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Ultrasound measurement of the optic nerve sheath diameter in traumatic brain injury: a narrative review

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Abstract : *Background* : Raised intracranial pressure (ICP) needs to be investigated in various situations, especially in traumatic brain injury (TBI). Ultrasonographic (US) measurement of the optic nerve sheath diameter (ONSD) is a promising noninvasive tool for assessing elevated ICP.
Objectives : This narrative review aimed to explain the history of and indications forUS measurement of ONSD. We focused on the detection of elevated ICP after TBI and discussed the possible improvements in detection methods.
Conclusions : US measurement of ONSD in TBI cases provides a qualitative but no quantitative assessment of ICP. Current studies usually calculate their own optimum cutoff value for detecting raised ICP based on the balance between sensitivity and specificity of the method when compared with invasive methods. There is no universally accepted threshold. We did not find any paper focusing on the prognosis of patients benefiting from it when compared with usual care. Another limitation is the lack of standardization. US measurement of ONSD cannot be used as the sole technique to detect elevated ICP and monitor its evolution, but it can be a useful tool in a multimodal protocol and it might help to determine the prognosis of patients in various situations.

Keywords : Ultrasonography ; optic nerve ; intracranial pressure ; intracranial hypertension ; traumatic brain injury.

Introduction

The primary goal in neurocritical care is to avoid secondary brain injury (SBI). The main clinical causes of SBI are hypotension, hypoxia, anemia, hypocapnia and hypercapnia, hypoglycemia, hyperthermia, and elevated intracranial pressure (ICP). These conditions may be responsible for the mismatch between metabolic needs and delivery of oxygen and glucose to the cells, which may lead to tissue ischemia and cellular death, resulting in worse outcomes. Therefore, these factors are closely monitored in routine practice and may be the target of different therapies (1). Other factors, such as excitotoxicity, mitochondrial dysfunction, inflammation, and production of cytotoxic agents, are also involved in SBI (2).

This review focuses on the detection of elevated ICP, especially after traumatic brain injury (TBI). Elevated ICP can lead to a decrease in cerebral perfusion pressure (CPP) and cause cerebral ischemia. CPP is defined as the difference between mean arterial pressure and ICP. It is the net pressure gradient driving oxygen delivery to the cerebral tissue. Elevated ICP can also cause brain herniation and lead to death in severe cases (3). The definition of intracranial hypertension varies in literature. Many authors use a threshold of 20 mmHg (1), while others use thresholds of 20, 25, or even 30 cmH_2O (4). The main techniques used to evaluate ICP are invasive. External ventricular drain (EVD) and intraparenchymal monitoring (IPM) are the gold standards, presenting different benefits and limitations. EVDs help to evacuate cerebrospinal fluid (CSF), thereby reducing ICP. Some IPMs do not only monitor ICP, but also brain tissue oxygen ($PbtO_2$). Moreover, with microdialysis technology, it is possible to measure lactate, pyruvate, glycerol, and glutamate levels (5). This allows for a better understanding of cerebral physiology and focused care. Invasive techniques may cause serious side effects such as cerebral hemorrhage or infections, but these seem less likely with IPMs than with EVDs (6). Intrathecal lumbar catheters are also

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Table 1

Glasgow Coma Scale

Points	Eye opening	Best verbal response	Best motor response
1	No eye opening	No verbal response	No motor response
2	Response to pain	Incomprehensible	Extension to pain
3	Response to verbal command	Inappropriate	Flexion to pain
4	Spontaneous	Confused	Withdrawal response to pain
5		Oriented	Localizing response to pain
6			Obeys commands

Adapted from Teasdale G., and Jennett B. 1974. Assessment of coma and impaired consciousness. A practical scale. Lancet. 2(7872):81-4 (143).

often used to evaluate ICP. They allow drainage of CSF to lower ICP, similar to EVD. However, they can cause local hemorrhage and infection, and there might be a risk of cerebral herniation with elevated ICP (7).

ICP monitoring has been questioned as there is no evidence of better outcomes in patients managed with it (8), particularly in the Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure (9). However, the 2016 Brain Trauma Foundation guidelines recommend invasive ICP monitoring for severe TBI cases (Glasgow coma scale score ≤8, see Table 1) with abnormal computerized tomography (CT) findings (1). A meta-analysis conducted in 2016 reported better survival among patients subjected to invasive ICP monitoring after 2007 (10). A recent prospective, observational, and multicenter cohort study also reported better outcomes in patients subjected to ICP monitoring (11). The prognosis with classical IPM and EVD seems equivalent (12), but more advanced multimodal IPMs that are not limited to ICP measurement – $PbtO_2$ monitoring and microdialysis – might lead to better outcomes (10). Therefore, ICP monitoring and treatment alone seem insufficient, which questions the relevance of a precise ICP threshold. Some hypotheses suggest that ICP and CPP-based care may be an oversimplification of a more complex problem (2, 13). Multimodal IPMs will probably become the next gold standard in the domain, in addition to other multimodal cerebral monitoring techniques. Unfortunately, some of these advanced methods are still under development or may not always be easily applicable, especially in low-income countries.

Many noninvasive methods for evaluating ICP have been proposed. Their main advantage is that they cause few or no side effects, especially in patients with coagulopathy, which is a major contraindication for invasive procedures. Some methods can also be useful for screening purposes.

The first noninvasive method for assessing ICP is clinical examination, however it can be limited and difficult to perform in unconscious or sedated patients. Pupillary dilation has shown a low sensitivity of 28.2% (95% confidence interval (CI) 16-44.8%), but high specificity of 85.9% (95% CI 74.9-92.5%) to detect elevated ICP (3). Nowadays, automated pupillometry enables more reliable pupillary examinations (14). A Glasgow coma scale score ≤8 and positioning may also lead to some degree of imprecision when assessing ICP (3).

Direct cerebral imaging by CT or magnetic resonance imaging (MRI) can present indirect signs of intracranial hypertension, such as midline shift, intracranial hemorrhage, ventricular and basal cistern compression or hydrocephaly, diffuse sulcal effacement, and brain herniation (3, 15).

Papiledema is a late sign of elevated ICP and requires ophthalmoscopy for detection (16).

Many other procedures have been developed, especially for pediatric patients (17, 18, 19, 20). Transcranial Doppler (TCD) sonography and ultrasonographic (US) measurement of the optic nerve sheath diameter (ONSD) are two promising techniques.

The optic nerve (ON) is surrounded by the pia mater, the arachnoid space filled with CSF, and the dura mater, from inside to outside respectively, which are collectively called the optic nerve sheath (ONS) (21). In case of elevated ICP, the CSF flows into the arachnoid space and the sheath is enlarged (22). This enlargement can be detected by various imaging techniques, including US, CT, and MRI.

Comparison between US, CT, and MRI

The main advantages of US are its repeatability and rapidity. Generally, this examination takes a few minutes, and it can be repeated without moving

the patient. Recent developments in portable US equipment may soon allow widespread pre-hospital screening. US examination does not cause side effects if the necessary protocols are rigorously followed. Theoretically, it can generate heat in the tissues. This can affect the lens, vitreous body, and retina of the eyes. The vibrations of the sound beam can also cause intense local variations in pressure or even cavitation, which can lead to tissue damage. It is advised to limit the power output and the examination time to as low as reasonably achievable (ALARA principle). Values of thermal index (TI) equal to 0 and mechanical index (MI) <0.23 are often observed (23, 24). As compared to CT and MRI, US is a relatively cheap procedure, even in low-income countries or small hospitals.

A CT examination is primarily indicated when an intracranial abnormality is suspected. ONSD can be measured with this technique, which is an additional indicator of elevated ICP, as described previously. However, CT examination requires moving the patient on the scanner table, which can be dangerous or even contraindicated in patients with hemodynamic instability. Moreover, it is a source of ionizing radiation, and CT may be less accessible than US in some areas.

Although MRI is not a source of ionizing radiation, as compared to CT, it is generally less accessible, takes longer to perform, and is more expensive. Additionally, it requires patient mobilization, and it is contraindicated in patients with ferromagnetic or other metallic implants, such as non-compatible pacemakers.

To assess their validity as an indirect and non-invasive method to determine ICP, these imaging procedures have been compared with both non-invasive andinvasive methods. Two meta-analyses concluded that US measurement of ONSD (US ONSD) can predict signs of raised ICP on CT (25, 26). Both meta-analyses included the same 12 studies (with a total of 478 patients) and reported a sensitivity of 95.6% (95% CI 87.7-98.5%), specificity of 92.3% (95% CI 77.9-98.4%), positive likelihood ratio (PLR) of 12.5 (95% CI 4.2-37.5), and negative likelihood ratio (NLR) of 0.05 (95% CI 0.016-0.14). This means that US ONSD might be used as a screening tool for better identification of patients requiring further investigations with CT, as such avoiding unnecessary radiation exposure. However, more research is required to ensure that omitting CT will not be harmful in some patients, as only using US ONSD is not yet recommended for evaluating ICP.

Comparing ONSD values obtained with two different imaging techniques is not feasible. MRI is often considered the most reliable imaging technique for soft tissues, as it has the best spatial resolution. Several studies have compared MRI and other techniques measuring the ONSD. Some studies reported good correlations, while others failed to do so. As we will discuss later, the right procedure to be followed for measuring ONSD with US is debated. The different methods of US ONSD can be a source of heterogeneity in literature, thus reducing the reliability of comparisons.

It is important to note that using one imaging procedure does not dismiss the use of another. In severe TBI cases, US screening might be performed first to detect elevated ICP, followed by CT to detect intracranial lesions, then US monitoring of ICP trend, and finally a semi-urgent MRI to diagnose lesions more accurately and for prognosis purposes. Each imaging technique has its own advantages and disadvantages. The aim of this review is to explain US ONSD to novices and discuss actual and future possible indications and limitations in the diagnosis and monitoring of elevated ICP, with a focus on TBI.

Main causes of ONSD increase

Apart from elevated ICP, variations in ONSD can be due to many other factors (27). The main intrinsic causes include tumors (meningioma, glioma, arachnoid cyst, etc.), inflammation (optic neuritis and ocular trauma), and Grave's neuropathy. Patients diagnosed with these pathologies are often excluded from studies aimed at detecting elevated ICP, because asymmetry in ONSD of both eyes may induce false-positive results. The concept of ICP is that the intracranial space behaves as a unicameral compartment, and ICP is equal at every point. CSF flows uniformly in each ONS and causes a symmetrical increase in ONSD. In fact, this has been observed in most cases, and it is usually advised to compare ONSD of both eyes to confirm symmetry. However, mass lesions can cause asymmetry in ICP (28). Some patients may thus present with asymmetrical ONSD after TBI.

History and description of US measurement of ONSD

In the 1970s, Karl Ossoinig proposed standardization of the US eye examination (29, 30). He was one of the main developers of the first US measurement technique of ONSD with A-scan US biometry. During A-scan, reflections of a linear US

Table 2

Differential diagnosis of the 30° test

Positive 30° test	**Negative 30° test**
Increased intracranial pressure	Grave's optic neuropathy
Optic neuritis	Optic neuritis
Apical mass lesion	Nerve sheath meningioma
Trauma	Optic nerve glioma
Uveal effusion syndrome	
Arachnoïd cyst	

Inspired from Atta H.R. 1988. Imaging of the optic nerve with standardised echography. Eye (Lond). 2 (Pt 4):358-366 (27).

beam are analyzed to measure reflective anatomical structures. The patient is in supine positionwith a fixed gaze. Anesthetic eye drops are required for conscious patients. The probe is placed directly on the eyeball at its equator on the temporal side and directed posteriorly, nasally, and slightly superiorly (27). The result is a graph where the peaks represent reflective structures, such as the sheaths. The distance between the peaks represents the size of the structures. Ossoinig, Cennamo, and Byrne postulated that ONSD measurement is always perpendicular to the nerve on its anterior portion, owing to refraction of the sound beam toward the nerve surface. They stated an accuracy of 0.5 mm (31). With A-scan, it is possible to perform a 30-degree test in order to differentiate whether thickening of the nerve is caused by liquid (CSF) or by solid tissue. The ONSD was recorded at the primary position and again at 30° lateral gaze (towards the probe). This creates a pull on the ON and its sheath, causing a shift in CSF and a reduction in ONSD. A reduction >10% is considered positive (27, 31). Table 2 summarizes the conditions in which positive and negative results were obtained in the 30-degree test. It is important to note that increased ICP is not the only cause of arachnoid space thickening and reversible ONSD increase.

A-scan has a relatively good accuracy and allows to perform dynamic tests to improve differential diagnosis. However, a thorough knowledge of ocular anatomy and techniques is required to obtain reliable and reproducible results. Unfortunately, only few practitioners are familiar with this method, possibly explaining the limited number of studies.

In the 1990s, the B-scan improved in accuracy and progressively replaced the A-scan for measurement of the ONSD, mainly due to the works of Hansen and Helmke (22, 32, 33, 34). The technology has gained popularity in various domains since then. Its

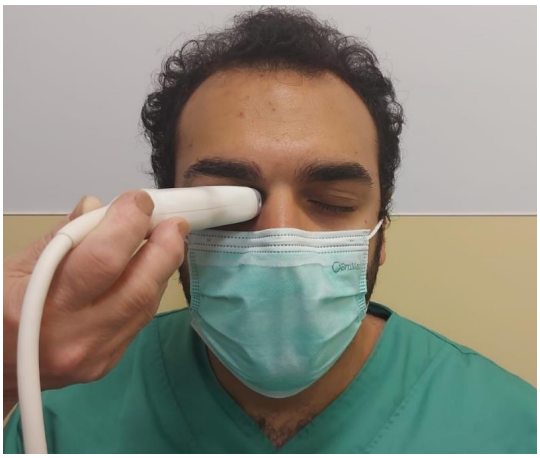

Fig. 1. — Transversal axis (also called horizontal axial).
Fig. 1a — Probe placement on the patient. The probe is placed slightly on the temporal side, aiming nasally to align the sound beam with the longitudinal axis of the ON. It is placed on the upper eyelid.

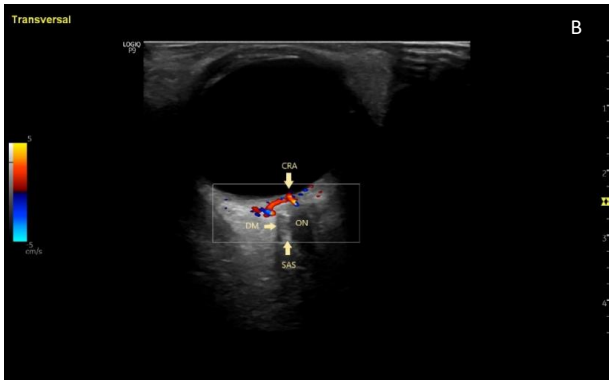

Fig. 1b — The hypoechogenic optic nerve (ON) emerges from the hyperechogenic optic disc. It is surrounded by the hyperechogenic subarachnoid space (SAS) and the hypoechogenic dura mater (DM). The peri-orbital fat is hyperechogenic. The central retinal artery (CRA) is identified with the Doppler function. It is situated in the center of the ON.

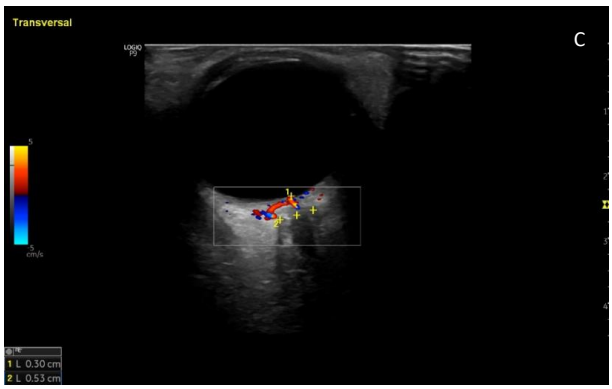

Fig. 1c — The optical nerve sheath diameter (ONSD) is measured 3 mm behind the papilla, inside the inner borders of the dura mater, perpendicularly to the nerve course.

main advantage is that it allows direct visualization of different structures and organs. It was already part of the standardized US eye examination but

it was not used to measure ONSD until then. An imaging resolution of 0.4 mm can be achieved with linear probes of ≥7.5 MHz, which is considered sufficient for ONSD measurement (35). Both axial and coronal views have been described, but there is no definitive proof that one is superior to the other (36). In all cases, the current procedures require the patient to lie supine, and the probe is placed on the closed eyelid with a coupling medium. Axial views are described first (27, 32). The transversal and sagittal planes are usually referred to as horizontal and vertical axial sections, respectively. In both cases, the probe is placed slightly on the temporal side, aiming nasally to align the sound beam with the longitudinal axis of the ON. For the transversal plane, it is placed on the upper eyelid (horizontal axial section; Fig. 1) and for the sagittal plane it is placed vertically on both eyelids (vertical axial section; Fig. 2). The hypoechogenic ON emerges from the hyperechogenic optic disc. The ONSD is usually measured 3 mm behind the optic disc, perpendicular to the ON longitudinal axis, because at this distance, the diameter of the sheath changes maximally when ICP varies (22, 33). It is advised to measure ONSD on both axial views (transversal and sagittal) in both eyes and to average the four measurements to limit errors.

There are two types of coronal views. The most common one is found with the probe placed vertically, more temporally, and aimed more nasally than for the sagittal view, to cut the nerve almost perpendicularly (Fig. 3). It appears almost circular on the screen. The craniocaudal diameter is measured (anatomically vertical but horizontal on the screen) because the mediolateral diameter might not be perpendicular to the longitudinal axis of the nerve and as such might be larger than the actual ONSD. It is not possible to determine the distance between the optic disc and the measured diameter. The best measurement is the largest craniocaudal diameter observed (36). The other coronal view is the oblique-transversal one (Fig. 4). The probe is placed horizontally on the lower eyelid to obtain an oblique cut of the ON. ONSD is measured mediolaterally (horizontally on the screen), because this axis should not be disrupted by the oblique view (37). Pediatric probes may be more adapted for coronal views, because it may be very difficult to fit adult probes correctly on the eye.

Available literature is divided based on the appearance on US of the different anatomical structures of the ONS. A group of authors described hypoechogenic central nerve fibers surrounded by a hyperechogenic pia mater (but it is usually too thin to be seen), a swollen hyperechogenic structure corresponding to the subarachnoid space filled with

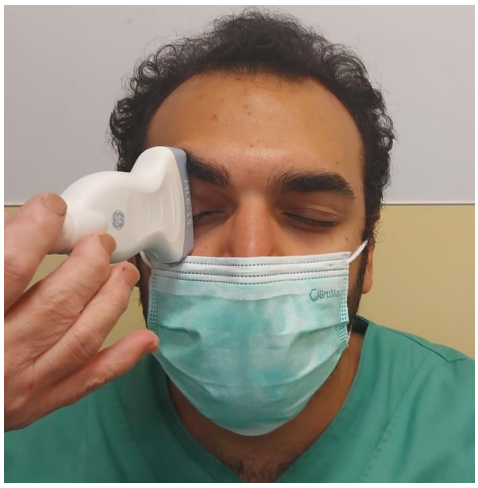

Fig. 2 — Sagittal axis (also called vertical axial).
Fig. 2a — Probe placement on the patient. The probe is placed slightly on the temporal side, aiming nasally to align the sound beam with the longitudinal axis of the optic nerve (ON). It is placed on both eyelids.

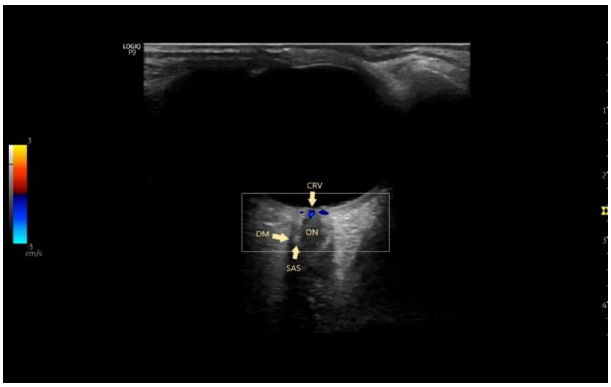

Fig. 2b — The hypoechogenic optic nerve (ON) emerges from the hyperechogenic optic disc. It is surrounded by the hyperechogenic subarachnoid space (SAS) and the hypoechogenic dura mater (DM). The peri-orbital fat is hyperechogenic. The central retinal artery (CRA) is identified with the Doppler function. It is situated in the center of the ON.

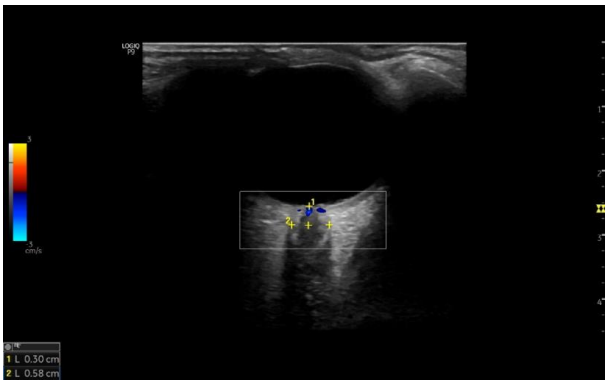

Fig. 2c — The optical nerve sheath diameter (ONSD) is measured 3 mm behind the papilla, inside the inner borders of the dura mater, perpendicularly to the nerve course.

Fig. 3 — Coronal vertical view.

Fig. 3a — Probe placement on the patient. The probe is placed vertically, more temporally, and aimed more nasally than for the sagittal view, to cut the nerve almost perpendicularly.

Fig. 4 — Coronal horizontal view.

Fig. 4a — Probe placement on the patient. The probe is placed horizontally on the lower eyelid to obtain an oblique cut of the optic nerve (ON).

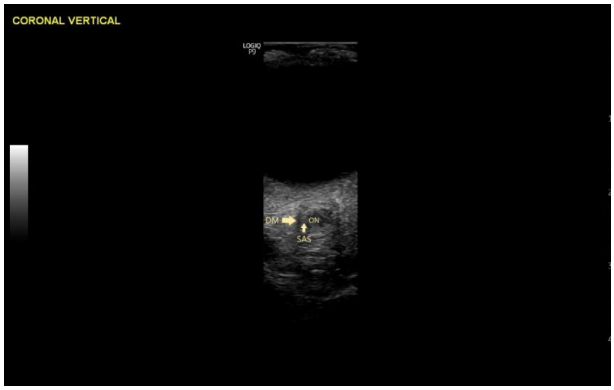

Fig. 3b — The optic nerve (ON) and its sheath appear almost circular on the screen. The hypoechogenic ON is surrounded by the hyperechogenic subarachnoid space (SAS) and the hypoechogenic dura mater (DM). The peri-orbital fat is hyperechogenic.

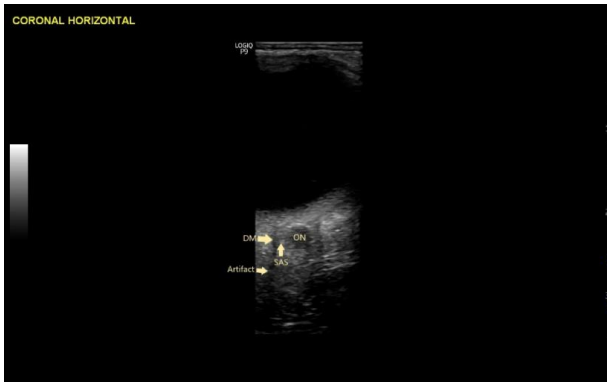

Fig. 4b — The optic nerve (ON) and its sheath appear almost circular on the screen. The hypoechogenic ON is surrounded by the hyperechogenic subarachnoid space (SAS) and the hypoechogenic dura mater (DM). The peri-orbital fat is hyperechogenic.

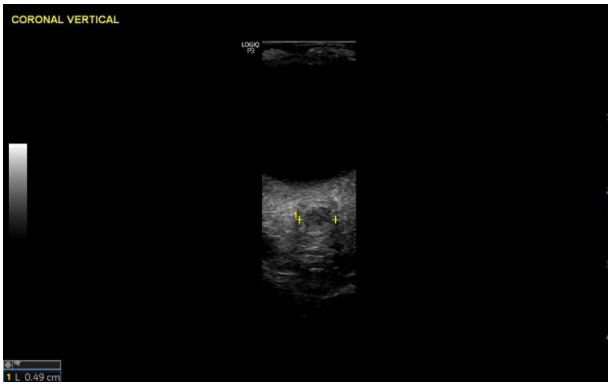

Fig. 3c — The craniocaudal diameter is measured (anatomically vertical but horizontal on the screen) because the mediolateral diameter might not be perpendicular to the longitudinal axis of the nerve and therefore might appear larger than the actual ONSD. It is not possible to determine the distance between the optic disc and the measured diameter. The best measurement is the largest craniocaudal diameter observed. The Doppler function is not needed. The optical nerve sheath diameter (ONSD) is measured inside the inner borders of the dura mater.

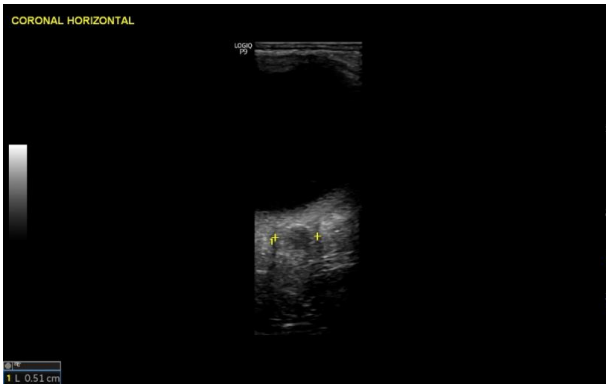

Fig. 4c — The optical nerve sheath diameter (ONSD) is measured mediolaterally (horizontally on the screen), because this axis should not be disrupted by the oblique view. It is not possible to determine the distance between the optic disc and the measured diameter. The best measurement is the largest mediolateral diameter observed. The Doppler function is not needed. The ONSD is measured inside the inner borders of the dura mater.

Fig. 5 —Artifact presenting as a black cone that makes the optic nerve sheath diameter measurement invalid. The optic nerve, the subarachnoid space and the dura mater cannot be recognized.

CSF, a thin hypoechogenic layer corresponding to the dura mater, and finally the periorbital fat that appears hyperechogenic (24, 38, 39). Other authors described hypoechogenic central nerve fibers, hyperechogenic pia mater, anechogenic or hypoechogenic subarachnoid space, and hyperechogenic dura mater and periorbital fat (40, 41, 42, 43). The problem with the latter description is that it does not conform to expected anatomy and images reported in recent literature. It was probably a correct description using the old sonographs (33, 34), but it has become outdated with new machines. In our opinion, the subarachnoid space has become hyperechogenic due to increase in resolution of sonographs, with the trabeculae adding heterogeneity (24, 39). Hence, we believe that the first description describes better what is observed nowadays.

ONSD is usually measured between the hyperechogenic subarachnoid space and the hypoechogenic dura mater, but Schroeder *et al.* noted that some authors also included the dura mater in their measurements (38). Generally, the ONS is the largest when measured 3 mm behind the globe, and becomes thinner as it moves away from it. It usually has an "S" shape. However, it is not rare to observe a hypoechogenic cone enlarging distally, where the ON is supposed to be (Fig. 5). The origin of this artifact is unclear. It could be the lens, lamina cribrosa, or the ONS itself. Moreover, there could be more than one possible origin (36, 44-47). Coronal views have the advantage of avoiding this artifact. In axial views, it is possible to search for the central retinal artery with Doppler in order to define the actual path of the ON and facilitate its identification (44, 48).

It is important to note that different values obtained with different views cannot be compared with one another (47, 49, 50). The ONS is not necessarily circular; therefore, transversal and sagittal views may give slightly different values. Since it is difficult to determine the exact depth of coronal views, they cannot be compared to transversal and sagittal measurements that are recorded precisely at a 3-mm depth.

In 2019, Aspide *et al.* published the "CLOSED protocol", with several recommendations to standardize the procedure (48). Their suggestions aimed to optimize the examination and limit its duration and potential side effects, thus improving patient security as well as intra-observer and inter-observer reliability. The key points of the procedure are as follows:

– *Color Doppler*: used to identify the central retinal artery, vein, and ophthalmic artery. The central retinal vessels are inside the ON, and their visualization aims to detect the actual nerve path. The ophthalmic artery runs outside the ONS.
– *Low power output*: to preserve the sensitive parts of the eye. As mentioned earlier, heat and vibration can cause tissue damage, especially to the lens, vitreous body, and retina. A power output of 20-25% is sufficient to obtain good images in compliance with TI and MI limits.
– *Optic disk clarity*: the nerve emerges from the optic disk (or papilla), which is hyperechogenic. The ONSD is measured 3 mm behind this structure, perpendicular to the nerve course.
– *Safety (short examination duration)*: to minimize the examination duration, the authors proposed recording the US video clip and conduct the measurements later.
– *Elevate frequency*: some studies compared different probes of different frequencies to identify the best one for ONSD measurement. A better spatial resolution is obtained with high-frequency probes, but tissue penetration, artifacts, and safety are equally important factors. Probes with frequency ≥7.5 MHz are often recommended (35, 49, 51).
– *Dual measurements*: if axial views are used, horizontal and vertical measures should be recorded, and their average values should be used to minimize imprecision.

The authors also suggested pre-settings such as the depth value set at 40-45 mm, focus at a depth of 25-30 mm, gain at 55-60%, and the Doppler value of the pulse repetition frequency at 1 kHz. The patient should be in supine position with a neutral head position and stable straight gaze.

This can be difficult because with closed eyes, the pupils naturally point upward and outward (Bell's phenomenon). The sonographer should sit behind the patient's head with the machine at the patient's side. Other authors suggest that the sonographer should sit at the patient's side with the machine behind the patient's head. Other suggestions can be found in their paper (48). It is important to note that these expert opinions are not guidelines and can be a source of debate.

Learning curve and reproducibility

The main advantage of the B-scan over the A-scan is its steep learning curve. Anatomical structures are directly visualized and the operator can easily evaluate if the right one is being measured correctly. In addition, the reproducibility is high with low intra-observer variability and high inter-observer reliability.

Tayal *et al.* reported that 10 patients with three abnormal scan results are sufficient for an experienced sonologist to learn the technique (52). For novices, 25 scans might be necessary. However, this is only a subjective estimation that is not evidence-based (53). Zeiler *et al.* reported that the intra-observer variability of a single operator reached a plateau after 21 patients with two axial measures for each eye (horizontal and vertical)(53). This suggests that approximately 80 measures are necessary to learn the technique comprehensively. Betcher *et al.* enrolled 23 special operations combat medics with minimal US experience for a 5-minute presentation on the ONSD and a 20-minute practical lesson (54). They then measured each other's ONSD in the transversal plane, and these measurements were compared with the instructor's measurements. No statistical difference was observed between the measurements by the trainees and the instructor, suggesting that the technique is easy to learn.

In a study assessing five novices, Potgieter *et al.* reported good inter-observer reliability after a 4-hour workshop on how to measure the ONSD of healthy volunteers with US in the transversal plane (55). The median intra-observer difference was ≤0.27 mm, standard deviation was ≤0.46 mm, and 95th percentile was ≤1.19 mm. For inter-observer reliability, the measurements by the novices were compared with those of an experienced operator. The median inter-observer difference was ≤0.3 mm and 95th percentile was ≤1.43 mm. Shrestha *et al.* compared three novice operators and one expert operator measuring three transversal measurements per eye in 27 healthy volunteers (56). They had a 2-hour practical session before the measurements, with 30 minutes of theoretical courses and a supervised training session, where they acquired at least 10 images of sufficient quality each. The mean inter-observer variations fluctuated largely in the first 17 cases (0.22-0.45 mm), but reduced in the last 10 cases (variability of 0.09-0.13 mm). Furthermore, the value of the Cronbach's alpha test improved after the 17th case: 0.40-0.98 for the right eye and 0.55-0.98 for the left eye in the first 17 cases, versus 0.93-0.99 and 0.74-0.91 in the last 10 cases for the right and left eye, respectively. This indicated good inter-observer reliability, suggesting that novices need 17 patients (102 measurements) to compete with an expert.

Ballantyne *et al.* reported low intra- and inter-observer variability when comparing three experienced sonographers performing transversal measurements on healthy volunteers (57). The median intra-observer variation was 0.1 mm (95% CI 0-0.4 mm) and the median inter-observer variation was 0.2-0.3 mm (95% CI 0-0.7 mm). Remarkably, the inter-observer variability reduced after the three sonographers had reviewed their methodology together, suggesting an initial lack of standardization that may have led to greater measurement variations. Bäuerle *et al.* also reported low intra- and inter-observer variability between two sonographers assessing healthy volunteers (58). ONSD was measured in the transverse plane. The intra-observer reliability analyzed with Cronbach's alpha ranged between 0.92 and 0.97. Pearson's correlation coefficient between the two investigators was 0.81-0.84. Lochner *et al.*'s study on healthy volunteers showed intra-observer agreement with a Cronbach's alpha value of 0.69-0.72, and inter-observer mean differences of 0.08 ± 0.28 mm and 0.09 ± 0.40 mm for the right ($p = 0.83$) and left bulb ($p = 0.47$), respectively (59). They also used only the transverse plane.

However, except for the study by Betcher *et al.*, the other studies included a small number of sonographers, and they all assessed healthy volunteers with normal ONSD. Among a group of emergency-medicine physicians, 10 ultrasound fellowship-trained physicians and 51 residents were compared (60). A database of US images was used, including both normal and abnormal ONSDs. Therefore, it was not the acquisition of the images that was compared, but the capability of measuring ONSD on the images. The authors evaluated the inter-rater reliability (IRR) using the intraclass correlation coefficient (ICC). The estimated IRR for the US fellowship-trained and resident emergency-

medicine physicians showed strong and moderate agreement with an ICC of 0.73 (95% CI 0.44-0.96) and 0.50 (95% CI 0.25-0.89), respectively. This was lower than in previous reports and it did not include the errors caused by the acquisition of images.

Literature is optimistic about the reproducibility of US ONSD. Except for the study by Oberfoell *et al.* (60), all studies concluded that the technique is easy to learn, and that intra- and inter-observer variability are low, although sometimes with wide CIs. However, as discussed earlier, standardization is lacking. The fact that the inter-observer variability in Ballantyne *et al.*'s study lowered after the three sonographers had reviewed their methodology together, suggests that this could be an influencing factor. As already stated before, some authors include the dura mater in the ONSD measurement (38). Another source of heterogeneity is the pathology of patients. Here, except for the study by Oberfoell *et al.*, only healthy individuals were included. In clinical practice, various pathologies are encountered, including TBI, subarachnoid hemorrhage (SAH), intracranial hemorrhage, stroke, idiopathic intracranial hypertension, acute liver failure, and sepsis. The absence of pathological images can influence the sonographers in what they expect to find, and they may correct themselves if they find an abnormally high ONSD. Another source of variability that is difficult to evaluate arises from the machine and different probes used (35, 49, 51).

ONSD variation and relationship with ICP

The first publication that studied the relationship between ONSD measured with B-scan and ICP was an *in vivo* study by Hansen & Helmke in 1997 (34). Two lumbar intrathecal catheters were used, one for Ringer's solution delivery and the other for continuous CSF pressure measurement. They demonstrated that the ONSD varied within minutes following infusion, and that CSF pressure increased. The average maximum difference in the ONSD between baseline and peak pressures was 1.8 mm (range 0.7-3.1 mm), corresponding to an average ONSD variation of 45% (range 15-89%). Regression analysis revealed a linear covariance between ONSD and CSF pressure with different slopes across the participants (0.019-0.071 mm/mmHg, mean r = 0.78). This linear relationship was only present above a threshold ranging between 15 and 30 mmHg with a plateau in ONSD at 30-40 mmHg. Moreover, they observed that ONSD returned to pre-infusion values after the experiment. Hansen *et al.* attempted to determine the distensibility and elastic characteristics of the ONS from autopsies (61). They calculated an ONSD increase of 0.025 mm for each mmHg increase in pressure in the subarachnoid space, which was consistent with previous findings. They also found that ONSD declined to baseline values within a few minutes when pressure was released, except when the pressure was ≥45-55 mmHg, in which case there seemed to be loss in elasticity. However, these two studies did not demonstrate a direct correlation between ONSD and ICP because of significant inter-individual variations. They mainly suggest that ONSD can rapidly increase and decrease depending on ICP variations.

In 2021, Sahu *et al.* determined the correlation between different ICP and ONSD values (62). Thirty adults undergoing surgical procedures for raised ICP due to mass lesions, congenital aqueductal stenosis, aneurysm, or infection, were included. They demonstrated that the optimum ONSD cutoff values predicting ICP at 20, 25, 30, and 35 mmHg were 5.5, 6.3, 6.5, and 6.7 mm, respectively. However, they noted that a higher ICP led to less significant results. There is still insufficient evidence to estimate the exact ICP based on ONSD values.

Maissan *et al.* measured US ONSD of 18 intubated and ICP-monitored patients before, during, and after tracheal manipulation (for essential nursing), which is known to increase ICP (63). They showed that acute changes in ICP in neurocritical patients may lead to concomitant changes in ONSD, confirming previous results. However, since acute and brief increases in ICP might be harmful after TBI (64), only a few studies have been conducted on this subject. It is easier to find papers on the acute decrease in ONSD after CSF evacuation or osmolar therapy in patients with intracranial hypertension (65-70). Fichtner *et al.* demonstrated that patients with intracranial hypotension caused by CSF leakage showed an acute decrease in ONSD when changing from supine to upright position (71). However, in case of SAH due to an arterial aneurysm rupture, some authors found no correlation between ONSD and ICP measured invasively (72, 73). The main hypothesis is that elasticity of the ONS is lost at very high ICP values, as described by Hansen *et al.* (61).

Clinical applications of US measurement of ONSD

US ONSD has been studied in various situations. Historically, its first use was in ophthalmology for ON pathologies. The works of Hansen and Helmke (22) focused on its utility in detecting intracranial

hypertension, and the technique is now being used by neurologists, neurosurgeons, intensive care providers, emergency medicine practitioners, anesthesiologists, pediatricians, etc.

In anesthesia, US ONSD has been used to assess ICP during specific surgeries or maneuvers. For example, laparoscopic procedures, when combined with the Trendelenburg position, are believed to cause an increase in ICP. Some authors evaluated the variation of ONSD in this setting (74, 75), while others evaluated the effect of different anesthetics on ONSD (76-79). Also the effect of low levels of positive end-expiratory pressure has been investigated (80). It is interesting to note that one study demonstrated that Trendelenburg and anti-Trendelenburg positions alone did not affect ONSD (81). In children, the effect of intubation, neck extension, and mouth-gag placement on US ONSD has also been investigated (82, 83). One study investigated the changes in ONSD during liver transplantation (84).

In emergency care, the effect of the cervical collar with or without elevation of the head of the bed (85) and the effect of patient positioning during helicopter transportation have been explored (86).

Also non-neurological conditions that can lead to cerebral edema and subsequently to increased ICP have been investigated, such as sepsis (87), acute liver failure, malignant hypertension (88), and pre-eclampsia or eclampsia (89-93). It is still unclear whether eclampsia is related to actual intracranial hypertension or to fluid status of patients (94). Since sepsis and liver failure may cause severe coagulopathy, noninvasive techniques to estimate ICP are very compelling in this context. Adult (95) and pediatric (96, 97) studies conducted on acute liver failure have shown contrasting results.

In neurosurgery, patients with CSF leakage can have decreased ONSD in upright position (71), which can be corrected with surgery (98). It can be useful to confirm the appropriate placement of a ventriculoperitoneal drain (99) or to diagnose its obstruction, but contrasting results have been reported (100, 101). The evolution of ICP after craniectomy also led to discordant results (102, 103). Its use as a means of detecting postoperative intracranial hypertension has also been investigated (104).

In neurology, including emergencies and neuro-critical care, US ONSD can be useful in detecting optic neuritis (105) or intracranial mass lesions with intracranial hypertension (106) and in the management of patients with migraine (107), idiopathic intracranial hypertension (66, 68, 108, 109), some types of meningitis (110, 111), and stroke (112-115). Hemorrhagic strokes are particularly common because aneurysmal SAH can cause irreversible distention of ONS, as discussed before. However, also patients with other types of hemorrhagic stroke might benefit from US ONSD. In patients with different types of intracranial bleeding, a correlation between ICP and ONSD has been shown (65, 116-118). Lee *et al.* demonstrated the prognostic value of ONSD measured on the first CT in SAH (119). We hypothesize that ONS distention caused by bleeding is associated with peak ICP, which might be linked to prognosis. Several studies have evaluated US, CT, and MRI measurements of ONSD to assess neurological prognosis after cardiac arrest of non-neurological causes (120, 121) or to predict brain death (122, 123).

Any sedated patient at risk of elevated ICP, but not meeting the criteria for invasive monitoring, could benefit from this technique. For example, a polytrauma patient without initial evidence of severe head trauma, who is placed under anesthesia for surgery, respiratory failure, shock, etc., could be monitored by US ONSD to detect late onset of intracranial abnormalities. This ensures more precise monitoring than when only relying on clinical examination (pupillary dilation).

Pathological ONSD threshold and diagnostic accuracy

There is no consensus regarding the best US technique for measuring ONSD. This probably contributes to the variability in threshold values proposed in literature. Another major problem arises from the different references used: intracranial devices (EVD and IPM), lumbar intrathecal catheters, or CT. ONSD threshold values clearly depend on the reliability of the reference used. Additionally, even when invasive devices are used as a reference, threshold pressure values defining intracranial hypertension may vary. In multiple studies patients with various pathologies were included. All these factors complicate their comparison. This is reflected in the meta-analyses, which often include few comparable studies.

A threshold of 5 mm was proposed in 1996 by Helmke and Hansen for ONSD measured with B-scan in patients aged ≥4 years (32). This threshold has been used for several years, and Kimberly *et al.* confirmed this threshold in an study in 2008 including 15 patients for an ICP threshold of 20 cmH_2O measured with EVD (124). Gradually, other

researches attempted to calculate the threshold with the best balance between sensitivity and specificity for their series of patients. Meta-analyses have been performed to calculate the sensitivity and specificity of US ONSD more precisely, but studies using different thresholds or even different references were included, which limits their scope.

The first meta-analysis on US ONSD was released in 2011 by Dubourg *et al.* (125). It included six studies with a total of 231 patients with TBI, intracranial hemorrhage, or ischemic stroke. The study revealed a sensitivity of 0.90 (95% CI 0.80-0.95) and specificity of 0.85 (95% CI 0.73-0.93) for the detection of raised ICP and a pooled diagnostic odds ratio (DOR) of 51 (95% CI 22-121) in comparison with invasive intracranial monitoring (EVD or IPM). However, the six studies used different thresholds of pathological ONSD, varying from 5 mm to 5.9 mm.

In 2018, Robba *et al.* performed a meta-analysis of seven studies including 320 patients with intracranial hypertension due to TBI, intracranial hemorrhage, or stroke (4). These studies useddifferent cutoff values for elevated ICP and pathological ONSD, and therefore the authors calculated pooled DOR, PLR, and NLR, which was more accurate than calculating the pooled sensitivity and specificity. DOR was 67.5 (95% CI 29-135), PLR was 5.35 (95% IC 3.76-7.53), and NLR was 0.088 (95% CI 0.046-0.152), without any significant heterogeneity.

In 2019, Koziarz *et al.* performed a meta-analysis of 61 studies, 18 of which focused on TBI (126). The sensitivity was 0.97 (95% CI 0.92-0.99), specificity was 0.86 (95% CI 0.74-0.93), PLR was 6.93 (95% CI 3.55-13.54), and NLR was 0.04 (0.02-0.1) for the TBI subgroup. The non-trauma group showed a sensitivity of 0.92 (95% CI 0.86-0.96), specificity of 0.86 (95% CI 0.77-0.92), PLR of 6.39 (95% CI 3.77-10.84), and NLR of 0.09 (95% CI 0.05-0.17).

In 2020, Lee *et al.* focused their meta-analysis on TBI studies only (127). It included five studies with 174 patients, four comparing US ONSD and one comparing CT measurement of ONSD with invasive methods. A pooled sensitivity of 0.91 (95% CI 0.87-0.94) and a pooled specificity of 0.77 (95% CI 0.63-0.88) were observed. The sensitivity and specificity of the US measurement were 0.91 and 0.82, respectively, whereas those of the CT measurement were 0.90 and 0.58, respectively. However, comparing the two methods with only one study evaluating CT is of limited use. Notably, sensitivity and specificity are comparable with those from the meta-analysis by Dubourg *et al.* using different studies. The same criticism could be directed to the other two meta-analyses. The studies included in the meta-analysis by Lee *et al.* did not use the same ONSD cutoff values. These varied from 5 mm to 6.4 mm. However, Lee *et al.* noted that the maximal ONSD value in the normal ICP group and the minimal ONSD value in the raised ICP group was the same (5.8 mm), suggesting that this could be a good cutoff value for TBI patients.

Overall, a sensitivity of 0.90 and a specificity of 0.80 have been frequently encountered in the literature with respect to US ONSD in the detection of raised ICP. This implies that one in every 10 patients suffering from raised ICP will not be diagnosed and that one in every 5 patients with increased ONSD will not have elevated ICP. Therefore, this technique must be used cautiously.

There is no clear evidence regarding variability in different population subtypes. The study by Wang *et al.* might question possible ethnic variations in ONSD (128). They assessed the ONSD threshold, linked with an opening pressure obtained with a lumbar puncture of ≥20 cmH_2O in the Chinese population. The reported threshold of 4.1 mm was lower than that noted in previous studies. Their measurement technique was criticized by Schroeder *et al.* in a meta-analysis that aimed to determine normal ON diameter (OND) and ONSD of healthy population (38). They argued that the authors had measured OND rather than ONSD. However, according to figure 1 in Wang *et al.*'s paper, it seems that they even included the dura mater in their measurement, which contradicts the criticism by Schroeder *et al.* We think that the lower threshold reported by Wang is due to the lower value of ICP (20 cmH_2O) that they considered as "elevated." Schroeder *et al.* calculated average normal values of 3.08 mm (95% CI 2.9-3.25) for OND and 4.78 (95% CI 4.63-4.94) for ONSD (38). They found no variability with sex, age, body mass index (BMI), or ethnicity, but the median age was low (36.1 years). Avci *et al.* evaluated ONSD of 195 healthy volunteers aged ≥65 years (129). Mean ONSD was 4.16 ± 0.69 mm. They found no differences with respect to age or sex. Some researchers have suggested influence of BMI on ONSD, but the evidence is insufficient. Pregnancy does not seem to modify ONSD (130), but carotid stenosis seems to reduce ONSD (131).

Multimodal US approaches have been developed, especially by Robba *et al.* These authors examined the combination of US ONSD, venous TCD of straight sinus systolic flow velocity (FV_{sv}), middle cerebral artery (MCA) pulsatility index (PI), and an estimator based on MCA diastolic FV (FV_d)

Table 3

Degrees and characteristics of head traumas

Degree	GCS* (< 24h)	Loss of consciousness	Alteration of consciousness	Imaging	Post-traumatic amnesia
Mild	13-15	0-30 min	< 24 h	Normal**	0-1 day
Moderate	9-12	30 min-24 h	> 24 h	Normal or abnormal	1-7 days
Severe	3-8	> 24 h	> 24 h	Normal or abnormal	>7 days

* GCS = Glasgow Coma Scale. ** In case of a patient who meets the mild traumatic brain injury classification by GCS, loss or alteration of consciousness and post-traumatic amnesia, but has abnormal imaging findings, some authors use the term "mild complicated TBI". Inspired from Capizzi A, Woo J, Verduzco-Gutierrez M. Traumatic Brain Injury: An Overview of Epidemiology, Pathophysiology, and Medical Management. Med Clin North Am. 2020;104(2):213-238 (134).

in 60 patients with TBI, SAH, or intracranial hemorrhage (132). They found that ONSD and FV_{SV} had the strongest correlation with invasive ICP and that their combination was even stronger, with a correlation coefficient (R) of 0.78 and an area under the curve (AUC) of the receiver operating characteristic (ROC) curve of 0.93 for prediction of ICP ≥20 mmHg. They proposed the following formula to estimate the noninvasive ICP (nICP; result in mmHg): $nICP_{ONSD+FVsv} = 4.23 \times ONSD + 0.14 \times FVsv-14.51$. In 2020, Robba *et al.* published another paper attempting to improve ICP estimation using noninvasive US techniques (133). They included 100 patients with TBI, SAH, or intracranial hemorrhage, and investigated US ONSD, PI, estimated ICP (eICP) using TCD, and neurological pupillary index (NPI) measured with automated pupillometry. A moderate Spearman correlation was found between the noninvasive techniques and invasive ICP, except for NPI that showed a weak correlation (ONSD: R = 0.54; PI: R = 0.50; eICP: R = 0.61; NPI: R = −0.41; $p < 0.001$ for all). The AUC to estimate intracranial hypertension was 0.78 (95% CI 0.68-0.88) for ONSD, 0.85 (95% CI 0.77-0.93) for PI, 0.86 (95% CI 0.77-0.93) for eICP, and 0.71 (95% CI 0.60-0.82) for NPI. The combination of ONSD with eICP had the highest AUC (0.91 (95% CI 0.84-0.97). These two studies suggest that a combination of several noninvasive techniques can improve detection of raised ICP in different pathologies. However, patients with SAH were also included, and as mentioned above, the validity of ONSD in these patients has been questioned. This means that the results could have potentially been better by excluding these patients.

TBI

TBI is a broad term comprising various types of brain injuries of varying severity. Medical care must suit specific needs of each patient, which requires the ability to identify and distinguish between different situations. TBI is usually divided into three categories: mild, moderate, and severe (Table 3) (134). Clinical monitoring is usually sufficient for mild TBI, but CT imaging or even surgery may be needed in some cases (134, 135). We did not find any specific study on ONSD for triaging patients with mild TBI, probably because they rarely present with elevated ICP. However, since US ONSD can be predictive of CT abnormalities suggestive of elevated ICP, including mass lesions and hemorrhage, this could be an interesting application in order to reduce exposure to ionizing radiations (25, 26).

Repeated mild TBI encountered in high-contact sports might affect ONSD. A study by Sadrameli reported an increase in ONSD in 24 female college soccer players without any history of concussion after the game season had begun (136).

Management of moderate and severe TBI is based on two major concerns: limiting the extension of primary lesions (when feasible) and preventing SBI. Elevated ICP is often encountered in these situations, especially in severe TBI cases (1). It can be caused by mass lesions (intracranial hemorrhage) or SAH or it can occur secondary to brain swelling. Guidelines usually propose prevention, detection, and treatment of elevated ICP. In the introduction, we have explained the gold standards for its detection. There are several studies focusing on US ONSD in severe TBI cases, but none of them actually gives it recognition in clinical practice. These studies are usually focused on determining the sensitivity and specificity of the technique, as discussed previously. Some studies linked ONSD measured on the initial CT to prognosis (137-139), but no study has evaluated the prognosis of patients in whom ONSD was compared with the gold standard. However, due to improvement of IPMs, it does not seem ethical to compare the prognosis of patients subjected only to US ONSD with those

subjected to IPMs with $PbtO_2$ measurements and microdialysis technology. However, because the variations of ONSD are prompt and well correlated to variations in ICP, and considering the multimodal approaches of Robba *et al.*, the technique can become an acceptable alternative. US ONSD is considered complementary to gold standards. It could be used as a decent alternative when EVD and IPM are contraindicated (coagulopathy), unavailable (absence of surgeon or material), or when there is a technical failure. However, it should be noted that there is no study showing that it improves outcome. Some authors suggested to use it as a screening utility in pre-hospital care (140) or in the emergency department to identify patients at high risk of raised ICP who might benefit from rapid therapy or further imaging. It could be possible to monitor patients who do not meet the criteria of invasive monitoring (moderate TBI cases) with this method, but there is no evidence demonstrating any benefit from this approach.

Conclusions

US measurement of ONSD is a noninvasive technique aimed to detect elevated ICP. It is quick, affordable, easily accessible, does not require patient mobilization, has no side effects if the correct safety measures are applied, and can be performed in pre-hospital settings and in all hospital departments. It seems quite easy to learn as shown by the studies on intra- and inter-observer reliability. However, these studies have limitations, and the lack of standardization of the technique does not support this idea. Moreover, there is debate about accordance between US images and the actual anatomy of ONS, and some artifacts may complicate measurements. It has been suggested that coronal views might avoid these artifacts, but axial and coronal views may provide different diameter values for the same ONS; hence, they cannot be directly compared. The B-scan measurement of ONSD is still evolving. Standardization or automation could be the next step to improve reliability and reproducibility of this technique (48, 141, 142).

Researchers often decide the best cutoff value based on the AUC of the ROC curve. As such, the actual practical diagnostic value of this technique is probably overestimated. Unfortunately, patients from different studies cannot be pooled to calculate a definitive cutoff due to sample heterogeneity. However, it is undoubted that this technique is less reliable than the invasive methods, especially when compared with the last multimodal IPMs that offer a better comprehension of cerebral physiopathology and seem to improve prognosis of patients. To date, there are no data concerning the prognosis of patients undergoing US ONSD.

De Bernardo, Rosa, and Vitiello proposed going back to the original A-scan technique, arguing that artifacts may be avoided and that ONSD measurement is more precise. However, recent evidence on its clinical value lacks.

Another limitation arises from the exclusion in all studies of patients with ocular trauma or pre-existing pathology. These patients cannot benefit from this technique because of the presence of important confounding factors.

Multimodal noninvasive approaches, as explored by Robba *et al.*, seem interesting and may improve the reliability of the techniques used alone. The combination of ONSD and TCD seems particularly promising.

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References

1. Carney N., Totten A.M., O'Reilly C., Ullman J.S., Hawryluk G.W.J., and Bell M.J., et al. 2017. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. Neurosurgery. 80(1):6-15.
2. Lazaridis C., Rusin C.G., and Robertson C.S. 2019. Secondary brain injury: Predicting and preventing insults. Neuropharmacology. 145(Pt B):145-152.
3. Fernando S.M., Tran A., Cheng W., Rochwerg B., Taljaard M., and Kyeremanteng K., et al. 2019. Diagnosis of elevated intracranial pressure in critically ill adults: systematic review and meta-analysis. BMJ. 366:l4225.
4. Robba C., Santori G., Czosnyka M., Corradi F., Bragazzi N., and Padayachy L., et al. 2018. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. Intensive Care Med. 44(8): 1284-1294.
5. de Lima Oliveira M., Kairalla A.C., Fonoff E.T., Martinez R.C., Teixeira M.J., and Bor-Seng-Shu E. 2014. Cerebral microdialysis in traumatic brain injury and subarachnoid hemorrhage: state of the art. Neurocrit Care. 21(1): 152-162.
6. Tavakoli S., Peitz G., Ares W., Hafeez S., and Grandhi R. 2017. Complications of invasive intracranial pressure monitoring devices in neurocritical care. Neurosurg Focus. 43(5):E6.
7. Tuettenberg J., Czabanka M., Horn P., Woitzik J., Barth M., and Thomé C., et al. 2009. Clinical evaluation of the safety and efficacy of lumbar cerebrospinal fluid drainage for the treatment of refractory increased intracranial pressure. J Neurosurg. 110(6):1200-1208.
8. Vella M.A., Crandall M.L., and Patel M.B. 2017. Acute Management of Traumatic Brain Injury. Surg Clin North Am. 97(5):1015-1030.
9. Chesnut R.M., Temkin N., Carney N., Dikmen S., Videtta W., and Petroni G., et al. 2012. A trial of intracranial-

pressure monitoring in traumatic brain injury. N Engl J Med. 367(26):2471-2481.
10. Shen L., Wang Z., Su Z., Qiu S., Xu J., and Zhou Y., et al. 2016. Effects of Intracranial Pressure Monitoring on Mortality in Patients with Severe Traumatic Brain Injury: A Meta-Analysis. PLoS One. 11(12):e0168901.
11. Robba C., Graziano F., Rebora P., Elli F., Giussani C., Oddo M., et al. 2021. Intracranial pressure monitoring in patients with acute brain injury in the intensive care unit (SYNAPSE-ICU): an international, prospective observational cohort study. The Lancet Neurology. 20(7):548-58
12. Volovici V., Huijben J.A., Ercole A., Stocchetti N., Dirven C.M., and van der Jagt M., et al. 2019. Ventricular Drainage Catheters versus Intracranial Parenchymal Catheters for Intracranial Pressure Monitoring-Based Management of Traumatic Brain Injury: A Systematic Review and Meta-Analysis. J Neurotrauma. 36(7):988-995.
13. Le Roux P. Evolution of neurocritical care. 2020. Curr Opin Crit Care. 26(2):83-86.
14. Romagnosi F., Bongiovanni F., and Oddo M. 2020. Eyeing up the injured brain: automated pupillometry and optic nerve sheath diameter. Curr Opin Crit Care. 26(2):115-121.
15. Jenjitranant P., Tunlayadechanont P., Prachanukool T., and Kaewlai R. 2020. Correlation between optic nerve sheath diameter measured on imaging with acute pathologies found on computed tomography of trauma patients. Eur J Radiol. 125:108875.
16. Freeman W.D. 2015. Management of Intracranial Pressure. Continuum (Minneap Minn). 21(5 Neurocritical Care):1299-1323.
17. Padayachy L.C. 2016. Non-invasive intracranial pressure assessment. Childs Nerv Syst. 32(9):1587-1597.
18. Khan M.N., Shallwani H., Khan M.U., and Shamim M.S. 2017. Noninvasive monitoring intracranial pressure - A review of available modalities. Surg Neurol Int. 8:51.
19. Zhang X., Medow J.E., Iskandar B.J., Wang F., Shokoueinejad M., Koueik J., and Webster J.G. 2017. Invasive and noninvasive means of measuring intracranial pressure: a review. Physiol Meas. 38(8):143-182.
20. Sallam A., Alkhatip A.A.A.M.M., Kamel M.G., Hamza M.K., Yassin H.M., and Hosny H., et al. 2021. The Diagnostic Accuracy of Noninvasive Methods to Measure the Intracranial Pressure: A Systematic Review and Meta-analysis. Anesth Analg. 132(3):686-695.
21. Liu D., and Kahn M. 1993. Measurement and relationship of subarachnoid pressure of the optic nerve to intracranial pressures in fresh cadavers. Am J Ophthalmol. 116(5):548-556.
22. Helmke K., and Hansen H.C. 1996. Fundamentals of transorbital sonographic evaluation of optic nerve sheath expansion under intracranial hypertension. I. Experimental study. Pediatr Radiol. 26(10):701-705.
23. Fowlkes J.B., and Holland C.K. 2000. Mechanical bioeffects from diagnostic ultrasound: AIUM consensus statements. American Institute of Ultrasound in Medicine. J Ultrasound Med. 19(2):69-72.
24. Lochner P., Czosnyka M., Naldi A., Lyros E., Pelosi P., and Mathur S., et al. 2019. Optic nerve sheath diameter: present and future perspectives for neurologists and critical care physicians. Neurol Sci. 40(12):2447-2457.
25. Ohle R., McIsaac S.M., Woo M.Y., and Perry J.J. 2015. Sonography of the Optic Nerve Sheath Diameter for Detection of Raised Intracranial Pressure Compared to Computed Tomography: A Systematic Review and Meta-analysis. J Ultrasound Med. 34(7):1285-1294.
26. Gottlieb M., and Bailitz J. 2016. Can Ocular Ultrasonography Be Used to Assess Intracranial Pressure? Ann Emerg Med. 68(3):349-351.
27. Atta H.R. 1988. Imaging of the optic nerve with standardised echography. Eye (Lond). 2(Pt 4):358-366.
28. Sahuquillo J., Poca M.A., Arribas M., Garnacho A., Rubio E. 1999. Interhemispheric supratentorial intracranial pressure gradients in head-injured patients: are they clinically important? J Neurosurg. 90(1):16-26.
29. Ossoinig K.C. 1977. Echography of the eye orbit and periorbital region. In: Orbital Roentgenology, by P.H. Arger. pp. 224-269. New York. Wiley.
30. Ossoinig K.C. 1979. Standardized echography: basic principles, clinical applications, and results. Int Ophthalmol Clin. 19(4):127-210.
31. Ossoinig K.C., Cennamo G., and Byrne S.F. 1981. Echographic differential diagnosis of optic nerve lesions. Doc. Ophthalmol. Proc. Ser. 29: 327-331.
32. Helmke K., and Hansen H.C. 1996. Fundamentals of transorbital sonographic evaluation of optic nerve sheath expansion under intracranial hypertension II. Patient study. Pediatr Radiol. 26(10):706-710.
33. Hansen H.C., Helmke K. 1996. The subarachnoid space surrounding the optic nerves. An ultrasound study of the optic nerve sheath. Surg Radiol Anat. 18(4):323-8.
34. Hansen H.C., Helmke K. 1997. Validation of the optic nerve sheath response to changing cerebrospinal fluid pressure: ultrasound findings during intrathecal infusion tests. J Neurosurg. 87(1):34-40.
35. Lochner P., Behnke S., Fassbender K., Andrejewski A., Knodel S., and Siniscalchi A., et al. 2019. Simulation and Experimental Characterization of Lateral Imaging Resolution of Ultrasound Systems and Assessment of System Suitability for Acoustic Optic Nerve Sheath Diameter Measurement. J Neuroimaging. 29(1):34-41.
36. Agrawal A., Cheng R., Tang J., and Madhok D.Y. 2019. Comparison of Two Techniques to Measure Optic Nerve Sheath Diameter in Patients at Risk for Increased Intracranial Pressure. Crit Care Med. 47(6):e495-e501.
37. Amini R., Stolz L.A., Patanwala A.E., and Adhikari S. 2015. Coronal Axis Measurement of the Optic Nerve Sheath Diameter Using a Linear Transducer. J Ultrasound Med. 34(9):1607-1612.
38. Schroeder C., Katsanos A.H., Richter D., Tsivgoulis G., Gold R., and Krogias C. 2020. Quantification of Optic Nerve and Sheath Diameter by Transorbital Sonography: A Systematic Review and Metanalysis. J Neuroimaging. 30(2):165-174.
39. Ertl M., Barinka F., Torka E., Altmann M., Pfister K., and Helbig H., et al. 2014. Ocular color-coded sonography - a promising tool for neurologists and intensive care physicians. Ultraschall Med. 35(5):422-431.
40. Bergès O., Koskas P., Lafitte F., and Piekarski J.D. 2006. Echographie de l'oeil et de l'orbite avec un échographe polyvalent. J Radiol. 87(4 Pt 1):345-353.
41. Merceron S., and Geeraerts T. 2008. Ocular sonography for the detection of raised intracranial pressure. Expert Review of Ophthalmology, 3(5):497-500.
42. Geeraerts T., Merceron S., Benhamou D., Vigué B., and Duranteau J. 2008. Non-invasive assessment of intracranial pressure using ocular sonography in neurocritical care patients. Intensive Care Med. 34(11):2062-2067.
43. Caccioppola A., Zoerle T., and Stocchetti N. 2020. The Authors Reply: Correlation Between Ultrasonographic Optic Nerve Sheath Diameter and Intracranial Pressure in Patients with Aneurysmal Subarachnoid Hemorrhage. Neurocrit Care. 33(3):862-863.
44. Copetti R., and Cattarossi L. 2009. Optic nerve ultrasound: artifacts and real images. Intensive Care Med. 35(8):1488-1491.
45. Teismann N.A., Lenaghan P., Stein J., and Green A. 2012. Will the real optic nerve sheath please stand up? J Ultrasound Med. 31(1):130-131.
46. Dubost C., and Geeraerts T. 2012. Possible pitfalls when measuring the optic nerve sheath with sonography. J Surg Res. 173(1):e43-44.

47. Blehar D.J., Gaspari R.J., Montoya A., and Calderon R. 2008. Correlation of visual axis and coronal axis measurements of the optic nerve sheath diameter. J Ultrasound Med. 27(3):407-411.
48. Aspide R., Bertolini G., Albini Riccioli L., Mazzatenta D., Palandri G., and Biasucci DG. 2020. A Proposal for a New Protocol for Sonographic Assessment of the Optic Nerve Sheath Diameter: The CLOSED Protocol. Neurocrit Care. 32(1):327-332.
49. Shah S., Kimberly H., Marill K., and Noble V.E. 2009. Ultrasound techniques to measure the optic nerve sheath: is a specialized probe necessary? Med Sci Monit. 15(5):63-68.
50. Raval R., Shen J., Lau D., Ferguson N., Kelly T., and Daniels J., et al. 2020. Comparison of Three Point-of-Care Ultrasound Views and MRI Measurements for Optic Nerve Sheath Diameter: A Prospective Validity Study. Neurocrit Care. 33(1):173-181.
51. Hewick S.A., Fairhead A.C., Culy J.C., Atta H.R. 2004. A comparison of 10 MHz and 20 MHz ultrasound probes in imaging the eye and orbit. Br J Ophthalmol. 88(4):551-555.
52. Tayal V.S., Neulander M., Norton H.J., Foster T., Saunders T., and Blaivas M. 2007. Emergency department sonographic measurement of optic nerve sheath diameter to detect findings of increased intracranial pressure in adult head injury patients. Ann Emerg Med. 49(4):508-514.
53. Zeiler F.A., Ziesmann M.T., Goeres P., Unger B., Park J., and Karakitsos D., et al. 2016. A unique method for estimating the reliability learning curve of optic nerve sheath diameter ultrasound measurement. Crit Ultrasound J. 8(1):9.
54. Betcher J., Becker T.K., Stoyanoff P., Cranford J., and Theyyunni N. 2018. Military trainees can accurately measure optic nerve sheath diameter after a brief training session. Mil Med Res. 5(1):42.
55. Potgieter D.W., Kippin A., Ngu F., and McKean C. 2011. Can accurate ultrasonographic measurement of the optic nerve sheath diameter (a non-invasive measure of intracranial pressure) be taught to novice operators in a single training session? Anaesth Intensive Care. 39(1):95-100.
56. Shrestha G.S., Upadhyay B., Shahi A., Jaya Ram K.C., Joshi P., and Poudyal B.S. 2018. Sonographic Measurement of Optic Nerve Sheath Diameter: How Steep is the Learning Curve for a Novice Operator? Indian J Crit Care Med. 22(9):646-649.
57. Ballantyne S.A., O'Neill G., Hamilton R., and Hollman A.S. 2002. Observer variation in the sonographic measurement of optic nerve sheath diameter in normal adults. Eur J Ultrasound. 15(3):145-149.
58. Bäuerle J., Lochner P., Kaps M., and Nedelmann M. 2012. Intra- and interobsever reliability of sonographic assessment of the optic nerve sheath diameter in healthy adults. J Neuroimaging. 22(1):42-45.
59. Lochner P., Coppo L., Cantello R., Nardone R., Naldi A., Leone M.A., and Brigo F. 2014. Intra- and interobserver reliability of transorbital sonographic assessment of the optic nerve sheath diameter and optic nerve diameter in healthy adults. J Ultrasound. 19(1):41-45.
60. Oberfoell S., Murphy D., French A., Trent S., and Richards D. 2017. Inter-rater Reliability of Sonographic Optic Nerve Sheath Diameter Measurements by Emergency Medicine Physicians. J Ultrasound Med. 36(8):1579-1584.
61. Hansen H.C., Lagrèze W., Krueger O., and Helmke K. 2011. Dependence of the optic nerve sheath diameter on acutely applied subarachnoidal pressure - an experimental ultrasound study. Acta Ophthalmol. 89(6):e528-e532.
62. Sahu S., Panda N., Swain A., Mathew P., Singla N., and Gupta S., et al. 2021. Optic Nerve Sheath Diameter: Correlation with Intra-Ventricular Intracranial Measurements in Predicting Dysfunctional Intracranial Compliance. Cureus. 13(1):e13008.
63. Maissan I.M., Dirven P.J., Haitsma I.K., Hoeks S.E., Gommers D., and Stolker R.J. 2015. Ultrasonographic measured optic nerve sheath diameter as an accurate and quick monitor for changes in intracranial pressure. J Neurosurg. 123(3):743-747.
64. Stein D.M., Hu P.F., Brenner M., Sheth K.N., Liu K.H., and Xiong W., et al. 2011. Brief episodes of intracranial hypertension and cerebral hypoperfusion are associated with poor functional outcome after severe traumatic brain injury. J Trauma. 71(2):364-73.
65. Moretti R., Pizzi B., Cassini F., and Vivaldi N. 2009. Reliability of optic nerve ultrasound for the evaluation of patients with spontaneous intracranial hemorrhage. Neurocrit Care. 11(3):406-410.
66. Bäuerle J., and Nedelmann M. 2011. Sonographic assessment of the optic nerve sheath in idiopathic intracranial hypertension. J Neurol. 258(11):2014-2019.
67. Launey Y., Nesseler N., Le Maguet P., Mallédant Y., and Seguin P. 2014. Effect of osmotherapy on optic nerve sheath diameter in patients with increased intracranial pressure. J Neurotrauma. 31(10):984-988.
68. del Saz-Saucedo P., Redondo-González O., Mateu-Mateu Á., Huertas-Arroyo R., García-Ruiz R., and Botia-Paniagua E. 2016. Sonographic assessment of the optic nerve sheath diameter in the diagnosis of idiopathic intracranial hypertension. J Neurol Sci. 361:122-127.
69. Chen L.M., Wang L.J., Hu Y., Jiang X.H., Wang Y.Z., and Xing Y.Q. 2019. Ultrasonic measurement of optic nerve sheath diameter: a non-invasive surrogate approach for dynamic, real-time evaluation of intracranial pressure. Br J Ophthalmol. 103(4):437-441.
70. Wang L.J., Chen L.M., Chen Y, Bao L.Y., Zheng N.N., Wang Y.Z., and Xing Y.Q. 2018. Ultrasonography Assessments of Optic Nerve Sheath Diameter as a Noninvasive and Dynamic Method of Detecting Changes in Intracranial Pressure. JAMA Ophthalmol. 136(3):250-256.
71. Fichtner J., Ulrich C.T., Fung C., Knüppel C., Veitweber M., and Jilch A., et al. 2016. Management of spontaneous intracranial hypotension - Transorbital ultrasound as discriminator. J Neurol Neurosurg Psychiatry. 87(6):650-655.
72. Bäuerle J., Niesen W.D., Egger K., Buttler K.J., and Reinhard M. 2016. Enlarged Optic Nerve Sheath in Aneurysmal Subarachnoid Hemorrhage despite Normal Intracranial Pressure. J Neuroimaging. 26(2):194-196.
73. Zoerle T., Caccioppola A., D'Angelo E., Carbonara M., Conte G., and Avignone S, et al. 2020. Optic Nerve Sheath Diameter is not Related to Intracranial Pressure in Subarachnoid Hemorrhage Patients. Neurocrit Care. 33(2):491-498.
74. Verdonck P., Kalmar A.F., Suy K., Geeraerts T., Vercauteren M., and Mottrie A., et al. 2014. Optic nerve sheath diameter remains constant during robot assisted laparoscopic radical prostatectomy. PLoS One. 9(11):e111916.
75. Robba C., Cardim D., Donnelly J., Bertuccio A., Bacigaluppi S., and Bragazzi N., et al. 2016. Effects of pneumoperitoneum and Trendelenburg position on intracranial pressure assessed using different non-invasive methods. Br J Anaesth. 117(6):783-791.
76. Choi E.S., Jeon Y.T., Sohn H.M., Kim D.W., Choi S.J., and In C.B. 2018. Comparison of the effects of desflurane and total intravenous anesthesia on the optic nerve sheath diameter in robot assisted laparoscopic radical prostatectomy: A randomized controlled trial. Medicine (Baltimore). 97(41):e12772.
77. Yu J., Hong J.H., Park J.Y., Hwang J.H., Cho S.S., and Kim Y.K. 2018. Propofol attenuates the increase of sonographic optic nerve sheath diameter during robot-assisted

laparoscopic prostatectomy: a randomized clinical trial. BMC Anesthesiol. 18(1):72.
78. Yu J., Park J.Y., Kim D.H., Koh G.H., Jeong W., and Kim E., et al. 2019. Dexmedetomidine attenuates the increase of ultrasonographic optic nerve sheath diameter as a surrogate for intracranial pressure in patients undergoing robot-assisted laparoscopic prostatectomy: A randomized double-blind controlled trial. Medicine (Baltimore). 98(33):e16772.
79. Geng W., Chen C., Sun X., and Huang S. 2021. Effects of sevoflurane and propofol on the optic nerve sheath diameter in patients undergoing laparoscopic gynecological surgery: a randomized controlled clinical studies. BMC Anesthesiol. 21(1):30.
80. You A.H., Song Y., Kim D.H., Suh J., Baek J.W., and Han D.W. 2019. Effects of positive end-expiratory pressure on intraocular pressure and optic nerve sheath diameter in robot-assisted laparoscopic radical prostatectomy: A randomized, clinical trial. Medicine (Baltimore). 98(14):e15051.
81. Romagnuolo L., Tayal V., Tomaszewski C., Saunders T., and Norton H.J. 2005. Optic nerve sheath diameter does not change with patient position. Am J Emerg Med. 23(5):686-688.
82. Yu J., Park J.Y., Kim D.H., Koh G.H., Kim S., and Hwang J., et al. 2020. Effect of neck extension on ultrasonographic optic nerve sheath diameter as a surrogate for intracranial pressure in patients undergoing palatoplasty: A prospective observational study. J Plast Reconstr Aesthet Surg. 73(2):369-375.
83. Altiparmak B., Toker M.K., Uysal A.İ., Köseoğlu S., and Gümüş Demirbilek S. 2020. Evaluation of the effect of the mouth gag use on optic nerve sheath diameter of pediatric patients undergoing tonsillectomy or Adenotonsillectomy: An observational study. BMC Anesthesiol. 20(1):163.
84. Seo H., Kim Y.K., Shin W.J., and Hwang G.S. 2013. Ultrasonographic optic nerve sheath diameter is correlated with arterial carbon dioxide concentration during reperfusion in liver transplant recipients. Transplant Proc. 45(6):2272-2276.
85. Sanri E., and Karacabey S. 2019. The Impact of Head of Bed Elevation on Optic Nerve Sheath Diameter in Cervical Collar Applied Healthy Volunteers. J Emerg Med. 56(4):371-377.
86. Maissan I.M., Verbaan L.A., van den Berg M., Houmes R.J., Stolker R.J., and den Hartog D. 2018. Helicopter Transportation Increases Intracranial Pressure: a Proof-of-Principle Study. Air Med J. 37(4):249-252.
87. Yang Z., Qin C., Zhang S., Liu S., and Sun T. 2020. Bedside ultrasound measurement of optic nerve sheath diameter in patients with sepsis: a prospective observational study. Crit Care. 24(1):235.
88. Roque P.J., Wu T.S., Barth L., Drachman D., Khor K.N., Lovecchio F., and Stapczynski S. 2012. Optic nerve ultrasound for the detection of elevated intracranial pressure in the hypertensive patient. Am J Emerg Med. 30(8):1357-63.
89. Dubost C., Le Gouez A., Jouffroy V., Roger-Christoph S., Benhamou D., Mercier F.J., and Geeraerts T. 2012. Optic nerve sheath diameter used as ultrasonographic assessment of the incidence of raised intracranial pressure in preeclampsia: a pilot study. Anesthesiology. 116(5):1066-1071.
90. Bržan-Šimenc G., Ambrozic J., Prokselj K., Tul N., Cvijic M., Mirkovic T., and Lucovnik M. 2018. Ocular ultrasonography for diagnosing increased intracranial pressure in patients with severe preeclampsia. Int J Obstet Anesth. 36:49-55.
91. Singh S.K., and Bhatia K. 2018. Ultrasonographic Optic Nerve Sheath Diameter as a Surrogate Measure of Raised Intracranial Pressure in Severe Pregnancy-induced Hypertension Patients. Anesth Essays Res. 12(1):42-46.
92. Ortner C.M., Krishnamoorthy V., Neethling E., Flint M., Swanevelder J.L., and Lombard C., et al. 2019. Point-of-Care Ultrasound Abnormalities in Late-Onset Severe Preeclampsia: Prevalence and Association With Serum Albumin and Brain Natriuretic Peptide. Anesth Analg. 128(6):1208-1216.
93. Assu S.M., Bhatia N., Jain K., Gainder S., Sikka P., and Aditya A.S. 2021. Sonographic Optic Nerve Sheath Diameter Following Seizure Prophylaxis in Pre-Eclamptic Parturients With Severe Features: A Prospective, Observational Study. J Ultrasound Med. Online ahead of print.
94. Bržan-Šimenc G., Ambrozic J., Prokselj K., Tul N., Cvijic M., and Mirkovic T., et al. 2018. Optic nerve ultrasound for fluid status assessment in patients with severe preeclampsia. Radiol Oncol. 52(4):377-382.
95. Rajajee V., Williamson C.A., Fontana R.J., Courey A.J., and Patil P.G. 2018. Noninvasive Intracranial Pressure Assessment in Acute Liver Failure. Neurocrit Care. 29(2):280-290.
96. Das M.C., Srivastava A., Yadav R.K., Yachha S.K., and Poddar U. 2020. Optic nerve sheath diameter in children with acute liver failure: A prospective observational pilot study. Liver Int. 40(2):428-436.
97. Vijay P., Lal B.B., Sood V., Khanna R., Patidar Y., and Alam S. 2021. Dynamic Optic Nerve Sheath Diameter (ONSD) guided management of raised intracranial pressure in pediatric acute liver failure. Hepatol Int. 2021 Feb 24. Online ahead of print.
98. Fichtner J., Ulrich C.T., Fung C., Cipriani D., Gralla J., and Piechowiak E.I., et al. 2019. Sonography of the optic nerve sheath diameter before and after microsurgical closure of a dural CSF fistula in patients with spontaneous intracranial hypotension - a consecutive cohort study. Cephalalgia. 39(2):306-315.
99. Bhandari D., Bidkar P.U., Adinarayanan S., Narmadhalakshmi K., and Srinivasan S. 2019. Measurement of changes in optic nerve sheath diameter using ultrasound and computed tomography scan before and after the ventriculoperitoneal shunt surgery in patients with hydrocephalus - A prospective observational trial. Br J Neurosurg. 33(2):125-130.
100. Hall M.K., Spiro D.M., Sabbaj A., Moore C.L., Hopkins K.L., and Meckler G.D. 2013. Bedside optic nerve sheath diameter ultrasound for the evaluation of suspected pediatric ventriculoperitoneal shunt failure in the emergency department. Childs Nerv Syst. 29(12):2275-2280.
101. Lin S.D., Kahne K.R., El Sherif A., Mennitt K., Kessler D., Ward M.J., and Platt S.L. 2019. The Use of Ultrasound-Measured Optic Nerve Sheath Diameter to Predict Ventriculoperitoneal Shunt Failure in Children. Pediatr Emerg Care. 35(4):268-272.
102. Gao Y., Li Q., Wu C., Liu S., and Zhang M. 2018. Diagnostic and prognostic value of the optic nerve sheath diameter with respect to the intracranial pressure and neurological outcome of patients following hemicraniectomy. BMC Neurol. 18(1):199.
103. Wang J., Li K., Li H., Ji C., Wu Z., Chen H., and Chen B. 2019. Ultrasonographic optic nerve sheath diameter correlation with ICP and accuracy as a tool for noninvasive surrogate ICP measurement in patients with decompressive craniotomy. J Neurosurg. 133(2):514-520.
104. Raffiz M., and Abdullah J.M. 2017. Optic nerve sheath diameter measurement: a means of detecting raised ICP in adult traumatic and non-traumatic neurosurgical patients. Am J Emerg Med. 35(1):150-153.
105. Lochner P., Leone M.A., Coppo L., Nardone R., Zedde M.L., Cantello R., and Brigo F. 2016. B-mode transorbital ultrasononography for the diagnosis of acute optic neuritis. A systematic review. Clin Neurophysiol. 127(1):803-809.

106. Blaivas M., Theodoro D., and Sierzenski P.R. 2003. Elevated intracranial pressure detected by bedside emergency ultrasonography of the optic nerve sheath. Acad Emerg Med. 10(4):376-381.
107. Canakci Y., Koksal O., and Durak V.A. 2018. The value of bedside ocular ultrasound assessment of optic nerve sheath diameter in the detection of increased intracranial pressure in patients presenting to the emergency room with headache. Niger J Clin Pract. 21(6):778-782.
108. Kishk N.A., Ebraheim A.M., Ashour A.S., Badr N.M., and Eshra M.A. 2018. Optic nerve sonographic examination to predict raised intracranial pressure in idiopathic intracranial hypertension: The cut-off points. Neuroradiol J. 31(5):490-495.
109. Lochner P., Fassbender K., Knodel S., Andrejewski A., Lesmeister M., and Wagenpfeil G., et al. 2019. B-Mode Transorbital Ultrasonography for the Diagnosis of Idiopathic Intracranial Hypertension: A Systematic Review and Meta-Analysis. Ultraschall Med. 40(2):247-252.
110. Nabeta H.W., Bahr N.C., Rhein J., Fossland N., Kiragga A.N., and Meya D.B., et al. 2014. Accuracy of noninvasive intraocular pressure or optic nerve sheath diameter measurements for predicting elevated intracranial pressure in cryptococcal meningitis. Open Forum Infect Dis. 1(3):ofu093.
111. Donovan J., Oanh P.K.N., Dobbs N., Phu N.H., Nghia H.D.T., and Summers D., et al. 2020. Optic nerve sheath ultrasound for the detection and monitoring of raised intracranial pressure in tuberculous meningitis. Clin Infect Dis. ciaa1823. Online ahead of print.
112. Gökcen E., Caltekin İ., Savrun A., Korkmaz H., Savrun Ş.T., and Yıldırım G. 2017. Alterations in optic nerve sheath diameter according to cerebrovascular disease subgroups. Am J Emerg Med. 35(11):1607-1611.
113. Seyedhosseini J., Aghili M., Vahidi E., and Shirani F. 2019. Association of optic nerve sheath diameter in ocular ultrasound with prognosis in patients presenting with acute stroke symptoms. Turk J Emerg Med. 19(4):132-135.
114. Lochner P., Fassbender K., Andrejewski A., Behnke S., Wagenpfeil G., and Fousse M., et al. 2020. Sonography of optic nerve sheath diameter identifies patients with middle cerebral artery infarction at risk of a malignant course: a pilot prospective observational study. J Neurol. 267(9):2713-2720.
115. Manouchehrifar M., Lakestani M., Kashani P., and Safari S. 2018. Sonographic diameter of optic nerve sheath in differentiation of ischemic and hemorrhagic strokes; a diagnostic accuracy study. Am J Emerg Med. 36(11):2064-2067.
116. Moretti R., and Pizzi B. 2009. Optic nerve ultrasound for detection of intracranial hypertension in intracranial hemorrhage patients: confirmation of previous findings in a different patient population. J Neurosurg Anesthesiol. 21(1):16-20.
117. Vaiman M., Sigal T., Kimiagar I., and Bekerman I. 2016. Noninvasive assessment of the intracranial pressure in non-traumatic intracranial hemorrhage. J Clin Neurosci. 34:177-181.
118. Naldi A., Pivetta E., Coppo L., Cantello R., Comi C., and Stecco A., et al. 2019. Ultrasonography Monitoring of Optic Nerve Sheath Diameter and Retinal Vessels in Patients with Cerebral Hemorrhage. J Neuroimaging. 29(3):394-399.
119. Lee S., Kim Y.O., Baek J.S., and Ryu J.A. 2019. The prognostic value of optic nerve sheath diameter in patients with subarachnoid hemorrhage. Crit Care. 23(1):65.
120. Lee S.H., and Yun S.J. 2019. Diagnostic performance of optic nerve sheath diameter for predicting neurologic outcome in post-cardiac arrest patients: A systematic review and meta-analysis. Resuscitation. 138:59-67.
121. Zhang Y.W., Zhang S., Gao H., Li C., and Zhang M.X. 2020. Prognostic Role of Optic Nerve Sheath Diameter for Neurological Outcomes in Post-Cardiac Arrest Patients: A Systematic Review and Meta-Analysis. Biomed Res Int. 2020:5219367.
122. Toscano M., Spadetta G., Pulitano P., Rocco M., Di Piero V., Mecarelli O., and Vicenzini E. 2017. Optic Nerve Sheath Diameter Ultrasound Evaluation in Intensive Care Unit: Possible Role and Clinical Aspects in Neurological Critical Patients' Daily Monitoring. Biomed Res Int. 2017:1621428.
123. Yazar M.A. 2019. Bedside Ultrasonography of the Optic Nerve Sheath in Brain Death. Transplant Proc. 51(7):2180-2182.
124. Kimberly H.H., Shah S., Marill K., and Noble V. 2008. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. Acad Emerg Med. 15(2):201-204.
125. Dubourg J., Javouhey E., Geeraerts T., Messerer M., and Kassai B. 2011. Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: a systematic review and meta-analysis. Intensive Care Med. 37(7):1059-1068.
126. Koziarz A., Sne N., Kegel F., Nath S., Badhiwala J.H., and Nassiri F., et al. 2019. Bedside Optic Nerve Ultrasonography for Diagnosing Increased Intracranial Pressure: A Systematic Review and Meta-analysis. Ann Intern Med. 171(12):896-905.
127. Lee S.H., Kim H.S., and Yun S.J. 2020. Optic nerve sheath diameter measurement for predicting raised intracranial pressure in adult patients with severe traumatic brain injury: A meta-analysis. J Crit Care. 56:182-187.
128. Wang L., Feng L., Yao Y., Wang Y., Chen Y., Feng J., and Xing Y. 2015. Optimal optic nerve sheath diameter threshold for the identification of elevated opening pressure on lumbar puncture in a Chinese population. PLoS One. 10(2):e0117939.
129. Avci M., Kozaci N., Komut E., Komut S., Caliskan G., and Tulubas G. The Measurement of Elderly Volunteers' Optic Nerve Sheath Diameters by Ocular Ultrasonography. Medicina (Kaunas). 55(8):413.
130. Kane S.C., Dennis A.T., Da Silva Costa F., Kornman L.H., Cade T.J., and Brennecke S.P. 2019. Optic nerve sonography and ophthalmic artery Doppler velocimetry in healthy pregnant women: an Australian cohort study. J Clin Ultrasound. 47(9):531-539.
131. Komut E., Murat M., Büyükşireci M., Komut S., and Kozaci N. 2021. Relationship between internal carotid artery stenosis grade and optic nerve sheath diameter measured by transorbital ultrasonography. J Clin Ultrasound. Online ahead of print.
132. Robba C., Cardim D., Tajsic T., Pietersen J., Bulman M., and Donnelly J., et al. 2017. Ultrasound non-invasive measurement of intracranial pressure in neurointensive care: A prospective observational study. PLoS Med. 2017;14(7):e1002356.
133. Robba C., Pozzebon S., Moro B., Vincent J.L., Creteur J., and Taccone F.S. 2020. Multimodal non-invasive assessment of intracranial hypertension: an observational study. Crit Care. 24(1):379.
134. Capizzi A., Woo J., and Verduzco-Gutierrez M. 2020. Traumatic Brain Injury: An Overview of Epidemiology, Pathophysiology, and Medical Management. Med Clin North Am. 104(2):213-238.
135. Blyth B.J., and Bazarian J.J. 2010. Traumatic alterations in consciousness: traumatic brain injury. Emerg Med Clin North Am. 28(3):571-594.
136. Sadrameli S.S., Wong M.S., Kabir R., Wiese J.R., Podell K., Volpi J.J., Gadhia R.R. 2018. Changes in Transcranial Sonographic Measurement of the Optic Nerve Sheath

Diameter in Non-concussed Collegiate Soccer Players Across a Single Season. Cureus. 10(8):e3090.
137. Legrand A., Jeanjean P., Delanghe F., Peltier J., Lecat B., and Dupont H. 2013. Estimation of optic nerve sheath diameter on an initial brain computed tomography scan can contribute prognostic information in traumatic brain injury patients. Crit Care. 17(2):R61.
138. Sekhon M.S., McBeth P., Zou J., Qiao L., Kolmodin L., and Henderson W.R., et al. 2014. Association between optic nerve sheath diameter and mortality in patients with severe traumatic brain injury. Neurocrit Care. 21(2):245-52.
139. Al-Hassani A., Strandvik G., Abayazeed S., Ahmed K., El-Menyar A., and Mahmood I., et al. 2020. Relationship of Optic Nerve Sheath Diameter and Intracranial Hypertension in Patients with Traumatic Brain Injury. J Emerg Trauma Shock. 13(3):183-189.
140. Houzé-Cerfon C.H., Bounes V., Guemon J., Le Gourrierec T., and Geeraerts T. 2018. Quality and Feasibility of Sonographic Measurement of the Optic Nerve Sheath Diameter to Estimate the Risk of Raised Intracranial Pressure After Traumatic Brain Injury in Prehospital Setting. Prehosp Emerg Care. 23(2):277-283.
141. Gerber S., Jallais M., Greer H., McCormick M., Montgomery S., and Freeman B., et al. 2017. Automatic Estimation of the Optic Nerve Sheath Diameter from Ultrasound Images. Imaging Patient Cust Simul Syst Point Care Ultrasound (2017). 10549:113-120.
142. Meiburger K.M., Naldi A., Michielli N., Coppo L., Fassbender K., Molinari F., and Lochner P. 2020. Automatic Optic Nerve Measurement: A New Tool to Standardize Optic Nerve Assessment in Ultrasound B-Mode Images. Ultrasound Med Biol. 46(6):1533-1544.
143. Teasdale G., and Jennett B. 1974. Assessment of coma and impaired consciousness. A practical scale. Lancet. 2(7872):81-84.