is a progressive optic neuropathy that causes visual field loss by affecting peripheral vision. The lamina cribrosa (LC) is a mesh-like connective tissue in the scleral canal of the optic nerve head (ONH) that contains retinal ganglion cell axons and retinal blood vessels.[1]

The LC forms a barrier between the two pressure compartments in the eye: intraocular pressure (IOP) in the intraocular space and cerebrospinal fluid (CSF) pressure in the intraorbital subarachnoid space.[2] The trans-laminar pressure difference (TLPD) across the LC is affected by pressure changes in any of these compartments (i.e., the TLPD corresponds to the IOP pressure minus the CSF pressure).

The identification of structural changes in the LC plays a role in the understanding of the pathophysiology of glaucomatous optic neuropathy.[3,4] Studies have shown that increased TLPD with increased IOP in glaucoma may be a risk factor in glaucomatous pathophysiology.[5-8] Deformation of the LC in glaucoma is considered to cause impairment of the axoplasmic flow in the optic nerve fibers and therefore apoptosis of the retinal ganglion cells.[9]

Studies have used enhanced-depth images of ONH with spectral-domain optic coherence tomography (EDI-OCT) to investigate the posterior displacement of the LC anterior surface in patients with glaucoma.[10-12]

Swept-source optic coherence tomography (SS-OCT), also known as high-penetration OCT, has been developed in recent years to enhance the visualization of deep ocular structures like the LC.[13]

The aim of this study was to compare the anterior lamina surface (ALS) depth, posterior lamina surface (PLS) depth, and LC thickness using SS-OCT in patients with primary open angle glaucoma (POAG) and normal controls.

METHODS

This retrospective, cross-sectional observational study included 26 eyes of 26 POAG patients and 20 eyes of 20 age-matched normal subjects. The study followed the tenets of the Declaration of Helsinki and was approved by the local ethics commitee. Informed consent was obtained from all patients. The study included patients who underwent SS-OCT as part of a work-up for glaucoma monitoring. Control subjects were recruited among hospital employees and friends.

In all cases, a complete ophthalmologic examination was performed, including best-corrected visual acuity, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, and dilated optic disc and fundus examination. Spectral-domain OCT (SD-OCT) imaging (OCT Spectralis, Heidelberg Engineering, Heidelberg, Germany) and standard automated perimetry were also performed (HFATM II; Humphrey Instruments Inc., San Leandro, California, USA).

The POAG was defined as a history of untreated IOP exceeding 21 mm Hg with an open iridocorneal angle as well as evidence of glaucomatous optic neuropathy associated visual field defect. Patients with early-stage glaucoma (2 dB ≤ perimetric mean deviation <6 dB) on IOP-lowering treatment were included into the study.[14] The patients who had undergone IOP-lowering laser therapy or had a history of ocular surgery other than cataract extraction, which may affect IOP level, or cases with poor image quality that prevents the visibility of LC were excluded from the study.

Swept-Source Optical Coherence Tomography

The LC measurements of the cases were performed by using a SS-OCT device (Topcon 3D, DRI OCT Triton). The SS-OCT probe light has a center wavelength of about 1050 nm with a repetition rate of 100,000 Hz, yielding an 8-μm axial resolution in the tissue. Longer wavelengths compared with SD-OCT enable deeper choroidal and scleral imaging by limiting light scattering in photoreceptors and retinal pigment epithelium.[15-17] Swept-source OCT scans were obtained using a 11 horizontal line raster scan protocol. For each line scan, 32 single images were recorded and averaged. Measurements were performed by the specialist investigator (IBP) using the manual caliper tool of the DRI-OCT viewer.

Measurement of LC depth and thickness

Among 11 horizontal B-scan images, the LC depth and thickness were measured at the seven locations equidistant across the vertical optic disc diameter. These seven horizontal B-scan lines were defined as plane 1 to plane 7 (from superior to inferior). The average LC depth and thickness were determined as the mean values of the measurements made at seven points of the LC.

The distance between the reference line connecting both edges of the Bruch membrane and anterior surface of the LC at the maximally depressed point was defined as the ALS depth, and the distance between the same reference line and the posterior surface of the LC again at the maximally depressed point was defined as the PLS depth. (Figure 1A-C)

The difference between the PLS depth and ALS depth was taken to be the LC thickness.

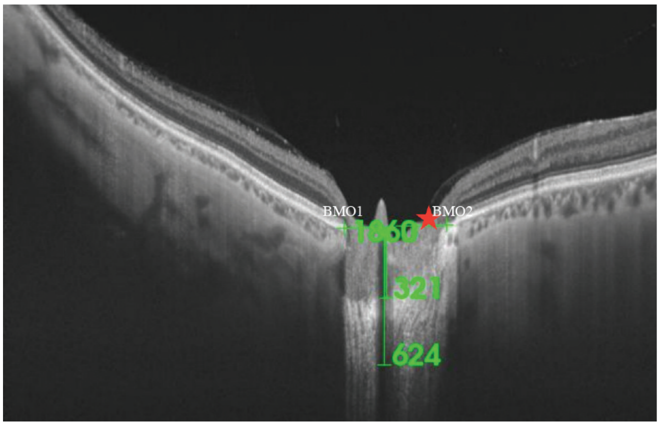

Figure 1A. *The reference line (horizontal line with star) connecting two points of Bruch's membrane opening on either side of the optic disc (indicated as BMO1 and BMO2).*

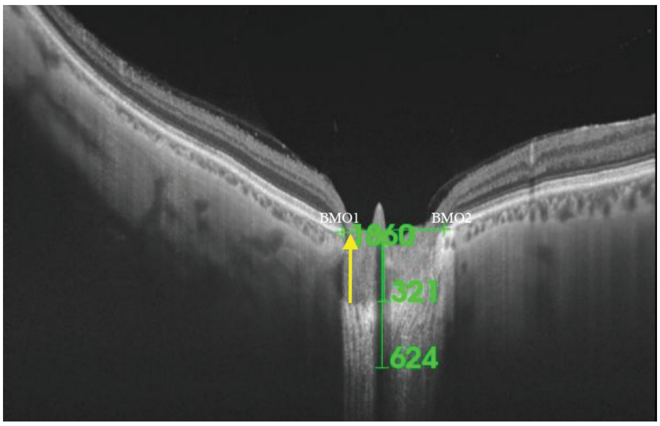

Figure 1B. *The arrow represents the anterior lamina surface depth which was defined as the distance between the reference line connecting two points of Bruch's membrane opening (BMO) on either side of the optic disc (indicated as BMO1 and BMO2) and anterior surface of the LC at the maximally depressed point.*

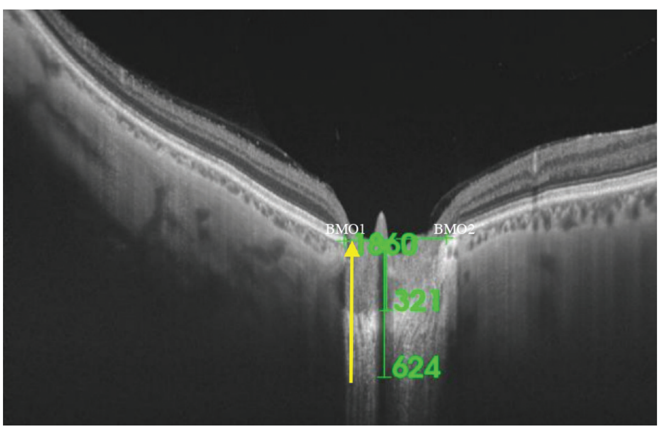

Figure 1C. *The arrow represents the posterior lamina surface depth which was defined as the distance between the reference line connecting two points of Bruch's membrane opening (BMO) on either side of the optic disc (indicated as BMO1 and BMO2) and the posterior surface of the LC at the maximally depressed point.*

Statistical analyses

Shapiro–Wilk test was used to determine whether the data were appropriate for normal distribution. Descriptive statistics included means and standard deviations for samples of normally distributed variables. The dependent variables (ALS and PLS depth, LC thickness) were analyzed using linear mixed effect models with disease (POAG with controls) as a random effect to control for correlations between measurements on the same subject. Pearson correlation coefficient was used to asses IOP's, retinal nerve fiber layer thickness's (RNFL) and perimetric mean deviation's (PMD) relationships to LC depth and thickness. Two-tailed p values less than 0,05 were considered to be statistically significant.

RESULTS

In all, 26 patients with POAG and 20 normal subjects were included. In the POAG group, 6 patients were women and 20 were men. The mean age of this group was 62,6±10,8 (49-73) years. In POAG patients; the mean PMD was -3,04±2,16 (-6,00-1,06), the RNFL thickness was 89±7,91 µm (76-118) and C/D ratio was 0,54±0,07 (0,4-0,6).

The mean IOP was 17.6±8,2 mm Hg (10-42) in the POAG group, and the mean IOP was 13,9±1,7 mm Hg (12-18) in the glaucoma control group (P = 0.17).

In patients with POAG, the mean ALS depth was 471,92±162,22 µm (236-861); the mean PLS depth was 673,19±158,24 µm (426-984); and the mean LC thickness was 201,26±53,33 µm (80-310). In the glaucoma control group, the corresponding values were 442,30±91,18 µm (200-587); 648,90±81,35 µm (483-768); and 206,60±50,41 µm (168-284), respectively. The difference in ALS depth, PLS depth and LC thickness between the POAG and control subjects were not statistically significant (p=0,66; p=0,59; p=0,79).

Correlation analyses in patients with POAG demonstrated that there was no correlation between IOP, PMD and ALS depth, PLS depth and LC thickness ($p > 0,01$). Retinal nerve fiber layer thicknesses were inversely correlated with ALS dept and PLS dept ($p<0.001$), $r = -0.41$.

Figure 2 A-B shows 2 representative cases illustrate the difference in the LC position among the study groups.

DISCUSSION

In this study, although the LC position differs and it was deeply located in patients with glaucoma, we could not find a statistically significant difference when compared with the control group.

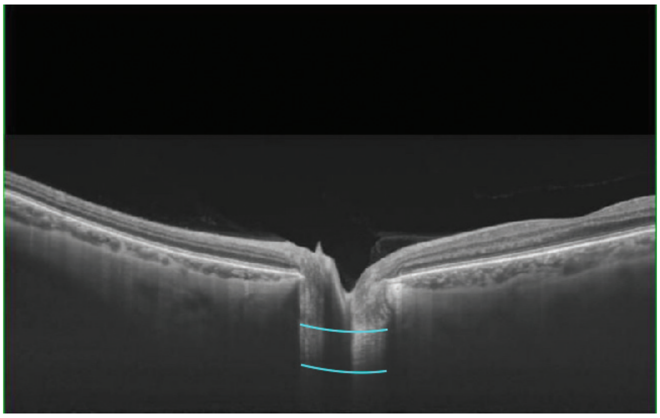

Figure 2A. *Posterior bowing of the lamina cribrosa (structure between the lines) position of a patient with primary open angle glaucoma.*

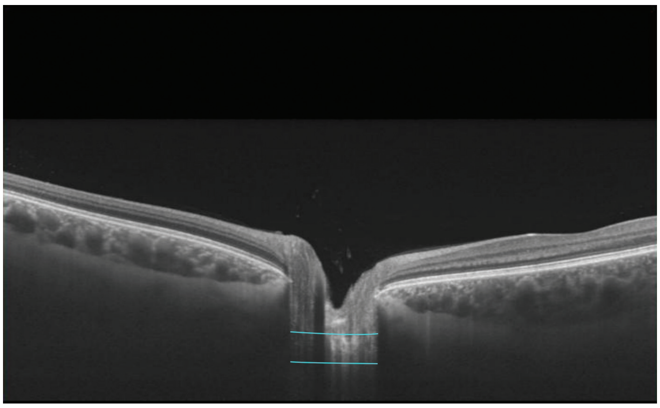

Figure 2B: *Straight lamina cribrosa (structure between the lines) position of a 40 year-old healthy control.*

Until now, the LC depth has been measured from BMO as the reference plane to the anterior surface of the LC.[18] This study represents in-vivo characterisation of the posterior lamina surface depth, and LC thickness using SS-OCT in POAG patients.

Our findings for POAG patients are consistent with the results of similar clinical studies, found that the LC was located deeper in glaucomatous eyes than in healthy controls.[10,11,19] We found that the LC in POAG patients tended to be more posterior than in normal subjects; however, the difference was not statistically significant.

Studies comparing LC depth before and after IOP-lowering therapy have suggested that the posterior LC displacement is somewhat reversed after IOP reduction in glaucomatous eyes. [20-22] In our study, POAG patients had received topical anti-glaucoma treatment with IOP-lowering drugs prior to the LC imaging. Since the glaucoma patients had not been recently diagnosed, the LC depth, which increases in hypertensive periods in these cases, may have been reversed after topical anti-glaucomatous treatment. Thus, if the LC depth were measured before IOP-lowering treatment begins, it might have greater diagnostic power.

Changes in the IOP may cause the LC to tilt and reformat. It is assumed that these structural changes impose shearing stress on axons passing through the pores, thereby causing retinal ganglion cell axon injury.[12]

In recent years, TLPD is thought to play a role in the progression of glaucomatous damage. Changes in LC position due to increased TLPD in glaucoma may occur before thinning of the peripapillary retinal nerve fiber layer.[23,24] Hence, evaluation of the LC position with SS-OCT may be useful in the early diagnosis and treatment monitoring of a progressive disease despite maintained target IOP.

Swept-source optical coherence tomography, currently used for research purposes, is capable of providing a more accurate and well-defined characterization of the choroid, sclera and LC. In-vivo visualization of the PLS, in addition to the ALS, is the superiority of SS-OCT.[25-28] These measurements are of particular interest in the pathogenesis of glaucoma. The limitations of this study include small sample size, patients who had undergone treatment with IOP-lowering medications prior to the time of LC imaging. Further prospective studies with a larger number of subjects are needed to assess the utility of the LC position as a diagnostic tool.

CONCLUSION

Eyes with POAG exhibited an increased LC surface depth compared with measurements in healthy controls, but this was not statistically significant. Additional studies with a larger number of subjects are necessary to determine whether LC surface depth measurements would be clinically useful in the diagnosis and management of patients with primary open angle glaucoma.

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