Original Article

Morphological assessment of lamina cribrosa in idiopathic intracranial hypertension

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Purpose: Technological development of optic coherence tomography has enabled a detailed assessment of the optic nerve and deeper structures and *in vivo* measurements. The aim of this study was to compare the lamina cribrosa morphology of the optic nerve in idiopathic intracranial hypertension (IIH) and healthy individuals. **Methods:** The lamina cribrosa morphology of optic nerve in 15 eyes with IIH and 17 eyes of healthy individuals were compared. Four parameters such as Bruch membrane opening (BMO), lamina cribrosa thickness (LCT), prelaminar tissue thickness (PTT), and anterior lamina cribrosa surface depth (ALCSD) were retrospectively evaluated. **Results:** By enhanced depth imaging-optic coherence tomography (EDI-OCT), PTT and BMO were found to be significantly greater (574,35 ± 169,20 µm and 1787,40 ± 140,87 µm, respectively) in IIH patients than healthy individuals (187,18 ± 132,15 µm and 1632,65 ± 162,58 µm, respectively), whereas ALSCD was found to be significantly less in IIH patients (234,49 ± 49,31 µm) than healthy individuals (425,65 ± 65,23 µm). There was not a statistically significant difference regarding LCT between the IIH patients (238,59 ± 17,31 µm) and healthy individuals (244,96 ± 15,32 µm). **Conclusion:** Increased intracranial pressure causes morphological changes in lamina cribrosa. Assessment of lamina cribrosa with EDI-OCT is important for diagnosis and follow-up of patients with IIH. EDI-OCT is objective, reproducible, and cost-effective assistive imaging tool in IIH patients.

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Idiopathic intracranial hypertension (IIH) is characterized by increased intracranial pressure (ICP) in the absence of an organic brain lesion and a pathological cerebrospinal fluid (CSF). Most common symptoms are headache, visual deterioration, and pulsatile tinnitus, and the most important complication is permanent vision loss.[1,2] Diagnostic criteria were first published by Dandy in 1937, later improved by Smith in 1985 and referred as "Modified Dandy Criteria".[3] First, a solid lesion by brain magnetic resonance imaging and sinus thrombosis by MR venography should be excluded to diagnose IIH. Exact diagnosis can be made by lumbar puncture (LP) after neuroimaging. CSF opening pressure of 250 mm H_20 is important in IIH diagnosis.[2]

Papilledema is caused by increased ICP and is a cardinal sign of IIH. It is present bilaterally in 93% and unilaterally in 5% of cases and causes vision loss both directly and indirectly. Increased CSF pressure is reflected on optic nerve sheath through the optic canal and the axons get exposed to pressure at lamina cribrosa (LC), where they leave the globe. With increased pressure, both slow and rapid axonal transport gets interrupted and edema develops on the nerve head. Owing to the pressure on vessels by edematous papilla, acute and subacute optic nerve ischemia and branch retinal arterial occlusion might occur. Most patients present with acute papilledema, whereas some might have chronic and atrophic discs. Visual acuity is generally preserved in the acute phase of papilledema. Visual deterioration usually starts with central vision loss and the visual field defects enlarge in chronic cases.[3]

Lamina cribrosa is placed deep in optic nerve head, and it is a network of type 1, 2, 3, 4, 5, and 6 collagen, laminin, elastin, and fibronectin. This layer consists of fenestrated, solid connective tissue, and elastic fibers. The glial tissue supporting the axons is maximized in LC and optic nerve begins to get extensions from the sclera. The fenestrae on LC are larger in superior and inferior poles, and axons travel through these. These fenestrae are normally 500 to 600 in number and their diameter change between 500–22.500 µm. This structure supports and protects retinal nerve fibers, after they leave the globe.[4]

The difference between intraocular and intracranial pressure is defined as the translaminar pressure difference.

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This translaminar pressure difference is increased in glaucoma patients and causes compression, deformation, and remodeling in LC.[5] Recent studies on glaucoma showed that morphological changes in LC appear early in the disease. The translaminar pressure difference also increases in patients with IIH and therefore, morphological changes occur in LC in IIH patients.

The aim of this study was to compare the lamina cribrosa morphology of the optic nerve in IIH and healthy individuals.

Methods

The records of patients diagnosed with IIH at University of Health Sciences Beyoğlu Eye Training and Research Hospital, Neuro Ophthalmology Clinic between June 2015 and June 2017 and the records of healthy patients applied to the same hospital's outpatient care and had prior optic nerve head EDI-OCT imaging to gather normative data were retrospectively reviewed. They were divided into two groups as IIH and control group. The right eyes of the patients whose birth year is an odd number and the left eyes of the patients whose birth year is an even number are involved in the trial.

Patients diagnosed with IIH by LP, without a history of ocular disease besides refractive error and IIH, and age over 18 years are included in the IIH group. Patients applied to routine eye examination to the outpatient care were matched with IIH group regarding age and gender, were included in the control group.

Exclusion criteria were pregnancy, myopia over 6 diopter (D), hyperopia over 4 D, co-existence of glaucoma and/or suspect of glaucoma, and history of any other optic nerve disease.

Patients in the IIH group were graded according to Frisen scale, as grade 1, 2, 3, 4, and 5.

Best-corrected visual acuity, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement with Goldmann applanation tonometry, fundus, and optic disc examination following pupil dilatation, central corneal thickness, and axial length of each eye were noted. SD-OCT of retinal nerve fiber layer and lamina cribrosa and EDI-OCT of lamina cribrosa were recorded.[6]

Optic nerve head was evaluated with EDI-OCT (15 × 10 degree, 97 B-scan, 20°CT frames). OCT images were obtained 48 days (mean) after the performance of LP. The measurements of Bruch membrane opening (BMO), lamina cribrosa thickness (LCT), prelaminar tissue thickness (PTT), and anterior lamina cribrosa surface depth (ALCSD) were obtained on LC. PTT was measured as the area from the optic nerve head surface to the beginning of high reflectance of LC [Fig. 1]. The beginning and the end of the high reflectance were used as reference points to measure LCT. To measure ALCSD, the distance between the imaginary line passing through Bruch membrane level and the anterior border of LC was measured from three different spots, which are 100 μm apart, and the mean value was noted. The measurements were made by two separate investigators, and the mean value of the two measurements was recorded. Retrospective ethical approval of this study was obtained from Gaziosmanpaşa Taksim Training and Research Hospital at 27.12.2017 and the study adhered to the tenets of Declaration of Helsinki.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, SPSS Inc. Chicago IL, USA) software (version 22.0).The continuous variables were expressed as mean ± standard deviation (SD). The categorical variables were expressed as number (n) and percentages (%). Categorical variables were presented as numbers and percentages, while numerical variables were expressed as the mean and standard deviation. First, the data were analyzed in terms of normality using Kolmogorov–Smirnov test. As the distribution of the data was found to be normal, independent sample t test was used. A *P* value of less than 0.05 was considered significant.

Results

Total of 33 eyes of 16 IIH patients and 17 healthy individuals were included in this study. There were 15 eyes in IIH group and 17 eyes in the control group. One eye in the IIH group was excluded from this study owing to an inaccurate evaluation of lamina cribrosa borders on EDI-OCT. Total of 32 eyes' lamina cribrosa morphology was included in the statistical analysis.

IIH group included 14 females, one male; the control group included 14 females, three males. In the IIH group, minimum and maximum ages were 19 and 55 and 21 and 53 in control group, respectively. Mean age of patients were 33.40 years and 33.03 years in IIH and control group, respectively, and there was not a statistically significant difference between the groups. BMI of IIH group was found to be 33.28 kg/m^2, and BMI of control group was 24.99 kg/m^2.

LCT was 238,59 ± 17,31 μm and 244,96 ± 15,32, in IIH and control group, respectively; there was no statistically significant difference present between the groups ($P > 0.05$). ALCSD was 234,49 ± 49,31 μm in IIH group, and 425,65 ± 65,23 μm in control group and was found to be significantly less in IIH group than the control group ($P < 0.05$).

Mean PTT was 574,35 ± 169,20 μm in IIH group and 187,18 ± 132,15 μm in control group, and it was significantly greater in IIH group than the control group. BMO was measured as 1787,40 ± 140,87 μm in IIH group, and 1632,65 ± 162,58 μm in control group. Mean BMO showed statistically significant difference between the groups and was greater in IIH group than control group ($P < 0,05$).

Our study included four eyes with grade 1, five eyes with grade 2, four eyes with grade 3, and two eyes with grade 4 papilledema. One eye was excluded owing to poor quality of lamina cribrosa imaging. LC parameters were evaluated comparing the grades, and there was no significant difference obtained for LCT. There was no statistically significant difference found between the grades regarding BMO; however, there was a significant difference between the control group and the IIH group. ALCSD was found to be significantly decreased in grade 1–3; however, there was no difference observed between grade 3 and 4. This might be owing to only two eyes being grade 4. PTT

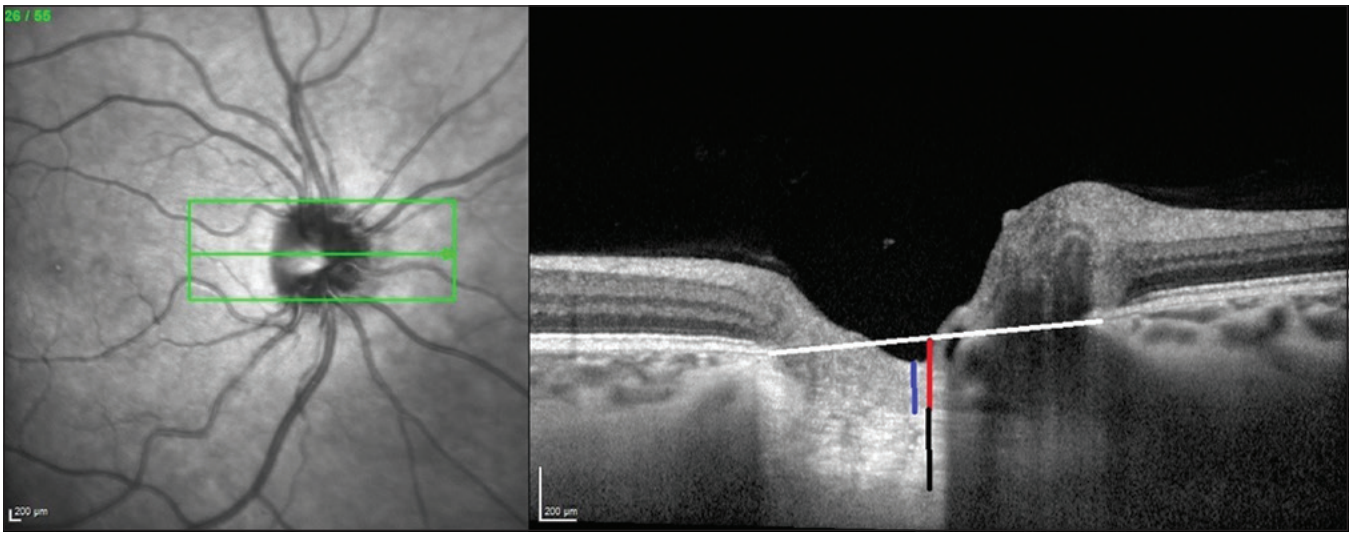

Figure 1: Optical cohorence tomogrophy-enhanced depth imaging of optic disc. White line is BMO. Red line is ALCSD. Black line is LCT. Blue line is PTT

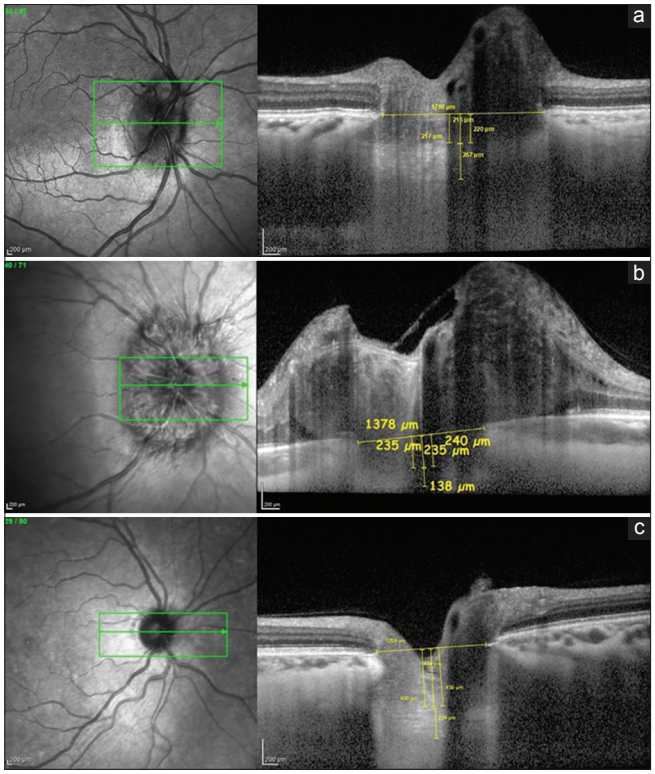

Figure 2: (a) Lamina cribrosa morphology of optic nerve in grade 2 idiopathic intracranial hypertension. (b) Grade 4 idiopathic intracranial hypertension. (c) Healthy individuals

was also found to be significantly decreased in grade 1–3; however, there was no difference observed between grade 3 and 4, as in ALCSD.

Discussion

Lamina cribrosa is collagen-based, network-like structure placed deep in optic nerve head, and it supports and protects retinal nerve fibers after they leave the globe.[4]

The difference between intraocular and intracranial pressure is defined as the translaminar pressure difference. LC separates intraocular and intracranial spaces and acts like a barrier between the two pressures, which makes it sensitive to both intraocular and intracranial pressure. The stress and the tension by increased IOP cause compression, deformation, and remodeling in LC.[5] Recent studies on glaucoma showed that morphological changes in LC appear early in the disease, and evaluation of LC, therefore, gained importance, especially in glaucoma patients. However, SD-OCT failed to show the posterior part of LC. In our study, deep optic nerve structures, including LC, have been clearly visualized by EDI-OCT.[7,8]

Translaminar pressure difference not only increases in glaucoma patients but also increases in IIH and causes morphological changes in LC. The posterior shift of LC in glaucoma patients have been shown with the measurements of LC depth by using Bruch membrane as a reference point.[9] Because the pressure forces are in opposite directions in IIH compared to glaucoma, LC was thought to anteriorly displaced. For this purpose, in the study of Morgan *et al*., intraocular or intracranial pressures of mixed-breed dogs were changed to increase translaminar pressure, and the position of lamina cribrosa was evaluated by confocal scanning laser tomography. In the case of increased IOP and stabile ICP, lamina cribrosa was displaced posteriorly; in the case of increased ICP and stabile IOP, lamina cribrosa was displaced anteriorly. In addition, they presented that the displacement of the LC was more likely to be related to the increased ICP.[10]

In their study investigating the depth of lamina cribrosa with 23 glaucoma and 6 IIH patients, Jenni M. Villarruel *et al*. reported that anterior surface of the lamina cribrosa was more anteriorly displaced in IIH patients, and they argued it was owing to the increased translaminar pressure difference. They also showed that the anterior displacement of LC disappeared following the reduction of translaminar pressure difference with IIH treatment. They added that the anterior surface of the LC of the glaucoma patients was posteriorly displaced.[11]

Perez-Lopez M. *et al*. presented an IIH case with lumboperitoneal shunt who had optic nerve fenestration performed due to newly developed vision loss and showed the preoperative and postoperative day 1 EDI-OCT of optic nerve images of the case. They established that following optic nerve fenestration, PTT decreased by 142.9 μm and ALCSD increased by 137 μm.[12]

Similar to all these reports, our results have shown that anterior lamina cribrosa depth is significantly less in IIH patients than the control group [Fig. 2].

In the study of Javier García-Montesinos *et al*. including 12 eyes with papilledema, BMO was found greater in the group with higher translaminar pressure difference, and they reported that with the reduction of translaminar pressure difference, BMO also reduced accordingly. They argued BMO was determined by the edema on the optic nerve.[13]

Sibony P. *et al*. reported no statistically significant difference in BMO between the measurements before the treatment and after the treatment when the optic disc edema resolved, in their study of 23 IIH patients with optic disc edema. However, the measurements were taken with SD-OCT in this study, not with EDI-OCT.[14]

In our study, BMO was found to be significantly greater in IIH group than the control group [Fig. 2].

We observed that PTT was thicker in the IIH group. Optic disc edema and anterior displacement of lamina cribrosa along with other anterior tissues might have been the reason for this measurement.

Our study had limitations. First, all IIH patients included were initially diagnosed by LP; however, they were receiving treatment of oral acetazolamide with a mean daily dose of 1.10 gm for 43 days, when their EDI-OCT images were obtained. We assumed their ICP was increased owing to their optic disk examination and symptoms; however, we did not know the exact value at that moment. Second, our control group was ruled as healthy according to their clinical optic disc examination. Patients with chronic headaches were excluded from the control group because of the recent studies showing IIH cases without papilledema; however, LP was not performed on any healthy individuals, which prevents us knowing the exact ICP of these patients. Third, there was a significant difference in BMI between the two groups. The effect of BMI on lamina cribrosa morphology remains unknown. The major advantage is that this study has been the largest series of IIH patients with their lamina cribrosa morphology evaluated in the literature that we know of.

Further prospective studies with a larger number of subjects and normal LC position and its thickness which is known to be varying in general population are needed to assess the utility of the LC position as a diagnostic tool.

Conclusion

ICP alterations cause structural changes in lamina cribrosa depth, BMO, and prelaminar tissue thickness. Evaluating the lamina cribrosa parameters of every patient whose ICP measurement was obtained with LP and the changes of those parameters over time might be helpful to follow-up patients with IIH.

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Conflicts of interest

There are no conflicts of interest.

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