Lack of Relationship between Central Corneal Thickness and Papilloedema in Idiopathic Intracranial Hypertension

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ABSTRACT

Translaminar pressure gradient abnormalities have been implicated in the pathogenesis and progression of glaucoma. A “reversed” translaminar pressure gradient may be related to papilloedema severity in idiopathic intracranial hypertension. Central corneal thickness is related to intraocular pressure measurements and, by extension, to translaminar pressure gradients. We evaluated if central corneal thickness could be a marker of worse papilloedema due to altered translaminar pressure gradients in patients with idiopathic intracranial hypertension. We found that central corneal thickness was not related to the severity of papilloedema in idiopathic intracranial hypertension.

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Introduction

Idiopathic intracranial hypertension (IIH), a disorder of elevated intracranial pressure without an identifiable cause, can lead to vision loss when increased pressure is transmitted to the anterior portion of the optic nerves causing papilloedema. The translaminar pressure gradient (TLPG), the difference between intraocular pressure (IOP) and intracranial pressure across the lamina cribrosa, may play a role in the pathophysiology underlying IIH and glaucoma, a disorder related to elevated IOP. Central corneal thickness (CCT) is an important metric in the evaluation of IOP and the risk of glaucoma.¹ Patients with thinner CCTs have higher true intraocular pressures than those measured by applanation tonometry (and are therefore at higher risk for developing primary open-angle glaucoma) because tonometers are constructed to measure IOP with an assumed normal corneal thickness. CCT influences IOP measurements and, by extension, TLPG measurements. Since the TLPG may influence the severity of optic nerve head damage in glaucoma,^{2,3} it is possible that a “reversed” TLPG may influence the severity of papilloedema in IIH.⁴

Therefore CCT, via its effect on IOP measurement, could be a marker of worse papilloedema in patients with IIH.

Methods

Participants

The Institutional Review Board of Emory University approved this study. We retrospectively reviewed the medical records of 100 consecutive patients diagnosed with IIH who had systematic CCT measurements between March 2015 and October 2016. Diagnosis of IIH was made using the updated modified Dandy criteria.⁵ Patients were excluded if the diagnosis of IIH was uncertain or if they presented with corneal disease that could modify CCT. Glaucoma patients were excluded.

Data collected included age, demographics, medications, body mass index (BMI), IOP, cerebrospinal fluid opening pressure (CSF-OP) measured by lumbar puncture at the time of diagnosis (before initiation of treatment), visual acuity, colour vision, CCT, visual fields, and Frisén grade of

papilloedema. Visual fields were graded as 0 = normal, 1 = enlarged blind spot, 2 = generalised depression, 3 = arcuate nerve fibre bundle defect, 4 = altitudinal defect, 5 = neurologic-like/other, 6 = central scotoma.

CCT was determined using handheld ultrasound pachymetry (DGH 550 Pachette 2, DGH Technology Inc., Exton, PA). The mean value of two readings was calculated for each eye. TLPGs were calculated by determining the difference between IOP and CSF-OP (following conversion of CSF-OP from cmH₂O to mmHg).

Statistical analysis

Controlling for age, race and sex, we examined associations between CCT and other variables of interest: BMI, CSF-OP, follow-up in months, visual acuity and visual field defects (at initial and final examinations), colour vision, IOP, TLPG, Frisén grade of papilloedema, and presence of papilloedema and/or optic nerve pallor (at initial and final examinations).

We used the following generalised estimating equation models to account for intereye correlations: linear for CSF-OP, CCT, cup-to-disc ratio, colour vision, IOP and TLPG; logistic for Frisén grade ≤ 4 , visual field defects at initial and final examinations, papilloedema or optic nerve pallor at initial and final visits; and ordinal for Frisén grade and visual field comparison between initial and final visit.

Results

Two-hundred eyes of 100 patients with IIH were included (median age at diagnosis 31.4 years [interquartile range 24.8–36.1]) [Table 1]. Patients had a median visual acuity of 0.0 logMAR at initial and final examinations.

Controlling for age, race and sex, CCT was not associated with any of the studied variables. No correlation was found between CCT and IOP, BMI, or TLPG. CCT was not associated with CSF-OP (Figure 1), severity of papilloedema, or optic nerve pallor at initial or final examinations. There was no correlation between CCT and final visual acuity or visual field defects [Table 2].

Table 1. Characteristics of 100 patients with idiopathic intracranial hypertension.

Characteristics	Value
Median age	31.4 years (IQR 24.8–36.1)
Gender	95/100 women (95%)
Race	56/100 black (56%) 35/100 white (35%)
Median follow-up	10.7 months (IQR 1.6–20.2)
Median BMI	35.7 kg/m ² (IQR 31.1–43)
Median CSF opening pressure	34 cmH ₂ O (IQR 29.6–41.7)
Median CCT	552 μ m (IQR 527.5–577.5)
Median IOP	15 mmHg (IQR 13–17)
Median TLPG (CSF OP-IOP)	9.4 mmHg (IQR 6.4–16.9)
Presence of papilloedema at presentation	142/200 eyes (71%)
Frisén Grade 1	39/142 eyes (20%)
Frisén Grade 2	39/142 eyes (20%)
Frisén Grade 3	40/142 eyes (20%)
Frisén Grade 4	16/142 eyes (8%)
Frisén Grade 5	8/142 eyes (4%)
Optic nerve pallor at presentation	30/200 eyes (15%)
Optic nerve pallor at final visit	43/170 eyes (25%)
Visual field defect at presentation	70/193 (36%)
Visual field defect at final visit	60/163 (36%)

IQR: interquartile range, BMI: body mass index, CSF: cerebrospinal fluid, OP: opening pressure, CCT: central corneal thickness, IOP: intraocular pressure, TLPG: translaminal pressure gradient (gradient across lamina cribrosa).

Discussion

We found that the median CCT for patients with IIH was in the normal range. There were no correlations between CCT and CSF-OP, TLPG, severity of papilloedema, or visual outcomes. However, it is not currently possible to directly measure TLPG in humans, as has been mentioned in a recent study evaluating IOP and CSF-OP in IIH patients on acetazolamide.⁶ This paper also used the difference between IOP and CSF-OP as a surrogate marker for direct TLPG measurement. However, opening pressure in the lumbar spine may not reflect the pressure in the immediate retrolaminar space due to CSF compartmentalisation, leading to incorrect assumptions about the actual TLPG.⁷ Further studies are necessary to evaluate the relationships among CCT, TLPG, IIH, and glaucoma. Although this was a negative study, we know CCT is an important variable in glaucoma, and we suspect TLPG is a factor in glaucoma severity. Due to the influence of CCT on IOP measurements, CCT may still change TLPG. Considering CCT as a variable in future studies may therefore be important in IIH studies involving TLPG.

Figure 1. Representative illustration of the overall study results: Scatter plot showing the correlation between central corneal thickness (CCT) and CSF opening pressure. No correlation was found between CCT and CSF opening pressure ($r = 0.00$).

Table 2. Association between central corneal thickness and listed variables controlling for age, sex, and race.

Variable	Mean change in CCT, μm (standard error)	<i>p</i> -Value
Frisén grade 4 or greater vs. lower grade	−0.003 (0.006)	0.68
Optic nerve pallor	−0.006 (0.006)	0.31
Visual acuity at final visit, per unit logMAR	−0.007 (0.005)	0.12
Visual field deficit at final visit, grade 2 or higher vs. lower	−0.008 (0.006)	0.16

Declaration of interest

The authors report no conflicts of interest.

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