Original Article

Lamina cribrosa surface position in idiopathic intracranial hypertension with swept-source optical coherence tomography

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Purpose: The purpose of this study is to compare the thickness and depth measurements of the lamina cribrosa (LC) obtained using a swept-source optical coherence tomography (SS-OCT) device in idiopathic intracranial hypertension (IIH) patients and healthy subjects. **Methods:** This retrospective, cross-sectional observational study included 16 eyes with IIH 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 IIH, the mean ALS depth was 225.00 ± 58.57 µm and the mean PLS depth was 449.75 ± 63.50 µm. In the IIH control group, the corresponding values were 359.40 ± 105.38 and 570.10 ± 99.41 µm ($P < 0.05$). The difference in LC thickness between the IIH and control subjects was not statistically significant. **Conclusion:** LC can be evaluated using an SS-OCT device. LC was displaced anteriorly in patients with IIH compared with normal controls. The assessment of LC level with SS-OCT in IIH cases is a valuable and reproducible adjunctive imaging method in terms of diagnosis and follow-up.

Key words: Idiopathic intracranial hypertension, lamina cribrosa, swept-source optical coherence tomography

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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).

Idiopathic intracranial hypertension (IIH) is a disease of unknown etiology that is characterized by increased intracranial pressure. It is most commonly observed in obese women of fertile age. It is thought that the decrease in TLPD in IIH, in which pressure forces change in the direction of increasing CSF pressure, plays a role in the pathophysiology of the disease. Recent studies have suggested that changes in LC are associated with papilledema.[3,4]

Studies have used enhanced-depth images of ONH with spectral-domain optic coherence tomography (EDI-OCT) to investigate the anterior displacement of the LC anterior surface in patients with IIH.[5] 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.[6]

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 IIH and normal controls. We hypothesize that the level of LC may be *in vivo* indicative of TLPD.

Methods

This retrospective, cross-sectional observational study included 16 eyes of 8 IIH patients with mild-to-moderate papilledema and 20 eyes of 10 age-matched normal subjects.

Patients who had headache, papilledema, and elevated lumbar puncture opening pressure (≥25 cmH_2O CSF), normal CSF composition, normal neurologic examination except for cranial six nerve abnormalities, and normal neuroimaging at the time of diagnosis were accepted as IIH.

At the third month of diagnosis, patients with Frisén grades 1–3 papilledema (minimal-moderate) under acetazolamide treatment who remained symptomatic (e.g., headache), indicating that CSF pressure was still elevated, were included into the study. SS-OCT imagings as part of a workup for IIH monitoring at that moment were used for measurements. Healthy controls were recruited among hospital employees and friends.

Patients with more than Frisén grade 3 papilledema, venous sinus thrombosis, or any other intracranial condition or diseases

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causing intracranial hypertension and who had undergone CSF-lowering surgery were excluded from the study.

The study followed the tenets of the Declaration of Helsinki and was approved by the local ethics committee. Informed consent was obtained from all patients.

In all cases, a complete ophthalmologic examination was performed, including best-corrected visual acuity, slit-lamp biomicroscopy, Goldmann applanation tonometry, and dilated optic disk 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, CA, USA).

The swelling of the ONH in papilledema causes light scattering and preventing accurate visualization of LC. To obtain better SS-OCT signal sensitivity under the papilledema, only modified Frisén grades 1–3 papilledema (minimal moderate) cases under acetazolamide treatment were included in the study.[7]

Swept-source optical coherence tomography

The LC measurements of the cases were performed by using an 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.[8-10] Swept-source OCT scans were obtained using an 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 deep range imaging optic coherence tomography (DRI-OCT) viewer.

Measurement of LC depth and thickness

Among 11 horizontal B-scan images, the LC depth and thickness were measured at the 7 locations equidistant across the vertical optic disk diameter. These seven horizontal B-scan lines were defined as planes 1–7 (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 ALS was defined as the anterior border of the highly reflective region beneath the internal limiting membrane at the optic disk cup on the B scans.[5] The posterior border of the same highly reflective region is defined as PLS. 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.[11] 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 [Fig. 1a–c]. The difference between the PLS and ALS depth was taken to be the LC thickness.

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. Pearson correlation coefficient was used to assess the lumbar puncture opening pressure relationship to ALS depth, PLS depth, and LC thickness, respectively. Two-tailed *P* values less than 0.05 were considered to be statistically significant.

Results

In all, 8 patients with IIH (16 eyes) and 10 normal subjects (20 eyes) were included. In the IIH group, six patients were women and two were men. The mean age of this group was 41.1 ± 7.1 years. The mean IOP was 13.2 ± 1.8 mmHg in the IIH group and 14.0 ± 1.1 mmHg in the age-matched control group ($P = 0.25$). In patients with IIH, the mean ALS depth was 225.00 ± 58.57 μm, the mean PLS depth was 449.75 ± 63.50 μm, and the mean LC thickness was 224.75 ± 45.98 μm. In the IIH control group, the corresponding values were 359.40 ± 105.38, 570.10 ± 99.41, and 210.70 ± 36.93 μm, respectively ($P = 0.00$; $P = 0.001$; $P = 0.42$). In patients with IIH, the mean ALS depth and PLS depth were highly significantly decreased compared with the age-matched controls ($P < 0.01$). However, there was no significant difference in mean LC thicknesses between the IIH patients and the patients in the control group. Fig. 2a and b show two representative cases in which the LC depth is measured to illustrate the difference in LC position among the study groups. Correlation analyses in patients with IIH demonstrated that the lumbar puncture opening pressure was inversely correlated with PLS depth ($P < 0.05$) and LC thickness ($P < 0.01$) with a correlation coefficient $r = -0.73$ and $r = -0.88$, respectively.

Discussion

In this study, we demonstrated that the LC position differs in patients with IIH when compared to control subjects. The LC in patients with IIH was shallower than the LC of patients in the control group.

Until now, the LC department has been measured from the Bruch membrane opening distance as the reference plane to the anterior surface of the LC.[12] This is the first study in the literature to evaluate the *in vivo* position of the entire LC structure in IIH. This study also represents the first in-vivo characterization of the PLS depth and LC thickness using SS-OCT in IIH patients.

The shallower position of the LC observed in IIH cases suggests that the LC was in an anterior position in these cases, which may be a result of TLPD. This difference is positively correlated with LC depth.[5] Therefore, our findings support previous studies.[13,14] Villarruel *et al.* reported the anterior displacement of the anterior LC surface position in patients with IIH compared with age-matched control subjects analyzed using EDI-OCT.[5] In our study, we demonstrated anterior displacement of the LC's anterior and posterior surfaces using high-penetration SS-OCT, which enhances the visibility of the entire structure of the lamina. SS-OCT uses a long-wavelength light source, that is less vulnerable to light scattering. This longer wavelength light has the ability to penetrate more deeply into tissue compared with the short-wavelength light used in SD-OCT devices. This feature enables better visualization of deeper structures like LC.[15] To date, our study is the first to use SS-OCT to assess the *in vivo* LC position and thickness in IIH patients.

A recent study showed that the optic nerve configuration does not return to baseline values after CSF pressure-lowering therapy.[16] Because all of the patients in our study with IIH had

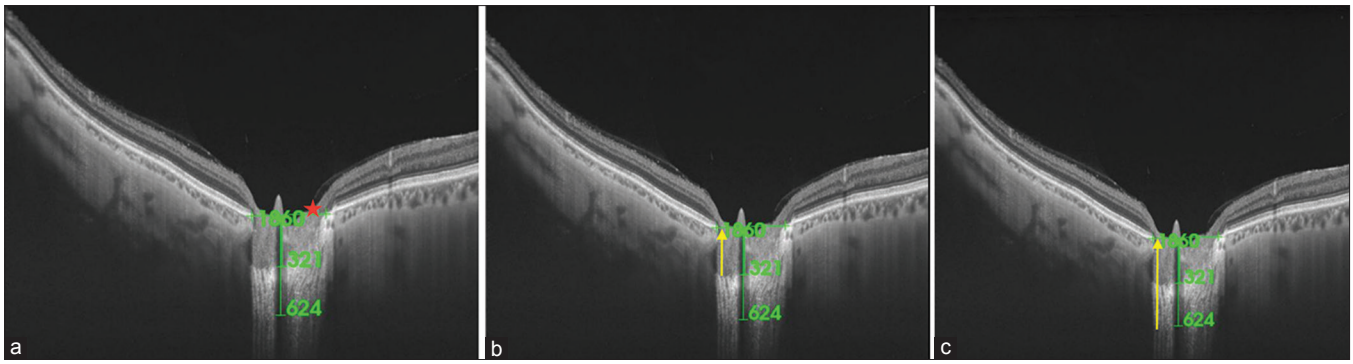

Figure 1: (a) The reference line (horizontal line with star) connecting both edges of the Bruch membrane, (b) arrow represents the anterior lamina surface depth, and (c) arrow represents the posterior lamina surface depth

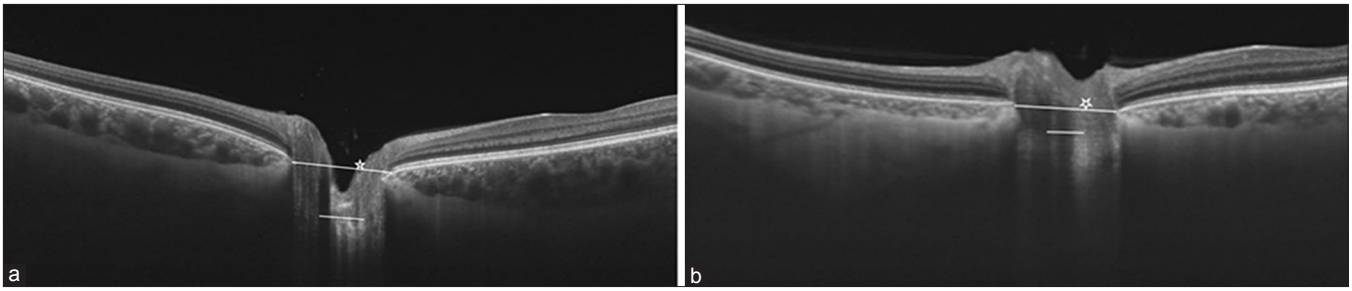

Figure 2: (a) Lamina cribrosa position of a 40-year-old healthy control. The horizontal line with star connecting both edges of the Bruch membrane and the inferior line represents the anterior lamina cribrosa surface, and (b) lamina cribrosa position of a patient with idiopathic intracranial hypertension. The horizontal line with star connecting both edges of the Bruch membrane and the inferior line represents the anterior lamina cribrosa surface

grades 1–3 papilledema at the time of imaging – indicating that the CSF pressure was still high – our LC measurements may reflect the chronic structural changes seen in IIH cases.

In clinical practice, identifying a mild papilledema can be a challenge for ophthalmologists. When the diagnosis is not certain, before invasive tests, evaluation of LC morphology with simple reliable and noninvasive methods such as SS-OCT may be important in diagnosis. In our study, it was shown that the LC was anteriorly displaced significantly compared to the control group in IIH cases.

In contrast, clinical studies found that the LC was located deeper in glaucomatous eyes than in healthy controls.[17] Changes in the IOP and therefore LC position, due to increased TLPD in glaucoma, may cause the LC to tilt posteriorly and these changes may occur before thinning of the peripapillary retinal nerve fiber layer.[18,19] Hence, evaluation of the LC position with SS-OCT may be useful in the early diagnosis of a glaucoma which is a progressive optic neuropathy.

Swept-source optical coherence tomography (SS-OCT), currently used for research purposes, is capable of providing a more accurate and well-defined characterization of the choroid, sclera, and LC. These measurements are of particular interest in the pathogenesis and investigation of optic neuropathies. The limitations of this study include small sample size and patients who had undergone treatment with CSF pressure-lowering medications prior to the time of LC imaging; also, the other known factors like refractive errors which can impact scleral thickness other than IOP were not evaluated.

Since this was the first study about visualization of the entire LC structure in the IIH patients, it was not comparable with similar publications. Further prospective studies with a larger number of subjects and normal LC position and its thickness which is known to be varying in the general population are needed to assess the utility of the LC position as a diagnostic tool.

Conclusion

Eyes with IIH exhibited a decreased LC surface depth compared with measurements in healthy controls. Additional studies with a larger number of subjects are necessary to determine whether LC surface depth measurements would be clinically useful in the early diagnosis and management of patients with IIH.

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Conflicts of interest

There are no conflicts of interest.

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