Evaluation of the lamina cribrosa morphology in correlation to retinal nerve fiber layer thickness
Ayser Abd El-Hameed Fayed

Department of Ophthalmology, Faculty of Medicine, Benha University, Benha, Egypt
Correspondence to Ayser Abd El-Hameed Fayed, MD, Department of Ophthalmology, Faculty of Medicine, Benha University, Kalyopia, Benha - 13512, Egypt
Tel: +20 013 316 6869; fax: +20 013 322 2817; e-mail: ayserfayed@yahoo.com
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Aim
The aim of this study was to assess the correlation between lamina cribrosa (LC) morphology and glaucoma severity using spectral domain optical coherence tomography.

Patients and methods
This is a comparative cross-sectional study that included 40 eyes divided into 20 eyes having primary open-angle glaucoma and 20 normal control eyes. Serial horizontal B-scan images of the optic nerve head were obtained using enhanced depth imaging optical coherence tomography. Images were analyzed using the Cirrus HD software. Statistical analysis was conducted to compare the lamina cribrosa depth (LD) and lamina cribrosa thickness (LT) with retinal nerve fiber layer (RNFL) thickness and visual field mean deviation.

Results
The mean±SD values of the LD, LT, and visual field mean deviation were 533.5±66.8, 188.4±15.8 μm, and −4.3±3.4 dB, respectively. On linear regression analysis, LD, LT, and intraocular pressure were significantly correlated with RNFL thickness (P<0.001, 0.001, and 0.01, respectively). The mean LD was significantly greater in the glaucoma group compared with the normal control group (P<0.001). In eyes with glaucoma, the LC was thinner and located more posteriorly compared with the normal control eyes.

Conclusion
There was a generalized decrease in LT and posterior displacement of the LC in the glaucomatous patients compared with healthy controls. Thus, the LC morphology can help differentiate glaucomatous from normal eyes.

Keywords:
glaucoma, lamina cribrosa, lamina cribrosa depth, lamina cribrosa thickness, optical coherence tomography

Introduction
Diagnosis of glaucoma requires ancillary tests that were designed to provide additional data for making diagnostic and therapeutic decisions. Cup/disc ratio evaluation cannot be used alone to make the diagnosis accurately, especially in cases with a large cup/disc ratio [1,2]. Retinal nerve fiber layer (RNFL) thickness measured by optical coherence tomography (OCT) is considered a solid early marker of glaucoma [1–3]. On the basis of findings from previous studies [3–7], the primary site of axonal damage in glaucoma is thought to be the lamina cribrosa (LC), which may happen by several means including mechanical damage, compromised vascular supply, and increased translaminar pressure gradient. Optic nerve head (ONH) cupping in glaucoma is thought to be a combination of the two components - prelaminar and laminar cupping [6–9]. Clinically, glaucomatous optic nerve damage is diagnosed by the deepening and extension of the optic cup, with thinning of the neuroretinal rim [1,10].

In recent years, OCT has been developed as a potential means using low-coherence interferometry to scan through the layers of the retina with very high axial resolution (3–15 μm). It is used for imaging disorders affecting the retina and optic nerve in vivo [11–15]. The present study aimed to discuss the morphological changes of the LC, including laminar thickness (LT) and posterior laminar displacement, in glaucomatous eyes in comparison with normal eyes.

Patients and methods
Forty eyes of 30 participants – 20 normal (control) eyes of 14 patients and 20 glaucomatous eyes having primary open-angle glaucoma (POAG) in 16 patients
were included in the present study. The study was approved by the Review Boards/Ethics Committee of Benha Faculty of Medicine at Benha University. Informed consent was obtained from all participants after the nature and consequences of the procedure had been fully explained to them.

Each participant underwent full ophthalmological examination including slit-lamp biomicroscopy, best-corrected visual acuity, fundus and ONH examination, intraocular pressure (IOP) measurement, visual field (VF) testing, fundus photography, and ONH imaging with spectral domain OCT device (Carl Zeiss Meditec Inc., Dublin, California, USA). Exclusion criteria included patients with spherical refractive error of more than −6.0 D, cylindrical error more than 2.0 D, IOP greater than or equal to 21 mmHg, patients with history of ocular trauma or intraocular surgery, cases with optic disc hemorrhages, two or more consecutive unreliable VFs, poor OCT quality images (defined by poor alignment on the OCT scans or signal strength <5), media opacity, poorly dilating pupil, and other retinal pathologies that might cause VF abnormalities such as diabetic retinopathy, cystoid macular edema, vein occlusion, or history of retinal laser treatment.

The normal control group was composed of 20 eyes (14 patients) that were randomly recruited as age-matched normal individuals. Eyes of the normal controls were used to establish normative data for the LC and standard automated perimetry.

The POAG sample consisted of 20 eyes (16 patients). All the patients exhibited characteristic ONH abnormalities (increase in vertical cup–disc ratio), untreated IOP greater than 21 mmHg, with characteristic VF (standard automated perimetry) loss.

All patients underwent imaging by Cirrus HD-OCT (Carl Zeiss Meditec Inc.). The ONH was imaged through the enhanced depth image (EDI) method. The Cirrus HD-OCT data sets used 3D cube, centered on the ONH. Cirrus OCT creates an array of 200×200 to determine the RNFL thickness. A 3.45-mm-diameter scan circle was positioned manually at the center of the optic disc. The Cirrus OCT software calculates the mean RNFL thickness for the overall globe (360°). The peripapillary RNFL thickness evaluated in this study was the mean RNFL thickness. Two to three ONH scans were acquired within the same visit for glaucomatous and healthy control patients. Once the image was aligned, the software was used to locate the center of the disc, and advanced visualization was obtained. After delineating the anterior LC surface, lamina cribrosa depth (LD) was determined by measuring the distance between the reference plane (Bruch’s membrane edges) and the anterior LC surface. LT was the distance from the anterior to the posterior border of LC in the middle of the horizontal plane of the ONH images. The LC was defined by the highly reflective structure below the optic cup (Fig. 1).

**Statistical analysis**

Comparison between glaucomatous and normal control eyes was performed using the independent $t$-test for continuous variables. The relationships between the laminar morphology (LD and LT) and VF MD were evaluated by linear regression analyses. All statistical analyses were performed using IBM SPSS statistics (version 20.0; SPSS Inc., Chicago, Illinois, USA). The level of statistical significance was set at $P$-value less than 0.05.

**Figure 1**

Delineating the anterior laminar surface. The maximum lamina cribrosa (LC) depth was defined as the perpendicular distance from the maximally depressed point to the reference line connecting the two Bruch’s membrane edges (white line). The LC thickness (red line).
Result
A total of 40 eyes of 30 patients were included in the present study. All participants were Egyptians and were classified into 20 normal eyes (14 patients; mean age, 51.3±11.4 years) and 20 POAG eyes (16 patients; mean age, 54.3±24.1 years). The patient characteristics are summarized in Table 1. With regard to RNFL average thickness and VF (MD), there were highly significant differences between the normal and glaucomatous eyes. The mean LC depth was more deeply located in the glaucomatous eyes compared with the normal control eyes. The mean LC depth was 533.5±66.8 μm in glaucomatous eyes and 306.4±51.9 μm in healthy controls, which was statistically significant (P<0.001). Correspondingly, the mean laminar tissue thickness was less in the eyes with glaucoma compared with the normal control eyes; this was statistically significant (P<0.001). Average LT was 395.6±20.6 μm in the normal eyes and 188.4±15.8 μm in eyes with glaucoma. After matching for RNFL thickness, 20 control and 20 glaucomatous eyes displayed a significant difference in LC parameters, including the depth and thickness (all P<0.001; Table 2 and Fig. 2a and b).

The correlation between the LT and RNFL thickness was statistically significant (P<0.001); the LC parameters (LT and LD) and the IOP were significantly correlated with the MD value.

Discussion
The main load-bearing tissue of the eye is the sclera. Its deformations due to the IOP changes are transmitted to the ONH [6–9]. As the LC is considered to be an important site of axonal injury in glaucoma, many researchers [15–18] have made efforts to visualize the LC and to analyze the structure–function relationship between the LC and glaucoma severity.

Table 2 Pearson’s correlation between both lamina cribrosa thickness and lamina cribrosa depth with retinal nerve fiber layer thickness in primary open-angle glaucoma

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>POAG (n=20)</th>
<th>Normal (n=20)</th>
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<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>LD (μm)</td>
<td>−0.188</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LT (μm)</td>
<td>0.190</td>
<td>&lt;0.001</td>
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<tr>
<td>IOP (mmHg)</td>
<td>0.188</td>
<td>0.011</td>
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IOP, intraocular pressure; LD, lamina cribrosa depth; LT, lamina cribrosa thickness; POAG, primary open-angle glaucoma; RNFL, retinal nerve fiber layer.

This is a prospective, comparative cross-sectional study, which provided significant correlation between glaucoma severity as measured by VF MD and LC parameters (LT and LD) in vivo using EDI spectral domain-OCT. The statistical analysis
of the present study found that the LT was thinned and the LD was deepened in the glaucomatous eyes compared with normal control eyes. The LT and IOP were significantly correlated with MD in the glaucoma group. Parallel to the thinning of the LC, the LD was significantly correlated with MD. Thinning and deepening of LC in the glaucomatous eyes compared with the normal eyes, in the present study, is in agreement with previous postmortem studies [19,20] in nonhuman primate experimental glaucoma, which had described the deformation and posterior migration of the LC in response to a chronic IOP elevation. Recently, Furlanetto et al. [21] demonstrated that the LC was located more posteriorly in glaucomatous eyes as compared with normal eyes.

In addition, the current study showed that the correlation between RNFL average thickness and mean LC depth in both the glaucomatous eyes and normal control group was significant. These findings suggest that posterior LC displacement occurs mostly at earlier stages of glaucoma, which may help in early detection and monitoring progression of the glaucoma. These findings are supported by Saman et al. [22], who explained the finding as LC defects that occur with localized axonal damage to retinal ganglion cell and consequently leads to corresponding VF defects. In contrast, Li et al. [23] found that neither RNFL average thickness nor VF MD was significantly correlated with average LC depth in both the high-tension glaucoma and normal-tension glaucoma groups, which was explained by the inability to consistently identify the posterior laminar surface, making it impossible to assess information regarding deformation of the entire lamina.

In conclusion, the LC was more deeply located, as well as thinner, in glaucomatous eyes than in healthy controls based on EDI OCT measurements. In addition, the LC could be an excellent diagnostic performance for glaucoma.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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