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Optic nerve sheath diameter asymmetry in healthy subjects and patients with intracranial hypertension

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Abstract

Background Ultrasonography of the optic nerve sheath diameter (ONSD) is used for the non-invasive assessment of increased

intracranial pressure (ICP). ONSD values are usually obtained by averaging the measurements of the two eyes, but asymmetric

ONSD dilation is possible, leading to potentially inaccurate ICP estimation when using binocular averaging. In addition, few data

are available about the asymmetry of the ONSD and the use of the maximum ONSD value between eyes for raised ICP detection.

The aim of the study was to evaluate the interocular ONSD asymmetry in healthy subjects and patients with intracranial

hypertension (IH) by ultrasonography and to investigate whether the maximum ONSD could be as useful as the binocular

assessment.

Methods Forty healthy subjects and 40 patients with IH (20 with idiopathic intracranial hypertension and 20 with intracerebral

hemorrhage) who underwent transorbital sonography were retrospectively enrolled. The prevalence and degree of ONSD

asymmetry were compared among groups; ONSD median binocular and maximum values were compared.

Results Forty-two out of 80 subjects (52.5%) showed significant ONSD asymmetry, without significant differences in prevalence

among groups (p = 0.28). The median asymmetry was higher in patients than in healthy subjects (0.45 mm vs 0.23 mm; p =

0.007), without significant differences between the two pathologies (p = 0.58). Both binocular and maximum ONSD measurements were significantly higher in patients with IH than in controls (p < 0.001).

Conclusions Interocular ONSD asymmetry occurs both in healthy subjects and, more consistently, in patients with IH. Both

binocular and maximum ONSD may be useful markers for increased ICP detection.

Keywords Optic nerve sheath diameter . Intracranial hypertension . Idiopathic intracranial hypertension . Intracerebral

hemorrhage . Transorbital sonography . Asymmetry

Introduction

Elevated intracranial pressure (ICP) may be indirectly evaluated by measuring the optic nerve sheath diameter (ONSD)

[1]. The rationale resides in the anatomical continuity between

the subarachnoid space of the optic nerve sheaths and that of

the brain, allowing the circulation of cerebrospinal fluid (CSF)

from the perichiasmatic cistern to the ocular regions [2]. With

increasing ICP, the pushing pressure drives a larger amount of

CSF toward the orbital spaces. As a result, the ONSDs enlarge

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and optic disc elevation develops over time. However, the

CSF transmission may be limited at the level of the optic

canals where the composition of the subarachnoid space

changes, becoming subdivided in small compartments and

narrowing its lumen to a capillary size [3]. This specific architecture, made of thick pillars and trabeculae, is assumed to be

responsible for the quantity and speed with which the CSF can

be transferred to the optic sheaths, and its large interindividual variability may explain the documented occurrence

of asymmetric ONSD enlargement and unilateral papilledema

[4, 5]. Furthermore, no data on individual interocular differences have been reported.

The ONSD may be explored with various techniques,

transorbital sonography being one of the most promising

due to its non-invasiveness, feasibility, and high diagnostic

accuracy [6]. The application fields of this method in the clinical practice have been recently described [7]. Despite the

anatomical remarks cited above, most ultrasonographic studies consider ONSD measurements as an average of binocular

values, rather than the maximum value between the two eyes,

leading to possible errors in estimating ICP, given the potential physiological asymmetry.

The aim of this study was to evaluate the variability, in term of symmetry, of the ONSD, by using ultrasonography in healthy subjects and patients with intracranial hypertension (IH), and to establish whether the maximum value of the ONSD could be as useful as the binocular assessment.

Materials and methods

Subjects

We retrospectively reviewed ONSD data from 80 subjects, collected from a dataset available from the authors [8, 9]. All participants were ≥ 18 years old; exclusion criteria were ocular trauma, glaucoma, and significant orbital mass. Forty normal subjects who underwent general medical, ophthalmological, and neurological evaluation to rule out signs and symptoms of IH and ocular pathologies were included in the healthy group.

Forty patients, matched for gender but not for age, composed the IH group, and included 20 consecutive subjects with idiopathic intracranial hypertension (IIH) and 20 consecutive patients with primary acute supratentorial intracerebral hemorrhage (ICH).

Patients with IIH were recruited at the BFranz Tappeiner^ Hospital of Merano Hospital between March 2014 and November 2015; raised ICP was established (after ONSD evaluation) by lumbar puncture with a CSF opening pressure ≥ 25 cm H20 according to the Friedmann diagnostic criteria [10]. ICH patients were admitted to the BMaggiore della Carità^ Hospital of Novara from January to December 2017; elevated ICP

was determined by clinical conditions and cerebral CT

scan. Radiologically, we considered only medium- to

large-size cerebral hemorrhages (≥ 30 ml) with at least

two of the following: midline shift ≥ 3 mm, collapsed

3rd ventricle, hydrocephalus, compression of cisterns,

and effacement of sulci with evidence of substantial edema [11, 12]. Hematoma size was calculated using the

ABC/2 score (if rounded or ellipsoid shape) or ABC/3

score (irregular or multinodular) [13, 14]. Contextually,

at least one clinical sign of elevated ICP had to be present, including bradycardia, altered consciousness, vomit,

headache, pupillary abnormalities, or uncontrolled

hypertension.

Transorbital sonography

Transorbital ONSD sonography was performed following a

previously described protocol using a Toshiba Medical

System Aplio 300 (Nasu, Japan; linear probe 7.5–11 MHz

with lateral resolution < 0.4 mm) for healthy subjects and

ICH patients, and a Toshiba Aplio ultrasound system XG

(Toshiba Medical Systems, Nasu, Japan; linear probe 7.2–

14 MHz, lateral resolution < 0.4 mm) for IIH patients [15].

Ultrasonographic evaluations were performed by two skilled

neurosonologists (A.N. and P.L.); all measurements were taken off-line by a single expert operator (P.L.) to reduce interobserver variability. ONSD was calculated as the distance

between the external hyperechogenic borders surrounding

the optic nerve, corresponding to the periorbital subarachnoid

space.

ONSD was evaluated on the axial plane in triplicate for

each eye. Binocular ONSD was obtained by averaging these

values between the eyes, while maximum ONSD was obtained by first averaging the three measurements for each eye and

then taking the maximum of the two values.

Statistical analysis

Statistical analysis was performed using the R software,

version 3.6.0 [16]. For each subject, the ONSD asymmetry was evaluated as the absolute value of the difference

between the mean ONSD of the two eyes; statistical significance was assessed using Welch's t test, with multiple

testing correction performed with the BenjaminiHochberg method at a false discovery rate of 5%. For

group comparison, categorical variables were expressed

as numbers and percentages and compared among groups

with Fisher's exact test. Continuous variables, expressed

as median and quartiles (Q1, Q3), were compared among

more than two groups with the Kruskal-Wallis test, and

between two groups with the Mann-Whitney U test.

Results

Demographic data, mean ONSD values, and asymmetry are

summarized in Table 1. The median age of subjects was 72.5

(range 44.75–79) and was significantly lower in IIH patients

(37 (29–47.25), $p < 0.001$), as expected for the pathology;

gender did not differ between the three subgroups ($p = 0.114$).

Forty-two out of 80 subjects (52.5%) showed a significant

ONSD asymmetry between eyes at a false discovery rate of

5%, and the difference in prevalence among groups was not

significant (16 for healthy subjects, 14 for ICH patients, and

12 for IIH; p = 0.28). The median asymmetry was higher in

patients with IH than in normal subjects (0.45 mm vs

0.23 mm, p = 0.007, Fig. 1a); when stratifying by pathology,

the significance was confirmed for ICH patients (p = 0.012),

while the result for IIH patients was close to significance (p =

0.07) when compared with the healthy group (Fig. 1b). There

was no significant difference between ICH and IIH patients

(p = 0.58). For ICH patients, there was no significant correspondence between the hemorrhage site and the side of the

larger ONSD (p = 0.41).

Both the binocular and maximum ONSD values were significantly higher in the IH group (independently of the pathology) compared with the healthy group (both p < 0.001,

Fig. 2a, b), with no significant differences among the two

pathologies (p = 0.12 and p = 0.15, respectively).

Discussion

This study documented for the first time in a clinical context

the occurrence and degree of interocular ONSD asymmetry by

using transorbital sonography in healthy and pathological subjects with IH. Ultrasonography of the ONSD has been proposed as a non-invasive technique to evaluate ICP and ONSD

behavior in various conditions. The sheath diameter may increase or shrink in response to ICP changes, but above a

dilation threshold the enlargement seems to be irreversible

[17, 18]. However, the exact reaction of the ONSD and the

optic disc upon ICP variation remains elusive and different

mechanisms may be involved in the orbital response, including optic atrophy, CSF and ocular pressure, and changes in the

lamina cribrosa or optic nerve structures [19]. Regarding the

anatomical aspects, some authors emphasized the role of the

optic canals in the transmission of the CSF toward the optic

sheaths [4]. Specifically, the thick arachnoid trabeculae and

pillars that compose the complex meshwork of the optic canals may limit or even prevent the flow of CSF in the course of

IH, determining a disproportionate expansion of ONSDs and

unilateral papilledema [20–22]. In addition, an elevated interindividual variability of optic canal conformation among

humans and animals has been described [5, 21]. However, to

our knowledge, no data are available about the interocular

asymmetry of the ONSD between eyes both in normal conditions and following elevated ICP, particularly in a clinical

setting where only isolated descriptions of asymmetry are

mentioned [22]. Nevertheless, most ultrasonographic and radiological studies related to this topic evaluated the binocular

ONSD value, without considering this anatomical variability,

which may limit the enlargement of the optic sheaths, thus

potentially leading to an inaccurate ICP estimation.

Our results documented an asymmetry of the ONSD of

the two sides, both in healthy individuals and in patients

with IH. The asymmetry increased following raised ICP,

confirming the anatomical finding of a different architecture of the optic canals: If the CSF may not be adequately

conveyed toward one of them because of a different composition in the trabecular network thickness, the two

ONSDs may enlarge asymmetrically. No differences

where observed between IIH and ICH subjects, suggesting that the asymmetry was independent on the cause and

mechanism of intracranial hypertension. In fact, while in

IIH increased ICP may be related to a pathological process involving the whole brain, in ICH it is a consequence

Table 1 Demographic

characteristics, binocular/

maximum ONSD values, and

asymmetry between eyes in

healthy and pathological subjects

Age Gender (F)

Healthy 75 (61.25–78.75) 47.5%

Patients 63 (38–79.25) 62.5%

ICH 79.5 (76.25–86.25) 50%

IIH 37 (29–47.25) 66.7%

ONSD binocular (mm) ONSD max (mm) Asymmetry (mm)

Healthy 4.72 (4.57–4.83) 4.73 (4.65–4.87) 0.23 (0.07–0.42)

Patients 6.54 (6.22–7.03) 6.65 (6.31–7.23) 0.45 (0.18–0.68)

ICH 6.66 (6.36–6.97) 6.77 (6.50–7.24) 0.53 (0.20–0.77)

IIH 6.37 (6.09–7.05) 6.48 (6.15–7.05) 0.40 (0.10–0.67)

All values are expressed as median (quartiles). F, female; ONSD, optic nerve sheath diameter; ICH, intracerebral

hemorrhage; IIH, idiopathic intracranial hypertension

of a focal event. Interestingly, there was no association

between the side of cerebral hemorrhage and the maximal

ONSD dilation, further suggesting that anatomical aspects

may influence the ONSD behavior.

The binocular ONSD assessment is a well-known technique for assessing increased ICP; conversely, only few studies evaluated the role of maximum ONSD for this purpose

[23–25]. In our series, both binocular and maximum ONSD

were significantly higher in patients than in healthy subjects;

thus, both measures could be useful for the detection of elevated ICP. However, considering the asymmetry and the

possibility of a missing or reduced enlargement of the

ONSD, ideally maximum ONSD could be a more precise

and quicker measurement, especially when asymmetry is

present.

There are some limitations to this study, mainly related to

its retrospective design and to the small sample size. In ICH

patients, diagnosis of IH was based on clinical and radiological findings, without directly measuring ICP. Finally, ONSD

values were recorded by using two different sonographic machines. Further studies in a larger population are needed to

confirm these results.

a b

Fig. 2 Binocular (a) and maximum (b) ONSD values in patients with intracranial hypertension and healthy subjects. ONSD, optic nerve sheath diameter;

ICH, intracerebral hemorrhage; IIH, idiopathic intracranial hypertension

a b

Fig. 1 Degree of asymmetry (expressed in millimeters) in healthy subjects and patients with intracranial hypertension (a) and subgroup analysis dividing

the cases by pathology (b). ICH, intracerebral hemorrhage; IIH, idiopathic intracranial hypertension

Conclusions

An interocular ONSD asymmetry exists in normal subjects

and patients with elevated ICP, with a larger extent in IH. If

present, the asymmetry should be considered for correct ICP

estimation. Both binocular ONSD measurements and maximum ONSD may be useful for the evaluation of raised ICP.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of

interest.

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