Influence of Translaminar Pressure Dynamics on the Position of the Anterior Lamina Cribrosa Surface

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PURPOSE. To determine how the translaminar pressure difference (TLPD) and gradient (TLPG) influence the position of anterior lamina cribrosa (LC) surface.

METHODS. Twenty-six eyes of 26 healthy subjects were subjected to enhanced-depth imaging volume scanning of the optic nerve using spectral-domain optical coherence tomography (SD-OCT). The anterior LC surface depth (LCD) relative to the Bruch’s membrane (BM) opening was measured at 11 equidistant planes, and the LC thickness (LCT) was measured at three locations (superior midperipheral, midhorizontal, and inferior midperipheral). Intraocular pressure and lumbar cerebrospinal fluid pressure (CSFP) were measured on the same day as the SD-OCT examination. The TLPD was defined as the difference between IOP and CSFP (i.e., IOP–CSFP), and the TLPG as the TLPD divided by LCT (i.e., TLPD/LCT).

RESULTS. Subjects were aged 63.4 ± 8.0 years and comprised 12 males and 14 females. Regression analyses revealed a significant association between a larger mean LCD and male sex (P = 0.002), and between a larger central LCD and male sex (P ≤ 0.012), larger TLPD (P = 0.048), and higher TLPG (P = 0.029). There was no significant association between IOP, CSFP, and LCT; and either the mean LCD (P = 0.438, 0.368, and 0.416, respectively) or central LCD (P = 0.284, 0.085, and 0.144, respectively).

CONCLUSIONS. A larger central LCD was associated with larger TLPD and higher TLPG in healthy eyes, which indicates that the translaminar pressure dynamics may play a role in the position of the anterior LC surface relative to BM opening in healthy human eyes.

Keywords: translaminar pressure gradient, translaminar pressure difference, lamina cribrosa

The lamina cribrosa (LC) is a key structure in the pathogenesis of glaucoma. It has been postulated that IOP-related stress may cause compression or posterior deformation of the LC, which may induce kinking or pinching of the axons that pass through the laminar pores, leading to a blockade of axoplasmic transport of the retinal ganglion cell axons. In addition, the compressive effect on the laminar capillaries in the course of LC deformation may confer ischemic insult to the axons. On the other hand, even in the absence of LC deformation, IOP can still increase the strain within the LC and induce laminar connective-tissue remodeling, which may compromise axon physiology. Moreover, the increased LC strain may have a substantial influence on the axonal flow where the LC is thin, because those axons may experience a steep transition between IOP and retrolaminar tissue pressure, termed the translaminar pressure gradient (TLPG).

Because the LC forms a barrier between two differentially pressurized compartments: the intraocular space with a higher pressure (IOP) and the retrolubar space with a lower pressure (retrolubar cerebrospinal fluid [CSF] pressure [CSFP]), a pressure gradient is formed across the LC. The pressure difference between the two compartments is termed the translaminar pressure difference (TLPD), and is defined as IOP–CSFP. At a given IOP, subjects with a lower CSFP have a larger TLPD, which can result in posterior deformation of the LC. Conversely, in subjects with a higher CSFP, the TLPD is smaller, and thus the LC is less likely to be deformed.

The ability of the LC to tolerate a given TLPD without being deformed may be associated with the material properties (e.g., compliance, stiffness, or structural rigidity) and geometry (e.g., thickness, shape, or curvature) of the LC and the peripapillary connective tissues. For example, eyes with a stiffer LC may be more resistant to deformation when the LC thickness is the same. Likewise, for a fixed LC stiffness, it is possible that eyes with a thinner LC are more susceptible to LC deformation. Regardless of its susceptibility to deformation, a thinner LC also contributes to a steeper TLPG as a result of the reduced distance between the intraocular space and the retrolaminar space, and may interrupt both orthograde and retrograde axoplasmic transport.

Studies have found a link between a larger TLPD or TLPG and glaucoma. It has been shown that patients with POAG...
Translaminar Pressure Dynamics and LC Position

that could affect the intracranial pressure (idiopathic intracranial hypo/hypertension, intracranial tumors, or medications (e.g., tetracycline, rofecoxib, mannitol, and carbonic anhydrase inhibitor)), or any contraindication for lumbar puncture (i.e., infectious diseases or infection around a lumbar puncture site, elongated prothrombin time [international normalized ratio > 1.7], thrombocytopenia < 50,000/mm³, uremia, hemophilia, or other impairment of the coagulation process). When both eyes of a subject were eligible for inclusion, one eye was randomly selected.

**METHODS**

This study was based on the data of healthy subjects included in the Study for Usefulness and Standardization of Cerebrospinal Fluid and Plasma Amyloid Biomarkers in Alzheimer's Disease, which is an ongoing prospective study of patients with Alzheimer's disease and healthy participants at the Neurocognitive Behavior Center in collaboration with Glaucoma Clinic of Seoul National University Bundang Hospital. The present study was approved by the Seoul National University Bundang Hospital institutional review board (Seoul, Korea). Informed written consent to participate was obtained from all subjects, according to the Declaration of Helsinki.

**Study Subjects**

Subjects were enrolled by the advertisement between May 2012 and April 2014. All subjects submitted to a complete ophthalmic examination, including visual acuity assessment, Goldmann applanation tonometry, refraction test, slit-lamp biomicroscopy, gonioscopy, dilated stereoscopic examination of the optic disc, fundus photography (VX-10 fundus camera; Kowa, Tokyo, Japan), measurement of central corneal thickness (Orbscan II; Bausch & Lomb Surgical, Rochester, NY, USA), corneal curvature (KR-1800; Topcon, Tokyo, Japan), and axial length (IOL Master; Carl Zeiss Meditec, Dublin, CA, USA), and EDI SD-OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) scanning of the optic disc and circumpapillary retinal nerve fiber layer (RNFL). Intraocular pressure was measured three times at 15-minute intervals, and the mean of the three values was considered as the baseline IOP. Subjects underwent CSFP sampling with CSFP measurement on the same day as the ophthalmic examination (see Evaluation of CSFP).

The inclusion criteria for eyes in this study were a best-corrected visual acuity of greater than or equal to 20/40, a spherical refraction of −8.0 to +5.0 diopters (D), cylinder correction of −3.0 to +3.0 D, and a normal-appearing optic disc without glaucomatous optic neuropathy, pallor, or swelling of the optic disc. The exclusion criteria were any ocular diseases other than cataract, a history of intraocular surgery including laser treatment other than cataract extraction, and subjects with a neurologic disease, a history of intracranial surgery or lumbar puncture prior to enrollment to this study, a condition

**EDI SD-OCT of the Optic Nerve Head**

The optic nerve head (ONH) was imaged using the Spectralis OCT system with the EDI technique. The details of the protocol for scanning of the optic nerve using EDI SD-OCT to evaluate the LC are available elsewhere. In brief, approximately 75 horizontal and vertical B-scan images covering the optic disc, separated by 30 to 34 μm (the scan-line distance being determined automatically by the instrument), were obtained for each eye. For each section, 42 OCT frames were averaged, which provided the best trade-off between image quality and patient cooperation.

**Measurement of LCD and LCT**

Lamina cribrosa depth was determined by measuring the distance from the Bruch's membrane (BM) opening plane to the level of the anterior LC surface in 11 equidistant planes that divided the optic disc diameter into 12 equal parts vertically in each eye. A reference line connecting the two termination points of the BM was drawn on each B-scan image. The distance from the reference line to the level of the anterior border of the LC was measured at three points: the maximally depressed point and two additional points (100 and 200 μm from the maximally depressed point in a temporal direction). Only the temporally adjacent points were selected because the maximally depressed point was often close to the central vessel trunk, the shadow of which obscured the LC. When there was insufficient space for measuring the LCD at three points (e.g., the uppermost or lowermost B-scans, or B-scans with a prominent vascular shadow), adjacent scans were used. The measurements from the 11 planes were used to calculate the mean LCD of the eye. The superior LCD was defined as the mean of three values obtained at the three uppermost B-scan images (from the first to the third scan), the central LCD as that obtained at the three central-most B-scan images (from the fifth to the seventh scan), and the inferior LCD as that obtained at the three lowermost B-scans (9th-11th scan).

The LC thickness (LCT) was measured at three locations in each eye (the midhorizontal and the superior and inferior midperipheral regions of the ONH) using thin-slab maximum-intensity projection (MIP) images. Thin-slab MIP images were used because they allow an easier detection of the posterior LC border. The technique of generating thin-slab MIP images is described in detail elsewhere. In brief, three-dimensional (3D) volumetric reconstruction of the ONH was performed from the B-scan images by MIP rendering using image-processing software (Amira 5.2.2; Visage Imaging, Berlin, Germany). The thin-slab image is then obtained by selecting two planes (separated by ~64 μm) inside the 3D volumetric image data; only the data within these two planes were displayed in the thin-slab image. Lamina cribrosa thickness was measured as the distance between the anterior and posterior borders at the central three points (each separated by 100 μm) in each thin-slab MIP image in the direction perpendicular to the anterior LC surface at the measurement point. The
measured from three thin-slab images were used to calculate the mean LCT of the eye.

Lamina cribrosa depth and LCT were measured using the manual caliper tool of the Amira 5.2.2 software by two observers (DSL and EJL) who were masked to clinical information about the subjects. All measurements were repeated three times each by the two observers, and the mean of the six values was used for the main analysis.

**Evaluation of CSFP**

Cerebrospinal fluid pressure was measured using the fluoroscopy-guided lumbar puncture technique, which was conducted on the same day as the ophthalmic examination. In brief, the participants were placed in the lateral decubitus position with their neck bent in full flexion and the knees bent in full flexion up to chest. A standard spinal needle (90-mm long, 20-G) was inserted into the subarachnoid space with fluoroscopic guidance under local anesthesia. A manometer was connected to a three-way stopcock, and the opening pressure was measured after the column was allowed to equilibrate. All of the CSF examinations were performed by an experienced radiologist (JWL), who was masked to the clinical information of the subjects.

**Determination of the TLPD and TLPG**

Translaminar pressure difference was defined as the difference between the baseline IOP and the CSFP (TLPD [mm Hg] = baseline IOP [mm Hg] – CSFP [mm Hg]). Translaminar pressure gradient was referred to as the TLPD divided by the LCT (TLPG [mm Hg/mm] = TLPD [mm Hg]/LCT[mm]).

**Statistical Analysis**

The interobserver reproducibility of measurements of the LCD and LCT was determined by calculating the intraclass correlation coefficients (ICC) and their 95% confidence intervals (95% CIs). The accuracy of detection of the posterior LC borders was determined by calculating the intraclass correlation coefficients (ICC) for LCD and LCT and their 95% CIs values were also calculated. The Shapiro-Wilk normality test was performed due to the relatively small number of subjects in this study. Comparison between groups for continuous variables was performed using the independent samples t-test for parameters that passed normality tests, and the Mann-Whitney U test for parameters that did not pass normality tests. For categorical variables, Pearson’s χ² test and Fisher’s exact test were performed for parametric and nonparametric comparisons, respectively. Linear regression analysis was performed to reveal the factors influencing the LCD including IOP, CSFP, TLPD, and TLPG. Statistical analyses were performed with SPSS software for Windows version 17.0 (statistical package for the social sciences; SPSS, Chicago, IL, USA). The cutoff for statistical significance was set at P less than 0.05.

**RESULTS**

**Demographics**

The study initially enrolled 30 healthy subjects. Of these, four were excluded due to a diagnosis of concurrent glaucoma (n = 1), poor B-scan quality that did not allow the delineation of the borders of the LC (n = 1), and failure to receive CSF examination (n = 2), leaving a final sample of 26 healthy subjects.

The finally included subjects (12 men and 14 women) were aged 63.4 ± 8.0 years (mean ± SD) and had a spherical error of 0.7 ± 1.6 D. The baseline clinical characteristics of the participants and a comparison thereof between sexes are presented in Table 1. The eyes in males were more myopic (P = 0.042) and had a greater axial length (P = 0.004) than those in females; there were no sex differences in any of the other clinical parameters, including age, central corneal thickness, RNFL thickness, body mass index, and presence of diabetes or systemic hypertension.

Table 2 gives the translaminar pressure parameters (i.e., baseline IOP, CSFP, TLPD, and TLPG) and the LC measurements (i.e., LCT and LCD). The mean LCD and all superior, central, and inferior LCDs were larger in males than in females (P < 0.012 for all); there were no differences between the sexes for any of the other translaminar pressure parameters. The interobserver ICCs for LCD and LCT were 0.949 and 0.920, respectively (95% CI = 0.929-0.964 and 0.904-0.954, respectively). The interobserver ICC for measuring the distance from the reference line to the posterior LC border was 0.911 (95% CI = 0.812-0.959).

**Factors Influencing the LCD**

Table 3 lists the factors influencing the mean and central LCDs. Male sex was significantly associated with a larger mean LCD (P = 0.002). None of the factors related to translaminar pressure dynamics (IOP, CSFP, TLPD, LCT, and TLPG) were associated with the mean LCD. Regarding the central LCD, univariate analysis revealed a significant association between a larger central LCD and male sex, a larger TLPD, and a higher TLPG (P = 0.022, 0.018, and 0.017, respectively). No association was found between central LCD and IOP, CSFP, or the mean LCT. The TLPD and TLPG had high variance.
inflation factors (44.61 and 50.01, respectively), and so multivariate analysis was performed in two ways to avoid multicollinearity. The multivariate analysis showed that sex, TLPD, and TLPG were all significant factors influencing the central LCD (P ≤ 0.012, 0.048, and 0.029, respectively; Table 5, Fig. 1).

Representative Cases

Figure 2 shows representative cases illustrating the relationship between the translaminar pressure dynamics and the LCD in healthy eyes. Eyes with a larger TLPD, and a higher TLPG had a deeper central LCD.

DISCUSSION

The influence of translaminar pressure dynamics on the position of anterior LC surface was investigated in healthy subjects in this study. It was found that both TLPD and TLPG significantly influence the central LCD, whereas IOP and CSFP do not. To the best of our knowledge, this is the first study to evaluate the relationship between LC characteristics and the translaminar pressure dynamics in human eyes.

Posterior deformation of the anterior LC surface is considered one of the key manifestations of glaucomatous optic neuropathy.6 Experimental studies have shown that LC displacement occurs at an early stage of glaucoma,31-35 and may precede the RNFL change as detected by SD-OCT.35 Such findings indicate that LC displacement is one of the earliest changes in glaucoma. It may therefore be meaningful to determine the factors associated with the LC position not only in glaucoma but also in healthy eyes. Of the various factors with the potential to influence the LC position, the focus of the present study was how the translaminar pressure dynamics affects the position of the anterior LC surface in healthy eyes.

The LC lies between two pressurized compartments, the intraocular space and the retrobulbar subarachnoid space. Functioning as a barrier between the anteroposterior force of IOP and the posteroanterior force of the CSFP within the orbit, the LC may deepen as either IOP increases or CSFP decreases. However, if elevation of the IOP is compensated by an increase in the CSFP, or reduction in the CSFP is compensated by a decrease in the IOP, the net pressure difference may be unchanged, and thus the LC may not be deformed. Hence, it can be postulated that the disturbance in the pressure balance between the two compartments is more important with respect to the position of anterior LC surface than either IOP or CSFP. Consistent with this concept, the findings of the present study revealed a significant influence of TLPD on the central LCD, but no effect of either IOP or CSFP. This finding partially agrees with the finding of Ren et al.22 that only TLPD was significantly associated with glaucomatous visual field damage, whereas IOP and CSFP were not. The absence of a relationship between IOP and LCD in the present study is comparable with what was reported recently by Seo et al.,35 which may be attributable to the present study only including healthy subjects with a normal IOP. It is possible that IOP-related stress did not exceed the load-bearing capacity of the LC of healthy subjects, and thus the LC was not collapsed to a pathological level.6 Together with TLPD, TLPG was also positively correlated with the central LCD. It is noteworthy that a higher TLPG was associated with a larger LCD, both of which are likely to be associated with impairment of axonal flow. Meanwhile, since the TLPG is inversely proportional to the pressure difference between the two compartments is more important with respect to the position of anterior LC surface than either IOP or CSFP. Consistent with this concept, the findings of the present study revealed a significant influence of TLPD on the central LCD, but no effect of either IOP or CSFP. This finding partially agrees with the finding of Ren et al.22 that only TLPD was significantly associated with glaucomatous visual field damage, whereas IOP and CSFP were not. The absence of a relationship between IOP and LCD in the present study is comparable with what was reported recently by Seo et al.,35 which may be attributable to the present study only including healthy subjects with a normal IOP. It is possible that IOP-related stress did not exceed the load-bearing capacity of the LC of healthy subjects, and thus the LC was not collapsed to a pathological level.6 Together with TLPD, TLPG was also positively correlated with the central LCD. It is noteworthy that a higher TLPG was associated with a larger LCD, both of which are likely to be associated with impairment of axonal flow. Meanwhile, since the TLPG is inversely proportional to the pressure difference between the two compartments, it can be postulated that a thinner LCT may be associated with LC deepening. However, in the present study, the thinner LCT was not an independent factor for the larger LCD. This may be explained by the complex interaction between the factors surrounding the optic nerve and their influence on the LCD. The position of the LC may be determined not only by the thickness itself, but also its material property and peripapillary scleral tension or stiffness,6,8,19,31 parameters that are not currently measurable in patients. It has been suggested that the influence of scleral tensile forces generated by IOP may be larger than that of the TLPD.36 It is possible that the IOP-related tensile forces within the sclera pulls the LC taut within the neural canal, which can affect the LCD.31-37,38

The present study found that only central LCD was associated with the TLPD and TLPG; neither mean LCD nor superior and inferior LCD (data not presented) were associated with either the TLPD or TLPG. Based on this finding, we speculate that the interaction between IOP and CSFP is centered mostly on the central portion of the optic nerve, resulting mainly in posterior bowing of the LC. However, it should be remembered that this assumption is only valid for healthy eyes, and might not be generalizable to patients with glaucoma. The region most likely to be damaged in glaucoma is regarded to be the superior and inferior ONH;45,46 thus, further studies including glaucoma subjects should be performed to clarify this matter.

**Table 2. Translaminar Pressure Parameters and LC Measurements**

<table>
<thead>
<tr>
<th>Translaminar pressure parameters</th>
<th>Overall Subjects, n = 26</th>
<th>Male, n = 12</th>
<th>Female, n = 14</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline IOP, mm Hg</td>
<td>12.9 ± 2.5</td>
<td>12.5 ± 2.2</td>
<td>13.2 ± 2.8</td>
<td>0.485</td>
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<tr>
<td>CSFP, mm Hg</td>
<td>14.4 ± 2.5</td>
<td>14.1 ± 2.8</td>
<td>14.5 ± 2.3</td>
<td>0.689</td>
</tr>
<tr>
<td>TLPD, mm Hg</td>
<td>−1.5 ± 3.1</td>
<td>−1.6 ± 3.1</td>
<td>−1.3 ± 3.3</td>
<td>0.809</td>
</tr>
<tr>
<td>TLPG, mm Hg/mm</td>
<td>−5.6 ± 12.9</td>
<td>−6.9 ± 12.7</td>
<td>−4.5 ± 12.9</td>
<td>0.654</td>
</tr>
<tr>
<td>LC measurements</td>
<td></td>
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<tr>
<td>Superior LCD, μm</td>
<td>242.9 ± 48.5</td>
<td>253.5 ± 50.9</td>
<td>249.3 ± 47.2</td>
<td>0.475</td>
</tr>
<tr>
<td>Central LCD, μm</td>
<td>263.7 ± 49.1</td>
<td>257.8 ± 58.1</td>
<td>268.7 ± 41.4</td>
<td>0.584</td>
</tr>
<tr>
<td>Inferior LCD, μm</td>
<td>244.5 ± 49.6</td>
<td>241.4 ± 60.0</td>
<td>247.2 ± 40.7</td>
<td>0.775</td>
</tr>
<tr>
<td>Average LCD, μm</td>
<td>250.4 ± 41.6</td>
<td>244.9 ± 47.2</td>
<td>255.1 ± 37.3</td>
<td>0.544</td>
</tr>
<tr>
<td>Superior LCD, μm</td>
<td>452.0 ± 102.1</td>
<td>521.2 ± 81.9</td>
<td>388.8 ± 72.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Central LCD, μm</td>
<td>419.9 ± 112.6</td>
<td>477.7 ± 105.1</td>
<td>370.3 ± 96.5</td>
<td>0.012</td>
</tr>
<tr>
<td>Inferior LCD, μm</td>
<td>402.9 ± 95.7</td>
<td>462.9 ± 87.9</td>
<td>351.3 ± 69.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Average LCD, μm</td>
<td>425.9 ± 100.2</td>
<td>486.2 ± 91.4</td>
<td>372.0 ± 80.6</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Values with statistical significance are shown in bold. Data are shown in mean ± SD, unless otherwise specified.
### Table 3. Factors Influencing the Mean and Central LCD

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Mean LCD</th>
<th>Central LCD</th>
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<tbody>
<tr>
<td>Age, per 1-y older</td>
<td></td>
<td></td>
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<tr>
<td>Female sex*</td>
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<tr>
<td>Male sex</td>
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<tr>
<td>Presence of diabetes mellitus</td>
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<tr>
<td>Presence of systemic hypertension</td>
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<td>BMI, per 1-kg/m² larger</td>
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<tr>
<th>Eye-specific characteristics</th>
<th>Mean LCD</th>
<th>Central LCD</th>
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<tr>
<td>CCT, per 1-µm thicker</td>
<td></td>
<td></td>
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<tr>
<td>AXL, per 1-mm longer</td>
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<tr>
<td>Global RNFL thickness, per 1-µm thicker</td>
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<table>
<thead>
<tr>
<th>Factors related with translaminar pressure dynamics</th>
<th>Mean LCD</th>
<th>Central LCD</th>
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<tbody>
<tr>
<td>IOP, per 1-mm Hg higher</td>
<td></td>
<td></td>
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<tr>
<td>CSFP, per 1-mm Hg higher</td>
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<td></td>
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<tr>
<td>TLPD, per 1-mm Hg larger</td>
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<td></td>
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<tr>
<td>TLPG, per 1-mm Hg/mm higher</td>
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<tr>
<td>Mean LCT, per 1-µm thicker</td>
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</table>

Values with statistical significance are shown in bold. β, regression coefficients; VIF, variance inflation factor.

* Mean LCD in female and male were 372.01 ± 80.59 and 486.23 ± 91.40 µm, respectively (P = 0.002, independent t-test). Central LCD in female and male were 362.65 ± 100.04 and 472.50 ± 128.16 µm, respectively (P = 0.022, independent t-test).
Yang et al. recently examined morphologic changes of the RNFL and optic nerve head in monkey eyes with experimentally reduced CSFP. They found that four of eight study eyes developed thinning of the RNFL and neuroretinal rim, while none of the control eyes exhibited any of these changes. A longitudinal study is required to validate whether this finding is also true in healthy human eyes with low CSFP.

In the present study, the male sex appeared to be significantly associated with a larger LCD. This finding is consistent with a recent study finding that the EDI-OCT-based LCD was larger in healthy male eyes than in healthy female eyes. Since the axial length was also found to be greater in males than in females, its influence on LCD was investigated, which did not find any correlation between the axial length and the LCD at any of the locations (data not presented). It is possible that this result is merely an anatomic difference between the sexes for which there is no clear explanation, and hence the clinical relevance of the apparent sex-related difference in LCD position remains to be elucidated.

One may argue that the translaminar pressure dynamics could also influence the LCT via a compressive effect on the LC. However, there was no significant association between the TLPD/TLPG and the LCT at any of the locations (data not presented). This absence of an association indicates that the TLPD/TLPG may not be a factor related to LC thinning in healthy eyes. We believe that the TLPD/TLPG represents the amount of anteroposterior force, which could influence the anteroposterior position of the LC but may not be able to compress the LC significantly. Rather, LC thinning may occur when both the IOP and CSFP are elevated and compress the LC from both directions. However, a simultaneous increase in IOP and CSFP may not necessarily be associated with a net increase in TLPD/TLPG. On the other hand, it can be speculated that a long-term increase in the strain within the LC from an increased TLPD/TLPG could cause failure of the laminar beam and subsequent LC thinning. However, this proposition needs to be confirmed in future studies involving glaucoma patients.

This study was limited by the smallness of the sample. Furthermore, since patients with glaucoma were not included, the influence of translaminar pressure dynamics on LCD and its relationship with glaucomatous damage could not be determined. However, given that LC displacement is one of the early changes in glaucoma, it is still important to determine the factors that can affect the LC position in healthy eyes. Secondly, this was a cross-sectional study; thus, the active displacement of the LC could not be evaluated, but only the position of the LC was measured. However, we believe that evaluation of the LC position is still important in that it may characterize the chronic...
remodeling and deformation of the LC. In addition, the LC position may represent the amount of glaucomatous damage, and may also predict the future glaucoma progression. Currently, the dynamic relationship between translaminar pressure parameters and the LC displacement could be addressed only by experimental studies. Thirdly, the IOP and CSFP were measured with the patients in different body positions. Both IOP and CSFP are dynamic parameters that change according to the body position, and so the estimation of the TLPD may not have been as accurate as it could be. However, the true TLPD can only be calculated from the difference between the IOP and the retrolaminar tissue pressure, which is not currently measurable. In the present study, the lumbar CSFP was used instead of the retrolaminar tissue pressure, based on the assumption that the lumbar CSFP is associated with the intracranial CSFP and the pressure in the optic nerve subarachnoid space, and therefore also with the retrolaminar tissue pressure. However, the lumbar CSFP is not equivalent to the intracranial CSFP, and the intracranial CSFP may not be equivalent to the pressure in the optic nerve subarachnoid space, because it may be buffered by the orbital tissue. Furthermore, since the pressure in the optic nerve subarachnoid space may itself be buffered by the pia mater, the pressure therein may not be equivalent to the retrolaminar tissue pressure. Fourthly, parameters potentially associated with the LC position, such as the material properties and geometry of the ONH and peripapillary scleral tissue, including the size of the BM opening and the scleral canal diameter, were not considered in the present study. As found previously in experimental studies that investigated laminar scleral dynamics, increased TLPD may not influence the LC position because the IOP-related tensile force within the sclera pulls the LC taut, thus acting as a counterforce against posterior LC movement. However, such a phenomenon is less likely to occur in healthy human eyes with a normal IOP and a low CSFP. Finally, the position of the LC was determined in the present study based on the level of the BM, and therefore the measurement could have been influenced by the thickness of the peripapillary choroid. It has recently been demonstrated that the LCD relative to the BM opening may be overestimated in eyes with a thick peripapillary choroid, and vice versa. However, the bias in the LCD measurements caused by the variability of peripapillary choroidal thickness may have been minimal in the healthy subjects included in the present study, since they exhibited little variation in the factors potentially associated with choroidal thickness, such as age and degree of myopia.

In conclusion, both a larger TLPD and a higher TLPG were significantly associated with a larger central LCD in healthy human eyes. This result suggests a potential role of translaminar pressure dynamics in determining the anterior LC position relative to BM opening.

Acknowledgments

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