The Literature

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β-Zone Parapapillary Atrophy and the Rate of Retinal Nerve Fiber Layer Thinning in Glaucoma
Lee EJ, Kim TW, Weinreb RN, et al

ABSTRACT SUMMARY
Lee et al used time-domain optical coherence tomography (OCT) to determine if the presence of, size of, and increase in β-zone parapapillary atrophy (βPPA) is associated with the rate of change in the thickness of the retinal nerve fiber layer (RNFL).

The retrospective cohort study evaluated 202 patients who had at least four previous OCT measurements. Of the participants, 177 patients had normal-tension glaucoma (NTG), and 25 had high-tension glaucoma. Subjects were divided into two groups according to the presence (n = 144) or absence (n = 58) of βPPA. Two masked investigators independently evaluated βPPA, which was defined based on stereophotographs. The outlines of the optic disc (inner border of Elschnig scleral ring) and βPPA (an inner crescent of chorioretinal atrophy with visible scleral and choroidal vessels) were plotted using imaging software, and the areas of total optic disc and βPPA were obtained. Peripapillary fast RNFL scans were performed with time-domain OCT. Values were obtained from 1 to 12 o’clock and in the global, temporal, superior, nasal, and inferior quadrants.

The RNFL thinned significantly faster in eyes with βPPA than in those without βPPA in the inferior quadrant and the 7-o’clock sector. In a comparison of the global rate of thinning of the RNFL, more patients showed faster rates of thinning in eyes with βPPA (46 of 144) than in eyes without βPPA (seven of 58; P < .001). Multivariate analysis showed that the presence of βPPA and the percentage increase in the βPPA to disc-area ratio significantly influenced the rate at which the RNFL thinned, as shown on OCT. The authors concluded that the presence and enlargement of βPPA were significantly associated with the rate of progressive thinning of the RNFL.

DISCUSSION
What is βPPA?
The association between parapapillary atrophy and glaucoma was first described by Elschnig and Bücklers in the early 1900s. In 1989, Jonas et al observed differences in the features of parapapillary atrophy and divided it into α and β zones. αPPA is characterized by irregular hypo- and hyperpigmentation of the retinal pigment epithelium and thinning of the chorioretinal tissue layer, and αPPA is peripheral to βPPA when the latter is present. βPPA is adjacent to the optic disc and is characterized by atrophy of the retinal pigment epithelium and choriocapillaris, thinning of chorioretinal tissues, and visible scleral and choroidal vessels. βPPA correlates with a marked loss of retinal pigment epithelial cells and retinal photoreceptors. Accordingly, αPPA produces a relative scotoma, and βPPA produces an absolute one.

Cerebrospinal Fluid Exchange in the Optic Nerve in Normal-tension Glaucoma
Killer HE, Miller NR, Flammer J, et al

ABSTRACT SUMMARY
Killer et al conducted an unmasked prospective series that studied the cerebrospinal fluid (CSF) exchange between the intracranial spaces (ie, basal cisterns) and the subarachnoid space (SAS) of the optic nerve in subjects with NTG compared with control subjects without NTG or other forms of glaucoma.

The investigators performed computed tomography cisternography of the brain and orbits of 18 patients (seven...
women, 11 men; mean age, 64.9 ±8.9 years) with NTG and four patients (four women; mean age, 62.8 ±18.4 years) without glaucoma. At the beginning of the cisternography, a lumbar puncture was performed to measure intracranial pressure. Subjects were in the lateral decubitus position to confirm that CSF pressure was 20 cm H2O or less. At the time of the lumbar puncture, 10 mL of CSF was obtained for analysis, and then 10 mL of contrast was injected intrathecally. The researchers then performed computed tomography cisternography and measured the density of contrast-loaded CSF in the intracranial spaces and in the SAS surrounding the optic nerve in Hounsfield units (HU).

The investigators found no difference in intracranial pressure between subjects in the NTG group (mean, 13.3 ±3.5 cm H2O) and the control subjects (mean, 13.0 ±5.7 cm H2O; \( p = .96 \)) or between men and women (\( p = .43 \)). In the control group (eight eyes), the densities of contrast medium by computed tomography cisternography in the SAS surrounding the optic nerve had a mean density of 529 ±285.3 HU, and the densities in the basal cisterns had a mean density of 531 ±208.3 HU. In the NTG group (36 eyes), the mean density of contrast medium in the SAS of the optic nerve was 144 ±88.4 HU and differed significantly from the densities in the control eyes (\( p = .006 \)). Mean contrast density in the basal cisterns of patients with NTG was 566 ±166.5 HU and did not differ from that of the control group (\( p = .67 \)). The difference between the measured contrast density in the SAS surrounding the optic nerve and the intracranial SAS in the basal cisterns revealed a significant difference between patients with NTG and the control subjects (\( p < .0001 \)).

The authors concluded that the difference in concentration gradients between the contrast-loaded CSF within the intracranial spaces and the SAS of the optic nerve in the NTG group supports the hypothesis of a disturbed CSF exchange between these spaces. This suggests that, in patients with NTG, the SAS of the optic nerve may become compartmentalized with different CSF dynamics, composition, and pressure. Such division could lead to CSF stasis, which might decrease the clearing from the CSF of toxic metabolites that might damage the optic nerve.

**DISCUSSION**

**Why is CSF pressure important in glaucoma?**

The optic nerve is exposed to two independent pressurized regions: the intraocular space anteriorly and the SAS posteriorly.\(^7\) IOP is approximately 10 to 21 mm Hg, and the CSF pressure in the SAS is approximately 5 to 15 mm Hg.\(^7\) The structure that separates these two pressurized regions is the lamina cribrosa, and the pressure difference between these regions is the translaminar pressure difference.\(^7\)

Studies have postulated that a low CSF pressure and high translaminar pressure difference may play a role in the pathogenesis of NTG.\(^8,9\) CSF pressure is important because it provides force from the SAS against the posterior surface of the lamina cribrosa. This counteracts the force from the IOP against the anterior surface of the lamina cribrosa. If a patient has a high IOP but a normal CSF pressure—a high translaminar pressure—the optic nerve may be susceptible to damage due to excessive force against the lamina cribrosa. Similarly, if a patient has a normal IOP but a low CSF pressure, the optic nerve may be subject to damage by the same mechanism.

**What is the significance of this article?**

There is much to be learned about the cerebrospinal system, including its various spaces and CSF flow, pressure, and composition. This study demonstrates that CSF may not flow freely in the cerebrospinal space. If it is compartmentalized, impaired circulation and stagnation of the CSF may lead to a buildup of toxic metabolites that could damage the optic nerve.