

Higher optic nerve sheath diameters are associated with lower ocular blood flow velocities in glaucoma patients

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Abstract

Purpose To investigate the relationship between optic nerve sheath diameter (ONSD) and retrobulbar blood flow velocities, as measured by color Doppler imaging (CDI) in glaucoma patients.

Methods We performed a prospective, randomized, observer-masked study involving a total of 197 subjects. Once enrolled, they were divided by three groups: healthy controls (n=51), normal-tension glaucoma patients (NTG, n=58), and primary, open-angle glaucoma patients (POAG, n=88). All subjects underwent a general ophthalmological examination, an ultrasound-based assessment of the ONSD, and a hemodynamic study of the retrobulbar vascularization using CDI. Non-parametric tests, chi-square contingency tables, and the

Deming correlations were used to explore differences and correlations between variables in the diagnostic groups.

Results ONSD was not different between experimental groups (p=0.28). ONSD correlated positively with the pulsatility index of the ophthalmic artery in healthy individuals (p=0.007), but not in glaucoma patients (NTG: p=0.41; POAG: p=0.22). In NTG patients, higher ONSD values were associated with lower end-diastolic and mean flow velocities in the short ciliary arteries (p=0.005 in both correlations). No such correlation was found in healthy nor POAG groups (p range between 0.15 to 0.96). ONSD was not associated with any CDI-related variable of the central retinal artery in any cohort. Venous outflow velocities were not associated with ONSD in any of the three groups.

Conclusions ONSD is negatively correlated with retrobulbar blood flow velocities in glaucoma patients, but not in healthy controls.

Koen Willekens and Luís Abegão Pinto contributed equally to the study, and should both be considered as first author.

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Keywords Optic nerve sheath diameter · Ocular blood flow · Normal tension glaucoma · Color Doppler imaging

Introduction

Globally, glaucoma is one of the leading causes of blindness [1]. A significant number of patients develop glaucoma or show signs of disease progression despite good intraocular pressure (IOP) control, thus raising the question that other mechanisms may contribute to the pathogenesis of this disease.

One of the possible mechanisms involved is an abnormal translaminal pressure gradient [2]. Recent studies have suggested that glaucoma patients may have an imbalance between the pressures on both sides of the lamina cribrosa [3, 4]. However, for both technical and ethical reasons, research on the forces acting behind the human globe has been limited to imaging the orbit, namely through MRI and ultrasound [5–7].

Neurologic and trauma-related research has suggested that optic nerve sheath diameter (ONSD) is strongly correlated with intracranial pressure (ICP). As the cerebrospinal fluid (CSF) around the optic nerve is in continuity with the rest of the central nervous system, a higher ICP could lead to an expansion and overall diameter increase of the meningeal sheath around the optic nerve. Accordingly, measuring ONSD has been broadly used as a surrogate for ICP [8]. Although not extensively studied in ophthalmology, ONSD has been linked to visual field damage and IOP levels [5, 9].

ICP is one of the major variables involved in the overall autoregulation process of the cerebral arteries [10]. Should the retrobulbar arteries share the same autoregulatory mechanisms as the intracranial vessels, then both regions would show the same behavior to changes in CSF pressure. As glaucoma patients appear to have an impaired autoregulation [11, 12], it is thus possible that fluctuations in ICP could affect ocular blood flow. Accordingly, the search for a possible correlation between ocular blood flow and ICP may provide further insight into the disease pathogenesis.

Therefore, our aim was to study the relationship between ONSD measurements as a proxy for ICP and the retrobulbar hemodynamics in glaucoma patients assessed by color Doppler Imaging (CDI).

Methods

Subject groups

Three groups were recruited for the study: healthy controls (n=51), normal-tension glaucoma (NTG, n=58) and primary open-angle glaucoma (POAG, n=88) patients. Healthy controls were recruited from non-blood related individuals who accompanied glaucoma patients to their consults. Glaucoma was defined as having characteristic glaucomatous visual field and optic disc changes: thinning of the inferior and/or superior rim, cup-to-disc ratio asymmetry of > 0.2 not due to optic disc size asymmetry), and based on matching glaucomatous visual field defects (specifically, a cluster of three or more test points with > 5 dB, or two points with > 10 dB sensitivity reduction compared to age-eccentricity corrected normal value) [13]. POAG and NTG were grouped considering a maximal, untreated IOP $>$ or ≤ 21 mmHg, respectively. An ophthalmological examination (including Goldmann applanation tonometry, GAT) and visual field testing were performed on the same day of the study visit.

Patients with ocular pathologies other than glaucoma (including vascular-related diseases such as central retinal artery (CRA) or central retinal vein (CRV) occlusion) were excluded. Exclusion criteria included known neurological or orbital diseases (such as Graves' ophthalmopathy) and vascular-related, systemic conditions other than arterial hypertension

(such as diabetes and heart failure). For ethical reasons, patients were not discontinued from their regular medical therapies (IOP-related or not), but individuals under direct vasodilator drugs (for instance, nitric oxide donors or peripheral-acting calcium channel blockers) or patients under systemic carbonic anhydrase inhibitors were not included.

All healthy controls were screened by a senior staff member (IS) and excluded from the study if: (1) there was a family history of glaucoma, (2) an increased or asymmetrical cup/disc ratio, or other optic disc structural abnormalities (notching, disc hemorrhage) were present, or (3) if an IOP higher than 21 mmHg was measured.

Measuring devices

Visual acuity was assessed by using the ETDRS chart, placed in the same room under the same lighting conditions at the same distance for all of the study subjects. IOP was measured using GAT and blood pressure by applying an automatic electronic sphygmomanometer (Omron, Schaumburg, IL, USA) to the right upper arm in sitting position. CDI measurement was performed using an ultrasound device with a B-scan, 7.5 MHz Doppler probe (Antares®, Siemens, Munich, Germany) by the same researcher (LAP), who was masked to the patient's diagnosis, and included the following variables: peak systolic velocity (PSV), end-diastolic velocity (EDV), mean flow velocity (MFV), maximum venous velocity (Vmax), minimum venous velocity (Vmin), resistivity index [$RI=(PSV-EDV)/PSV$] and pulsatility index [$PI=(PSV-EDV)/MFV$] of the CRA, CRV, the short nasal and temporal, posterior ciliary arteries (NPCA and TPCA), and the ophthalmic artery (OA), according to the published methodology of CDI image capture [14]. The ONSD was measured using the following technique [5]: in brief, the patient is in the supine position, with the head in a neutral position and both eyes closed and in primary gaze position. After coupling gel is applied and the insonation depth is set to 5–8 cm, the transducer is softly placed over the upper eyelid in an axial plane. The ONSD is calculated perpendicular to the vertical axis of the scanning plane, 3 mm behind the globe.

Experimental design

The study was approved by the ethical committee (institutional review board) at the University Hospitals Leuven, and was conducted in accordance with Good Clinical Practice within the tenets of the Helsinki agreement. An informed consent statement was signed by every subject prior to any investigation. During the study visit, the following examinations were performed sequentially: visual acuity, IOP measurement, blood pressure and heart rate measurement, and ultrasound measurement of the ONSD and CDI for retrobulbar flow velocity assessment. Only one eye per patient was included

in the study; the one with greater glaucomatous damage or a random eye for the healthy subjects.

This study was registered on clinicaltrials.gov with the following number: NCT01802463.

Statistical analysis

The Kruskal-Wallis test with Dunn's correction was used to compare continuous variables between the three diagnostic groups, while the Mann-Whitney test was used for pairwise comparisons. The Deming correlation was used to test for a relationship between continuous variables. Pearson's chi-squared tests (for 3×2 contingency tables) were used for categorical items. Statistical significance was considered when $p < 0.05$. Values are depicted as mean ± standard deviation unless otherwise indicated. Analyses were performed using Graphpad Prism_ver. 5.0 (Graphpad Software Inc, La Jolla, CA, USA).

Results

Patients characteristics

Table 1 summarizes the patients' characteristics and their comparative p values. Age, gender, visual acuity, and mean ocular perfusion pressures [MOPP – calculated as: (2/3 diastolic + 1/3 systolic blood pressures)*2/3-Goldmann tonometry] were not statistically different between the three groups (p ranged from 0.18 to 0.67). IOP was statistically different between the groups ($p < 0.01$), with Dunn's correction confirming a significantly lower IOP in the NTG group than in the POAG group ($p < 0.05$). Both glaucoma groups presented with similar visual field mean defect ($p = 0.11$).

Topical IOP-lowering medication in the glaucoma group is summarized in Table 2.

Optic nerve sheath diameter

No differences were found between the ONSD of the three groups (Healthy: 6.14 ± 0.77 mm; NTG: 6.00 ± 0.78 mm; POAG: 5.89 ± 0.78 mm; $p = 0.28$). A test for correlation between ONSD and IOP revealed a positive correlation in POAG patients (slope 23.5 ± 10.9 , CI 1.78 to 45.2, $p = 0.03$), but only a borderline association in the NTG group (slope 10.5 ± 5.25 , CI -0.006 to 21.1 $p = 0.05$). In healthy subjects, no correlation was detected ($p = 0.45$). There was no correlation between ONSD and the severity of visual field deficits in the glaucoma groups (NTG: $p = 0.27$; POAG: $p = 0.47$).

Table 1 Patients characteristics by experimental group

	Healthy	NTG	POAG	p-value
N	51	58	88	
Age (years)	73.8 ± 13.3	70.9 ± 11.3	70.4 ± 11.8	0.18
Gender (female) ^a	24	32	49	0.58
IOP (mmHg)	13.6 ± 2.6	11.9 ± 3.0	14.5 ± 4.3	0.001
Visual acuity (logMar)	0.18 ± 0.3	0.20 ± 0.3	0.16 ± 0.2	0.67
MD (dB)	-	-5.71 ± 6.8	-8.7 ± 8.7	0.11
MOPP (mmHg)	56.3 ± 7.7	59.4 ± 8.5	57.9 ± 9.2	0.43

Mean values (and SD) are depicted. Comparison between continuous variables was made through Kruskal-Wallis and Mann-Whitney tests. ^a denotes the use of a χ^2 test. IOP = intraocular pressure; MD = mean defect (visual field); MOPP = median ocular perfusion pressure [(2/3 diastolic+1/3 systolic blood pressures]*2/3-Goldmann tonometry]

Color Doppler imaging

Table 3 depicts the hemodynamic variables obtained by CDI for every experimental group. Individuals from the control group presented with higher PSV values in the OA, and higher Vmax and RI in the CRV, when compared to the other two groups ($p = 0.04$, $p < 0.01$ and $p = 0.02$, respectively). In pairwise comparison between glaucoma groups and healthy individuals, the CRV Vmax was found to be significantly higher in healthy individuals when compared to both groups (NTG: $p = 0.02$; POAG: $p = 0.004$). Furthermore, POAG patients had both lower CRV RI and PI values (vs. healthy, $p = 0.02$ in both comparisons), whereas no significant differences were found in these two variables between NTG and healthy individuals ($p = 0.23$ and $p = 0.27$, respectively). The OA PSV values in the healthy group were significantly higher than those in NTG patients ($p = 0.02$), but similar to the POAG group ($p = 0.10$). No other flow velocity differences were found between the three groups or in the glaucoma groups' pairwise comparison (p ranging from 0.10 to 0.87).

Correlation of ONSD and CDI measures

Healthy individuals presented with a positive association between ONSD and the OA's PI ($p = 0.007$; Fig. 1.a), which was not detected in the two glaucoma groups (NTG: $p = 0.41$; POAG: 0.22). In NTG patients, however, we found that higher ONSD values were associated with a decrease in blood flow velocities in the short ciliary arteries (TPCA EDV: $p = 0.005$; TPCA MFV: $p = 0.005$; Fig. 1b and c, respectively). These correlations between ONSD and CDI-related variables in the short ciliary arteries were not seen in the POAG nor in the healthy cohorts (p range 0.15-0.96). No other correlation between ONSD and retrobulbar hemodynamic parameters reached statistical significance (p range 0.06-0.096). Table 4

Table 2 Topical medications in the glaucoma groups

		Healthy	NTG (n=58)	POAG (n=88)
Number of patients and percentages (between brackets) are depicted. P values from pairwise comparison ranged between 0.18 and 0.73	Topical			
	Beta blockers	-	26(44)	42(48)
	Prostaglandin analogs	-	23(40)	45(51)
	Carbonic anhydrase inhibitors	-	19(33)	23(26)
	α -adrenergic agents	-	8(14)	9(10)

details the correlations between ONSD and the retrobulbar hemodynamic CDI variables in the three groups.

Discussion

ONSD appears to have a different association with retrobulbar hemodynamics in healthy individuals than in glaucoma patients. In healthy individuals, higher ONSD values were associated with a higher PI level in the OA, which was not observed in the glaucoma groups. Assuming that ONSD accurately reflects ICP in healthy individuals, these results would suggest that the ophthalmic artery would show a similar behavior as the cerebral arteries to fluctuations in ICP. Indeed, large intracranial arteries (such as the middle cerebral artery) show a remarkable correlation between PI and ICP

[15]. Accordingly, this Doppler variable has been extensively used as a noninvasive surrogate for pathological increases in ICP [16]. The rationale behind this increase has been suggested to be an ICP-induced compression of the smaller arterioles downstream of the measurement, which would lead to an increase in downstream resistance and a significant decrease in mean flow. As the latter is the denominator for PI calculations, PI rises significantly [15]. In contrast, no correlations were seen between ONSD and OA-related hemodynamic variables in glaucoma patients. Of note, there have been reports that the cerebral vasoreactivity is also impaired in glaucoma patients [17]. While the nature of these findings is not completely understood and a variety of mechanisms could be involved (ranging from autonomic dysfunction to an endothelial-related vascular relaxation impairment [18]), it is possible that this abnormal behavior by the cerebral arteries

Table 3 Comparison of flow velocities and resistance indexes between diagnostic groups

		Healthy	NTG	POAG	Overall	NTG vs. POAG	
Data are shown as mean \pm SD. Velocities depicted as cm/s. Overall comparison between the subgroups was made using the Kruskal-Wallis test. Mann-Whitney tests were used in pairwise comparison. NTG indicates normal tension glaucoma; POAG, primary, open-angle glaucoma; CRA, central retinal artery; CRV, central retinal vein; NPCA and TPCA, short posterior ciliary arteries (nasal and temporal, respectively); OA, ophthalmic artery; PSV, peak systolic velocity; EDV, end-diastolic velocity; RI, resistive index; MFV, mean flow velocity; PI, pulsatility index; Vmax, maximum velocity; Vmin, minimum velocity	CRA	PSV	11.16 \pm 4.6	10.31 \pm 3.1	9.94 \pm 2.9	0.52	0.61
		EDV	3.00 \pm 1.3	2.92 \pm 1.0	2.72 \pm 0.8	0.66	0.37
		MFV	5.47 \pm 1.8	5.58 \pm 1.8	5.37 \pm 1.5	0.95	0.75
		RI	0.73 \pm 0.1	0.71 \pm 0.1	0.72 \pm 0.1	0.58	0.63
		PI	1.36 \pm 0.3	1.33 \pm 0.3	1.33 \pm 0.3	0.78	0.87
	CRV	Vmax	5.89 \pm 1.6	5.16 \pm 1.6	5.05 \pm 1.3	<0.01	0.84
		Vmin	3.33 \pm 0.8	3.04 \pm 0.7	3.10 \pm 0.6	0.12	0.45
		MFV	3.93 \pm 1.4	3.43 \pm 1.3	3.45 \pm 1.3	0.07	0.77
		RI	0.42 \pm 0.1	0.37 \pm 0.1	0.35 \pm 0.1	0.02	0.48
		PI	0.66 \pm 0.2	0.62 \pm 0.2	0.59 \pm 0.2	0.04	0.15
	NPCA	PSV	10.29 \pm 3.3	9.22 \pm 2.7	9.68 \pm 2.9	0.25	0.40
		EDV	3.28 \pm 1.3	3.16 \pm 1.0	3.25 \pm 1.1	0.84	0.57
		MFV	5.91 \pm 1.7	5.35 \pm 1.6	5.87 \pm 1.8	0.27	0.17
		RI	0.67 \pm 0.1	0.65 \pm 0.1	0.66 \pm 0.1	0.33	0.69
		PI	1.18 \pm 0.3	1.10 \pm 0.2	1.12 \pm 0.3	0.41	0.87
	TPCA	PSV	10.1 \pm 3.5	9.07 \pm 2.3	9.75 \pm 2.7	0.44	0.23
		EDV	3.31 \pm 1.4	3.00 \pm 0.8	3.30 \pm 1.0	0.29	0.11
		MFV	5.74 \pm 2.1	5.50 \pm 1.3	5.95 \pm 1.8	0.49	0.38
		RI	0.66 \pm 0.1	0.66 \pm 0.1	0.66 \pm 0.1	0.83	0.51
		PI	1.14 \pm 0.3	1.14 \pm 0.3	1.11 \pm 0.2	0.68	0.33
OA	PSV	36.63 \pm 14.5	30.25 \pm 10.5	32.42 \pm 12.7	0.04	0.35	
	EDV	6.55 \pm 4.1	5.24 \pm 2.3	6.34 \pm 3.3	0.27	0.10	
	MFV	15.8 \pm 8.8	13.2 \pm 5.0	15.3 \pm 7.4	0.49	0.23	
	RI	0.82 \pm 0.1	0.82 \pm 0.1	0.80 \pm 0.1	0.19	0.10	
	PI	2.01 \pm 0.6	1.95 \pm 0.5	1.88 \pm 0.6	0.25	0.23	

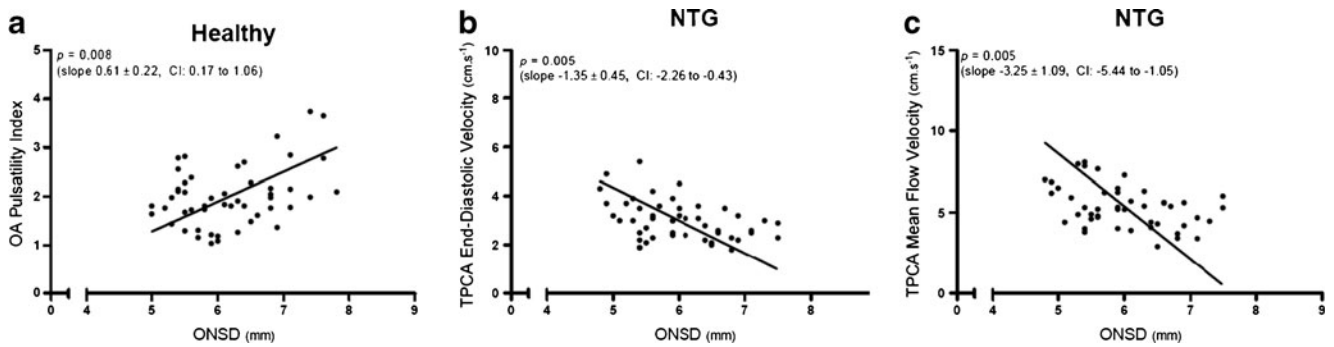


Fig. 1 Statistically significant associations between color Doppler imaging variables of the retrobulbar vessels and the optic nerve sheath diameter (ONSD). A positive correlation was detected between ONSD and the

ophthalmic artery pulsatility index (**1.a**), while in NTG, a higher ONSD was associated with lower blood velocities in the short ciliary arteries (TPCA end-diastolic velocity – **1.b**; TPCA mean flow velocity – **1.c**)

reflects a wider vascular dysfunction and an inability to adapt to external, non-vascular factors such as ICP.

Interestingly, no correlations were observed between ONSD and the CRA or CRV hemodynamic variables in any of the three groups. It would have been intuitive that, as these vessels pass directly through the CSF fluid, they would be more directly affected by ICP than other vessels. However, CSF-related pressures are not the only forces at play in the

blood flow of these central retinal vessels. The CRA seems to be strongly autoregulated, with local factors involved in the regulation of blood flow (from O₂ and CO₂ levels to neurotransmitters involved in neurovascular coupling [19–21]). In addition, the rigidity of the retinal arteries themselves may be of particular importance in influencing blood flow, as demonstrated in untreated NTG patients [22]. This increase in regulation downstream to the site of CDI measurement could

Table 4 Correlation between ONSD and hemodynamic variables

			Optic nerve sheath diameter		
			Healthy	NTG	POAG
Color Doppler imaging	CRA	PSV	0.66	0.32	0.19
		EDV	0.71	0.85	0.06
		MFV	0.74	0.46	0.11
		RI	0.93	0.18	0.26
		PI	0.79	0.14	0.31
	CRV	Vmax	0.56	0.55	0.21
		Vmin	0.18	0.41	0.13
		MFV	0.87	0.88	0.11
		RI	0.55	0.95	0.25
	NPCA	PI	0.75	0.31	0.50
		PSV	0.25	0.16	0.41
		EDV	0.28	0.14	0.22
		MFV	0.13	0.11	0.30
		RI	0.96	0.96	0.73
	TPCA	PI	0.46	0.93	0.54
		PSV	0.22	0.09	0.20
		EDV	0.18	0.005 (−1.35±0.45)	0.81
		MFV	0.23	0.005 (−3.25±1.09)	0.41
RI		0.90	0.84	0.15	
OA	PI	0.96	1.00	0.25	
	PSV	0.69	0.83	0.49	
	EDV	0.18	0.24	0.33	
	MFV	0.48	0.52	0.23	
	RI	0.06	0.52	0.29	
		PI	0.007 (0.61±0.22)	0.41	0.22

Data shown as p-values using the Deming regression (best-fit slope depicted if p value <0.05). NTG indicates normal tension glaucoma; POAG, primary, open-angle glaucoma; CRA, central retinal artery; CRV, central retinal vein; NPCA and TPCA, short posterior ciliary arteries (nasal and temporal, respectively); OA, ophthalmic artery; PSV, peak systolic velocity; EDV, end-diastolic velocity; RI, resistive index; MFV, mean flow velocity; PI, pulsatility index; Vmax, maximum velocity; Vmin, minimum velocity

potentially render some factors, such as CSF-compression around the retrobulbar portion of the CRA, less important in the overall flow regulation. On the other hand, the CRV is a very fragile vessel and could potentially be subject to outside compression. However, even in healthy individuals, the pores of the lamina cribrosa have been suggested to act as a “throttle” around the CRV as it leaves the globe [23]. This physiological obstruction around the lamina cribrosa has been suggested to be hemodynamically significant. Indeed, the high shear-stress over the CRV wall in the region immediately downstream to the lamina cribrosa has been reported to induce an arterial-like morphology of its endothelial cells [24]. As with the CRA, the location of the measurement may explain our findings. By measuring the vessels downstream from the first significant hemodynamic obstruction (the lamina cribrosa), the relevance of further obstacles to flow is reduced (similar to the concept that a first dyke supersedes the importance of a second dyke). This could potentially explain our findings, where no association was detected between CRV Doppler-related variables and the ONSD.

Unlike the CRA or the CRV, the short ciliary arteries are not as capable of autoregulation, nor have they such physiological obstructions to flow. Accordingly, flow in these much smaller vessels could more accurately reflect changes in the extravascular compartment. Indeed, our results showed a negative correlation between blood velocities in the short ciliary arteries and the ONSD, albeit only in NTG patients. There could be several, non-exclusive explanations for this: either NTG patients have a different retrobulbar anatomy/physiology that may particularly expose these ciliary arteries to outside compression, or these vessels have a lower regulation threshold. There have been reports from clinical and animal-based models to support both theories, as these patients may have a less elastic optic nerve sheath, a different CSF distribution, an abnormal response to external stimuli, and/or even a different retrobulbar remodeling [3]. The combination of these factors could make these dysregulation-prone vessels more susceptible to ONSD changes.

In our study, we did not observe differences in ONSD between both groups. This finding is in agreement with our previously reported data [5], as well as with a recent meta-analysis that reports a significant overlap between the CSF pressure measured by lumbar puncture in healthy subjects and in NTG patients [25]. However, there have been other ONSD-related studies using other imaging methods that reported different results (CT scan, by Jaggi GP et al. [6] and MRI scan by Wang N et al. [9]). While the former publication suggests that NTG patients have a higher ONSD than control subjects, the latter study suggests that these patients have a narrower ONSD. These discrepancies between reported results could reflect differences in patient selection criteria, age distribution, head position, sample size and—importantly—different imaging techniques. Consistent methodologies

between centers should be used if comparisons between ONSD studies are to be made. Another aspect of the use of ultrasound B-scan measurements is that it allows the measurement to be coupled with a Doppler probe, thus allowing a detailed, reproducible, validated, but operator-dependent study of the retrobulbar blood flow [14, 26] that is not yet possible with other imaging technologies.

One important limitation of our work is the working assumption that ONSD may reflect orbital ICP. Despite the numerous publications asserting the strong association between ICP fluctuations and ultrasound-based ONSD measurements, including a recent meta-analysis showing high levels of specificity and sensitivity with this technique to detect raised ICP [8], these studies have been conducted in patients where little is known about their ophthalmological conditions. For instance, if the elasticity or compliance of the optic nerve sheath is indeed altered in glaucoma patients [6], then the same ONSD might represent a large range of pressures. Nevertheless, more studies involving anatomical and histological assessment of the orbital tissues in glaucoma patients are still needed to fully understand the nature of the mechanisms involved in retrobulbar pressures. Furthermore, the study protocol involved performing measurements in two different body positions (IOP and blood pressure recorded with patient sitting and ONSD/CDI measurements done in the supine position). As IOP is suggested to increase from sitting to supine [27], the precise IOP value is unknown at the time of the ONSD/CDI measurements, which is a common limitation to the majority of the CDI-based ocular blood flow studies [14]. Accordingly, assumptions about the translaminal pressure gradient in this setting should be made cautiously. Moreover, another potential source of IOP fluctuation is the transducer-induced ocular compression during the ultrasound measurements. While the magnitude of this IOP increase is uncertain, there have been suggestions that IOP changes would have little effect on the CDI-related measurements [28]. Nevertheless, and perhaps more importantly, all measurements were done by the same observer, which would have decreased the degree of variability since the same technique, execution, and pressure would have been similar in all patients, therefore minimizing this bias as much as possible. More studies with larger sample sizes are still needed to further characterize this intriguing correlation between hemodynamic parameters and ONSD.

In conclusion, our results suggest that the pressures determining ONSD can have a significant impact on ocular blood flow. This may be particularly important in NTG patients, where it could affect the optic nerve head arterial supply.

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Conflict of interest None of the authors have any conflict of interest to declare.

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