The role of cerebrospinal fluid pressure in glaucoma and other ophthalmic diseases: A review

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Abstract

Glaucoma is one of the most common causes of blindness in the world. Well-known risk factors include age, race, a positive family history and elevated intraocular pressures. A newly proposed risk factor is decreased cerebrospinal fluid pressure (CSFP). This concept is based on the notion that a pressure differential exists across the lamina cribrosa, which separates the intraocular space from the subarachnoid fluid space. In this construct, an increased translaminar pressure difference will occur with a relative increase in elevated intraocular pressure or a reduction in CSFP. This net change in pressure is proposed to act on the tissues within the optic nerve head, potentially contributing to glaucomatous optic neuropathy. Similarly, patients with ocular hypertension who have elevated CSFPs, would enjoy a relatively protective effect from glaucomatous damage. This review will focus on the current literature pertaining to the role of CSFP in glaucoma. Additionally, the authors examine the relationship between glaucoma and other known CSFP-related ophthalmic disorders.

Keywords: Cerebrospinal fluid pressure, Translaminar pressure, Glaucoma, Papilledema, Idiopathic intracranial hypertension, Microgravity

Introduction

Glaucoma is a distinct optic neuropathy, which results in a characteristic nerve damage and a typical pattern of visual field loss. Intraocular pressure (IOP) is one of the most important risk factors. One approach to the classification of glaucoma is open versus closed angle forms. Closed-angle variants of glaucoma have elevated IOP that is caused by primary or secondary pathologies that share anatomic crowding or closure of the aqueous humor drainage system or angle. In open-angle forms of glaucoma the drainage angle is open, but for a variety of reasons the IOP may be elevated or remains in the normal range. Regardless of the type of glaucoma, intraocular pressure reduction by a medical or surgical approach has been shown to decrease incidence and progression of glaucoma.

Why glaucoma occurs with normal tension glaucoma (NTG) or does not occur in some patients with ocular hypertension (OHT) has been debated for decades. Explanations for NTG include hypotheses of a “susceptible optic nerve,” intrinsic retinal or ganglion cell pathology, inflammatory causes, undocumented elevations in IOP, and others. There is likely an interplay of susceptibility factors that decreases the threshold for glaucomatous injury in these patients despite seemingly normal intraocular pressures, or alternatively causes a different type of glaucoma. Vascular or perfusion abnormalities may be important, perhaps in concert with pressure fluctuations, neuronal excitotoxicity, genetic
mutations or predisposition, or other pressure-independent factors. However, it has been determined that reducing IOP is beneficial in patients with normal tension glaucoma. Conversely, a variety of explanations have been offered for the observation that a relatively small percentage of patients with documented elevation of IOP out of the normal range ultimately develop glaucomatous damage. For these reasons it has become clear that factors in addition to IOP play an important role in glaucoma pathogenesis.

Recent studies have implicated the role of pressure of the primary fluid within the central nervous system, the cerebrospinal fluid (CSF), as a major contributor to glaucoma. The anatomical landmark of interest is the lamina cribrosa, a thin area of scleral tissue that separates two differentially pressurized compartments – the intraocular space and the orbital subarachnoid space. The difference in pressure between these two fluid spaces is termed the translaminar pressure. When described as a function of pressure across the lamina cribrosa, the CSF pressure can be a determinant factor in the pathogenesis of glaucoma.

**Figure 1.** Histologic anatomy of the posterior globe and optic nerve with surrounding tissue. The lamina cribrosa (red) is a thin section of scleral tissue that acts as a sieve and allows the passage of exiting retinal ganglion cell axons and the retinal vessels. The cerebrospinal fluid (blue) flows within the subarachnoid space between the dura mater and the pia mater investing the optic nerve. Modified and reproduced with permission, Boston University Histology Learning System (Deborah W. Vaughan, PhD).

**Figure 2.** Spectrum of cerebrospinal fluid pressure-related ophthalmic disease.
tissues of the optic nerve and lamina cribrosa the term is more accurately stated as the translaminar pressure gradient. It is hypothesized that an elevated posteriorly-directed pressure differential may contribute to optic nerve damage and produces posterior bowing of the lamina cribrosa, which is often seen in patients with glaucoma. At the other end of the spectrum, increased posterior pressure, a pressure vector in the anterior direction toward the intraocular fluid compartment, associated with elevated intracranial hypertension, can cause papilledema. (Fig. 2).

We review here the risk factors for glaucoma in the context of this glaucoma–CSFP model. The relevant anatomy is reviewed, as are plausible mechanisms that could result in glaucomatous optic neuropathy as well as conditions on the other end of the CSFP spectrum that are also explained by this model.

Primary open-angle glaucoma, normal tension glaucoma, ocular hypertension – and the translaminar pressure difference

The earliest evidence that CSFP may play a role in glaucoma was reported by Yablonski and colleagues. In the cat model, CSFP⁴ was lowered to −4 mm Hg. One eye was then cannulated to produce a pressure of 0 mm Hg, while the other eye was unchanged and maintained at a normal pressure. After 3 weeks, the uncannulated eye developed optic nerve damage consistent with glaucomatous optic neuropathy. The eye that was cannulated and maintained at a low pressure similar to the CSF pressure did not develop optic neuropathy. Morgan and colleagues later performed elegant studies that examined the effect of altering pressure of the intraocular and subarachnoid spaces on the lamina cribrosa in a dog model. They reported that varying CSFP was similar to altering IOP on the lamina cribrosa, and therefore may be relevant in the pathogenesis of glaucoma.⁵ A follow-up study determined that this effect was possibly similar in human donor eyes.⁶

Berdahl and colleagues reported a large-scale retrospective study based on electronic records available from the Mayo Clinic. Medical records were obtained on over 30,000 patients who underwent diagnostic lumbar punctures. Those with a diagnosis of primary open-angle glaucoma were compared to age-matched patients without glaucoma as controls. Intracranial pressure in POAG patients was lower than those without glaucoma (9.2 ± 2.9 mmHg versus 13.0 ± 4.2 mmHg respectively, p < 0.0001).⁷ A second study examined ocular hypertensive patients, as well as normal tension glaucoma patients. Compared to age-matched controls, patients with POAG were again found to have a statistically lower CSFP compared to controls (9.1 ± 0.77 mmHg versus 11.8 ± 0.71 mmHg, respectively). Patients with NTG had even lower pressures compared to standard POAG patients (8.7 ± 1.16 mmHg). Ocular hypertension patients were found to have higher CSFP compared to the control patients (12.6 ± 0.85 mmHg versus 10.6 ± 0.81 mmHg, respectively; p < 0.05).⁸

Ren et al. examined this in a prospective study conducted in Chinese subjects. Patients with POAG (N = 43, 29 POAG; 14 NTG) were compared to 71 non-glaucomatous controls. This study confirmed the finding that patients with high-pressure POAG had lower CSF (11.7 ± 2.7 mmHg) compared to normal patients (12.9 ± 1.9 mmHg). They also noted that patients with NTG had lower CSF compared to either POAG or non-glaucomatous controls (9.5 ± 2.2 mmHg). Given the prospective nature of this study, the examiners were able to calculate the translaminar pressure difference (CSFP – IOP) and were able to correlate this measurement to the mean deviation of patient’s visual fields. In this study larger translaminar pressure differences were positively correlated with visual field loss.⁹ A second study by the same group examined ocular hypertension patients compared to normal patients. Similar to the study by Berdahl et al., a statistically significant difference between CSFP in OHTN and non-glaucomatous control subjects was found with OHT patients having significantly higher pressures (16.0 ± 2.5 mmHg versus 12.9 ± 1.9 mmHg, respectively; p < 0.001).¹⁰

Risk factors for glaucoma: a different perspective

The studies cited above provide evidence of a relationship between CSFP and glaucoma, which raises additional questions about other factors that may be related to CSFP and, by association, with glaucoma pathogenesis. Therefore, the effect of factors such as age, sex, and body mass index (BMI) has been studied to better understand how these may affect CSFP as a potential risk factor for glaucoma and other ocular diseases.

Age

Among the multiple risk factors for primary open-angle glaucoma, age is one of the most noteworthy. Numerous studies in the United States and around the world have identified age as an independent risk factor.¹¹–¹⁹ A recent study by Fleischman et al. found a relationship between CSF and age, which may offer an explanation for age as a risk factor for POAG.²⁰ Electronic medical records of all patients who had a lumbar puncture performed at the Mayo Clinic in Rochester, Minnesota during a 13-year period (1996–2009) were screened. Patients using medications or having medical diagnoses known to affect CSFP were excluded from analysis. After all entry criteria were met, 12,118 patients were qualified for investigation. It was found that mean CSFP was stable from ages 20–49 years. However, mean CSFP progressively declined after age 49, from 11.5 ± 2.8 mmHg in the 20–49 age group to 8.4 ± 2.4 mmHg in the over 90 year age group (p < 0.001), a 27% reduction.

Assuming a stable IOP, this decline in CSFP with age would result in a significant increase in the translaminar pressure gradient. Morgan’s studies suggest that the mechanical effect of changes in CSFP plays a significant role on the morphology of the lamina cribrosa.²¹,²² Assuming that a decrease in CSFP is equivalent to a similar increase in IOP, we can evaluate this effect in reported population studies that have examined the prevalence and IOP measurements of persons diagnosed with glaucoma and controls (Fig. 3). For example, the Baltimore Eye Survey revealed a 4-fold increase in risk in the development of glaucoma by a change in IOP of +3 mmHg.¹¹,²³ The Beaver Dam Eye Study found that, on average, there was a 5 mmHg difference in IOP between patients with glaucoma and those without.¹³ In Tajimi, Japan, researchers found that a 4 mmHg rise in IOP increased risk for POAG in twofold, even within a normal range of...
IOP. These data suggest that the observed 3 mmHg mean reduction of CSFP with advancing age may be an important risk factor for glaucoma that has not been accounted among populations.

Body mass index

Body Mass Index (BMI) is another variable that has been reported as a risk factor for glaucoma. A positive correlation between increased BMI and glaucoma, especially in women, was identified in Newman-Casey and colleagues’ large longitudinal cohort study in a mostly Caucasian population (86.7%). In their study of the relationship between POAG and components of the metabolic syndrome, an elevated BMI in women had a 6% increased hazard of developing OAG. The study revealed no increased risk for glaucoma in men. The Tajimi Eye Study (Japan) compared 119 patients with POAG and 2755 controls, and found no statistically significant difference between BMI in either group (22.5 vs. 22.9 respectively, p = 0.28). On the other hand, Leske’s Barbados Eye Study identified that a decreased BMI was associated with greater risk for glaucoma in the Barbados population of African ancestry. Other studies have had similar findings to Leske’s, except in NTG patients or based on sex.

In their prospective study of CSFP and POAG, Ren and colleagues found a positive correlation between BMI and CSFP. In this study, the mean age was 45.7 ± 11.3 years, and the mean BMI was 23.7 ± 2.7. Univariate analysis revealed CSFP was significantly correlated with higher BMI (r = 0.50; p < 0.001). In a retrospective study, Berdahl et al., reported results from an analysis of electronic medical records obtained from 4235 patients with measured BMI. (Fig. 4) Women had a slightly lower BMI (mean 26.0 ± 5.8) while men had a slightly higher BMI (27.4 ± 4.6). Univariate regression models identified a positive linear relationship between BMI and CSFP (r² = 0.20, p < 0.001). There was a 37.7% increase in BMI from BMI 18 (8.6 ± 2.1 mmHg) to 39 (14.1 ± 2.5 mmHg).

Since BMI is positively associated with CSFP the question arises as to whether higher BMI may be protective for POAG and the converse, if lower BMI may increase risk for glaucoma. The studies cited above found that increased BMI appeared to be protective for POAG in female subjects,
although this protection was not conferred upon male sub-
jects. The reason for this discrepancy is unclear. It is possible
other factors, such as some hormonal element, may be
involved.34

Race

Race is a well-documented risk factor for glaucoma. It is of
great interest to determine whether CSFP varies among dif-
ferent populations and whether this may be part of the expla-
nation for differences in prevalence of glaucoma between
various ethnic groups. Unfortunately, there is no study pow-
ered to determine if there is any differential effect of race
on CSFP. Future large-scale studies of various populations
will be necessary to determine the effect, if any, of race on
CSFP.

Physiology of CSFP

The translaminar pressure difference is a relatively simplis-
tic term that does not account for what is clearly a complex
relationship between pressure within and surrounding varied
tissue compartments, body position, and other known and
unknown factors. The pressures within the orbital subarach-
noid space, which comprise the retrolaminar pressures, are
likely different than the pressures in the cranial vault and
the remainder of the neuraxis. CSF pressures are directly
responsive to changes in body position as well as diurnal var-
iation. For example, when humans are upright, intracranial
fluid pressure, due to hydrostatic fluid shifts, may drop to
−5 mmHg. Why would the pressure measured by a lumbar
puncture have any relevance?

Embryology of the optic nerve, flow of the CSF

The development of the optic vesicle begins at day 22
with an evagination from the wall of the diencephalon, which
creates the optic vesicle. The optic vesicle invaginates and
forms the optic cup and the optic stalk. The cavity of the op-
tic stalk is eventually filled with the axons of the retinal gan-
glion cells as well as the retinal vessels. The optic nerve, of
course, is an extension of the central nervous system, and
as such is invested by the meninges. The optic nerve, as it ex-
its the eye, is enclosed in dural, arachnoid and pial sheaths, as
well as the circulating fluid of the central nervous system, the
cerebrospinal fluid (CSF). The CSF originates in the choroid
plexus within the third, fourth, and inferior horn of the lateral
ventricles, and drains into the arachnoid villi of the cerebral
venous system, as well as through lymphatic channels.35–39
The fluid flows freely throughout the neuraxis within the sub-
arachnoid space, which includes the optic nerve.

Anatomy and physiology

For the glaucoma-CSF model to make sense, it is essential
to understand the anatomy of the optic nerve head. This must
be done in the broader context of the central nervous system
as well as the intraocular space. The anatomical landmark
of interest is the lamina cribrosa, a thin sieve-like perforation
of the posterior sclera through which the axons of the retinal gan-
glion cells exit the eye. It is generally believed that the lamina
cribrosa is the major site of injury for vision loss related to glau-
coma.40–43 This is also the site that experiences the pressure
gradient between the intraocular and extracurcular spaces.5,44
The difference between these two spaces is termed the trans-
laminar pressure difference. The resulting force imparted by
the difference of the two pressures is dependent on the thick-
ness of the lamina cribrosa. Jonas et al., in a histomorphometric
study of the lamina cribrosa in glaucomatous and non-glauco-
matous eyes noted that the central lamina cribrosa thickness in
a control group was nearly 250 micrometers thicker than the
glaucoma group. These investigators concluded that this in-
crease in the translaminar pressure gradient in these cases
might be important contributors to the glaucomatous patho-
physiological process.

Effect of posture on CSFP

The CSF measured in the supine position is a static mea-
sure of a dynamic process. Lenfeldt found that CSF mea-
sured by lumbar puncture accurately represents intracranial
pressure in the lateral decubitus position.45 However, the
CSF in the intracranial vault decreases and even falls to sub-
zero values in a standing position, and then approaches
equivalence in a prone position. Additionally, the dynamics
of the orbital CSF flow may be different than that of the rest
of the neuraxis. While a different pressure may exist within
the orbital CSF compartment, it is nevertheless continuous
with the rest of the spinal column, and there is evidence that
pressure is transmitted to the optic nerve sheath from fluid
changes elsewhere in the contiguous subarachnoid space.46
Although a formulaic relationship between the orbital CSF
and intracranial pressure has not been elucidated to this
point, the fact that there is pressure transduction between
the neuraxis and the orbital CSF suggests that these two
compartments should not be considered separately. There-
fore, for the purpose of considering the translaminar pressure
difference, it is more useful to relatively interpret lumbar
puncture data, as opposed to considering the retrolaminar
pressure strictly as the lumbar puncture opening pressure.

Idiopathic intracranial hypertension (IIH) and papilledema
serve as useful examples. In describing IIH, Corbett and Meht-
ta considered an abnormally elevated CSF to be greater
than 250 mm H2O (or 18.4 mmHg) as measured in the lateral
decubitus position.47 A pressure under 200 mm H2O
(14.7 mmHg) is considered normal however. Therefore, less
than 4 mmHg is clinically significant, even before taking into
account gross overestimates of the retrolaminar pressure in
the upright position, which is the case approximately two-
thirds of a typical day. The measurement of the opening pres-
sure from a lumbar puncture is important, however it is not
possible currently to assess the impact of postural changes
on the biomechanics and physiology of the lamina cribrosa.

What contributes to the pressure of the cerebrospinal
fluid?

In most simplistic terms, much like the eye, the CSFP is a
product of production and drainage of fluid. If we look at
the relationship of age and CSFP described above, the
change in pressure may be a product of decreased resistance
to CSF outflow or decreased CSF production with advancing
age. There is no evidence that outflow resistance decreases
with age – on the contrary, studies report CSF flow resistance
increases with age. However, the choroid plexus undergoes aging changes that lead to decreased CSF production. Current evidence suggests that vasopressin, a hormone that regulates the choroid plexus, is responsible for a reduction in CSF production. Further, vasopressin-secreting neurons show increased activity with aging. This is speculative, of course, but these data do support the role of reduced CSF production rather than increased drainage as a possible cause of decrease in CSFP with age.

BMI and CSFP

The effect of body mass index on the cerebrospinal fluid pressure likely involves a biomechanical explanation. BMI is positively and independently associated with CSFP. It is useful to look at the conceptual opposite of glaucoma—idiopathic intracranial hypertension. Studies of IIH suggest that obesity, in particular central obesity, increases intra-abdominal pressure. This results in an increase in venous pressure from compression of the large central veins, and this ultimately increases intracranial venous pressure with a corresponding increase in intracranial pressure. A similar mechanism may be responsible for the effect of BMI in general. However, it is likely that other factors may play a role in this relationship.

Diurnal variation

Diurnal variation of intraocular pressure has been identified as a normal physiological process, but also an independent risk factor for the progression of glaucoma. This is just one factor in the transmamellar pressure gradient, so it is useful and necessary to understand if changes exist in CSFP as a product of the circadian rhythm. To date, it is still unknown to what extent, if any, diurnal variability has an influence on the spinal fluid pressure. Severs’ group identified a significant diurnal fluctuation in CSFP in rats, with pressures nearly 4 mmHg higher during the nighttime compared to the daytime (p < 0.05). Conversely, Lin and Liu found no significant circadian intracranial pressure variation in Sprague–Dawley rats. The latter authors conclude that the transmamellar pressure difference is projected to be higher during the dark period only due to the change in IOP.

A recent study by Samuels and colleagues investigated central control of the individual elements of the transmamellar pressure difference—CSFP and IOP—in the context of the circadian rhythm. The dorsomedial and perifornical hypothalamic neurons receive input from the suprachiasmatic nucleus, the main regulator of the circadian rhythm. These dorsomedial and perifornical nuclei, in turn, contain many efferent sympathetic neurons that likely have an important role in carrying out the characteristic physiological changes. Diurnal changes in CSFP and IOP are discussed in greater detail elsewhere.

Genetics

Evidence is rapidly mounting on the importance of a genetic basis for glaucoma. In the context of the CSFP–glaucoma model, there is early evidence that genetic loci associated with risk for POAG may also be involved in CSF regulation. In a study by Wiggs et al., researchers found that a single nucleotide polymorphism (SNP) located on chromosome 8q22 falls in a region that is known to be actively transcribed by choroid plexus epithelial cells, nonpigmented ciliary epithelial cells, and iris pigment epithelial cells. It is intriguing that cells responsible for the production of the two circulating fluids of the central nervous system, the respective contributors to the transmamellar pressure difference, have been strongly associated with NTG.

Imaging studies

MRI

Mostly stemming from the desire to approximate intracranial pressures in idiopathic intracranial hypertension, neuro-imaging has been utilized in an attempt to detect elevated intracranial pressures. The only ways to accurately assess the spinal fluid pressures to date are through invasive techniques, including lumbar puncture. Since there is some risk associated with lumbar punctures or other intraventricular pressure measurements, non-invasive techniques for estimating cerebrospinal fluid pressures are highly coveted. Magnetic resonance imaging (MRI) may be one possibility. Many studies have advocated the use of MR imaging in the estimation of either increased or decreased intracranial pressure. If retrolaminar pressures are indeed important, then the pressure in the orbital subarachnoid space must be investigated more closely. Therefore, the diameter or changes in the optic nerve subarachnoid space width could be useful in assessing relative pressures for the retrolaminar component of the transmamellar pressure gradient. (Fig. 5) Wang et al. found that patients with NTG patients have a significantly smaller optic nerve subarachnoid space width (ON-SASW) compared to non-glaucomatous patients. These findings are consistent with the hypothesis that lower CSFP may play a role in POAG.

Ultrasound

Ultrasound, while not able to provide for posterior optic nerve sheath measurements, can reliably reveal nerve sheath diameters in the most anterior aspect of the intraorbital nerve. Again, interest in this field stems from finding a surrogate for lumbar puncture in patients with papilledema and presumed idiopathic intracranial hypertension; to date no studies on glaucoma patients have been performed. This may be an important imaging modality for studying CSF and pressure dynamics in the orbital nerve. Based on Wang’s MR imaging study, even at 3 mm posterior to the globe, there were significant differences in nerve sheath diameters between glaucomatous and non-glaucomatous patients. This is within the range that ultrasound could accurately image. While unable to provide a quantitative estimation of pressure (no more than MR imaging could provide), a qualitative estimation has significant utility.

Fluid, compartment and pressure dynamics would likely best be measured with ultrasonography due to its flexibility, easy use—especially in comparison to MRI. As humans spend
most of their day in an upright position, intracranial and orbital nerve pressures fall to subatmospheric pressures.\textsuperscript{75,76} Even differences in the prone and supine position, due to hydrostatic effects and gravity, may result in changes in the orbital CSFP. While it is possible to perform MRI in a variety of positions, it is far more challenging. Therefore, ultrasound offers a potentially more available and practical method to study orbital fluid dynamics in multiple positions.

The CSF model in idiopathic intracranial hypertension and microgravity-induced visual impairment/intracranial pressure

**Idiopathic intracranial hypertension**

If glaucoma is a disease that is due in part to decreased intracranial pressure, it then serves as the conceptual opposite to idiopathic intracranial hypertension (IIH). Idiopathic intracranial hypertension is a potentially blinding condition that results in papilledema from increased intracranial pressure. Interestingly, both IIH and glaucoma produce similar visual field defects. As described above, there are some anatomical explanations for a transient increase in CSFP. Clinical studies also implicate medications such as antibiotics, vitamin A, retinoid analogues, and hormonal contraceptives.\textsuperscript{77–80} In addition, there are multiple case reports of patients with ocular hypertension who were treated with pressure-lowering surgery and subsequently developed papilledema; they were later found to suffer from IIH.\textsuperscript{81–83} This suggests that intraocular pressure may actually be another element in this disease. This raises an intriguing idea of increasing the intraocular pressure for the purpose of treating papilledema.\textsuperscript{84,85} Much like the findings of Berdahl and Ren, an elevated cerebrospinal fluid pressure, as found in ocular hypertension, could potentially be protective for glaucoma.

An interesting observation of CSFP trends from the Mayo Clinic database places IIH and glaucoma at opposite ends of a spectrum. A study performed using the Mayo Clinic medical record system from 1976 to 1990 identified nine patients with IIH.\textsuperscript{86} Although the sample size is small, the highest rate of the disease occurred between ages 15 and 44, and patients with a BMI over 26 had a 7–8-fold increased risk of IIH compared to the general population. Generally, patients with IIH tend to be younger females with an increased body mass index.\textsuperscript{87} Glaucoma patients tend to be older and thinner. These pressures are essentially reference ranges per age and BMI group. It could be imagined that those patients at the higher end of the reference range, perhaps over two standard deviations in the age and BMI charts, would have significantly higher CSF pressures. This, coupled with decreased intraocular pressure, could contribute to IIH. An opposite scenario may exist in glaucoma.

**Microgravity-induced visual impairment/intracranial pressure**

A newly described clinical condition resulting from prolonged space travel may also highlight the importance of the translaminar pressure difference. Mader et al. reported that seven astronauts who were in prolonged space missions returned with visual disturbances and found to have elevated intracranial pressures and papilledema.\textsuperscript{88} We have suggested that papilledema may be due in part to a cephalad fluid shift of the CSF which would provide a persistent higher-than-normal retrolaminar pressure.\textsuperscript{89} This does not explain the elevated CSFP recorded, however. There are likely biomechanical and physiological metrics for baroregulation that are altered by prolonged microgravitational exposure. For example, just as the carotid sinus contains baroreceptors that regulate blood pressure, perhaps a similar system exists which regulates cerebrospinal fluid pressures. After months in a microgravitational environment, the baroreceptors could require a significant period of time to return to normal. It has also been suggested that the valveless venous system within the intracranial space may cause stagnant venous flow in microgravity causing a decrease in CSF outflow.\textsuperscript{90} Again, a safe increase in intraocular pressure may be an option to decrease the translaminar pressure gradient and simulating ocular hypertension.\textsuperscript{84,85} Finding or developing medications or devices that could safely and transiently increase intraocular pressure may be of interest.
Conclusion

A decreased cerebrospinal fluid pressure may act in a similar manner as an increased intraocular pressure by increasing the transliminar pressure difference. Reduced CSFP may offer a partial explanation for POAG that occurs in the presence of normal IOP and may be a contributing factor for most other forms of glaucoma. Our current inability to quantify the retrolaminar pressure gradient limits efforts to explore this hypothesis. However, if it was possible to account for IOP, lamina cribrosa thickness, and CSFP a formulaic calculation could be developed that might help predict glaucoma risk, risk of glaucoma progression, as well as contribute to our understanding of other CSFP-related ocular diseases and provide novel therapeutic opportunities.

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References


