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Review Article

Point-of-care ultrasound of optic nerve sheath diameter to detect intracranial pressure in neurocritically ill children - A narrative review

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ABSTRACT

The rapid diagnosis of increased intracranial pressure is urgently needed for therapeutic reasons in neurocritically ill children, however this can rarely be achieved without invasive procedures. Point-of-care ultrasound of the optic nerve sheath diameter has been proposed as a non-invasive and reliable means to detect increased intracranial pressure in adults. Accordingly, clinicians may be able to use this technique to initiate early treatment and monitor the effectiveness of treatment in conjunction with other clinical examination and diagnostic modalities. Two meta-analyses and a systematic review have been published on this topic in adults. However, data on the correlation between optic nerve sheath diameter and intracranial pressure in neurocritically ill children are scarce. The aim of this review was to briefly describe what is being measured with point-of-care ultrasound of the optic nerve sheath diameter, summarize the most recent findings from adult literature, and provide an update of current work in children.

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Many underlying pathologies are associated with increased intracranial pressure (ICP) in children with acute encephalopathy. Increased ICP is an important cause of secondary brain injury, and it has been associated with poor neurological outcomes after a traumatic brain injury [1]. Therefore, monitoring and treating increased ICP is crucial in the management of neurocritically ill children. Invasive ICP measurements are currently the gold standard for the initial diagnosis and follow-up evaluations of ICP in terms of accurate and real-time measurements. However, invasive techniques are associated with a risk of complications such as hemorrhage and infection. Furthermore, most children with acute encephalopathy do not receive invasive ICP monitoring. Therefore, a reliable, simple, non-invasive bedside method to detect ICP in children is needed.

Some non-invasive methods for measuring ICP can be used as alternatives to invasive techniques, including transcranial Doppler, tympanic membrane displacement, optic nerve sheath diameter (ONSD), computed tomography (CT), magnetic resonance imaging (MRI), and fundoscopy [2]. These non-invasive techniques do not carry the risk of complications as with invasive methods. Recently, adult studies have reported that measuring ONSD with non-invasive imaging technologies such as CT, MRI and ultrasound can be used as an alternative method to evaluate increased ICP [3–6]. However, CT and MRI for ONSD measurements are time-consuming, costly and usually require patient transportation. Thus, ultrasound assessments of ONSD could be a better option because of the low cost and rapid bedside operation without the need for radiation exposure, especially for cases that are unstable and require real-time monitoring of ICP in an intensive care unit [4,7].

A point-of-care testing is defined as an investigation taken near the patient at the time of the consultation with instant availability of results to make immediate and informed decisions about patient care. Point-of-care ultrasound (POCUS) of ONSD has been proposed as a non-invasive and quick method to identify increased ICP. Two meta-analyses and a systematic review have shown that bedside POCUS of ONSD can be used to detect increased ICP with good diagnostic test accuracy in adults [5,8,9]. However, data on the correlation between POCUS of ONSD and ICP in

neurocritically ill children are scarce. Therefore, the aim of this review was to briefly describe what is being measured with POCUS of ONSD, summarize the most recent findings from adult literature, and provide an update of current work in children.

Signs of increased ICP can manifest in the eye: what do we know?

Papilledema, optic disc swelling caused by increased ICP due to any cause, has often been used for screening suspected increased ICP. However, as optic disc swelling in cases of increased ICP takes time [10], papilledema on fundoscopic examination is not used in emergency situations such as an acute increase in ICP [2,11].

ICP has been correlated with ONSD. The optic nerve is enveloped by the optic nerve sheath which surrounds the optic subarachnoid space and is directly linked to the intracranial subarachnoid space [12]. An increase in ICP causes cerebral spinal fluid to move from the intracranial cavity into the optic subarachnoid space, thereby resulting in distension of the optic nerve sheath and widening of its diameter [12,13]. Therefore, changes in ICP are reflected in the ONSD [13–15]. Cadaveric studies have shown that maximal sheath distension occurs at 3 mm behind the papilla [13,14]. In addition, an abnormally wide ONSD may be an early finding of increased ICP, preceding the development of papilledema [15].

Ultrasound technique and the relevant anatomy of ocular sonography

Image acquisition

In general, a high frequency high-resolution (5–14 MHz) linear array probe is used for examinations. For ocular ultrasound, an ocular preset should be used with a limit of thermal index (TI) ≤ 1 , mechanical index (MI) ≤ 0.23 , and an intensity limit of ≤ 50 mW/cm² according to the As Low As Reasonably Achievable (ALARA) principle of ultrasonic instrumentation [16].

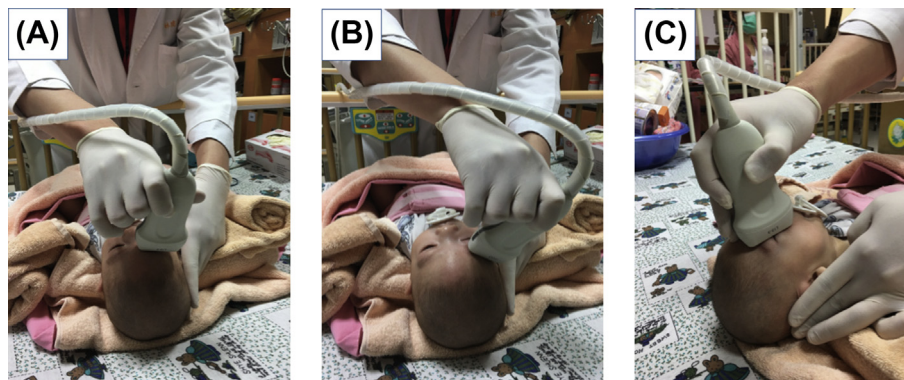


Fig. 1 Technique for measuring sonographic optic nerve sheath diameter using an (A) anterior axis, (B) lateral axis, and (C) vertical axis transbulbar approach.

The patients are examined in a supine relaxed position. The probe is gently placed on the closed eyelid with a standard ultrasound gel and adjusted to a suitable angle to display the optic nerve entry into the eyeball. There are no serious side effects or risks of ultrasound gel, but only unpleasant side-effects. Some ultrasound gels can leave behind a greasy, sticky, or tacky residue or cause drying of the skin. This is typically true of oil-based gels or those that use propylene glycol as a conditioning agent. A clear film adhesive strip can be placed over the eye for added protection with care to avoid trapping of air bubbles underneath. With the patient in this supine position, images used to measure ONSD are obtained via horizontal (anterior axial and lateral axial) and vertical axial transbulbar approaches (Fig. 1) [15–17]. We should avoid scanning through the lens in order to avoid theoretical thermal damage to lens. The relevant anatomy to be identified with ocular ultrasound is shown in Fig. 2. The probe has to be adjusted in order to display the entrance of the optic nerve into the ocular globe. ONSD is determined by measuring the diameter from the inner-edge to inner-edge of the optic nerve sheath at 3 mm behind the globe, using the optic disc as a reference point. Each of three or more such measurements using horizontal and vertical transbulbar approaches are averaged to calculate a final value of ONSD [15–17]. Besides, there has also been described a coronal approach that gives a cross sectional cut of the optic nerve which usually makes it easier to measure the true ONSD and avoids problems with measurement when the nerve is tortuous as it often is in kids (Fig. 3) [18,19].

Papilledema, optic disc swelling, is also a sign for increased ICP. Ocular ultrasound has been also used to detect papilledema. Optic nerve head elevation which has been correlated with optic disc swelling, and is one of the easiest things to see.

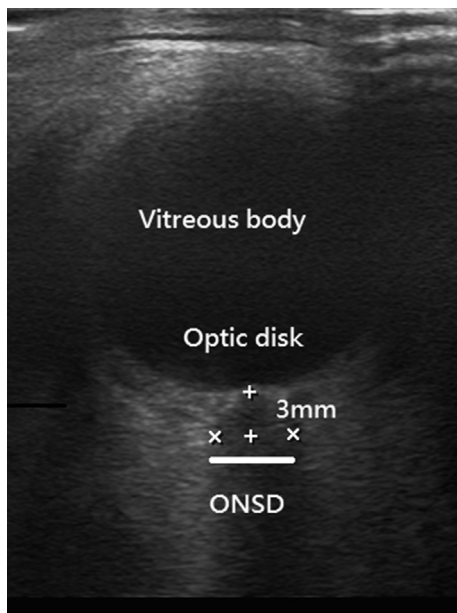


Fig. 2 Representative ultrasound images from anterior transbulbar ultrasonography. ONSD is determined by measuring the diameter from the inner-edge to inner-edge of the optic nerve sheath at 3 mm behind the globe, using the optic disc as a reference point. (+..+ : 3 mm behind the globe; x..x : ONSD: optic nerve sheath diameter).

Optic disc elevation was defined as elevation 1 mm or greater above the retina in either the horizontal or vertical axial orientation [18,20]. One caveat is that benign drusen can mimic this. Optic disc elevation (>1 mm) as a secondary sign may worth investigating more in future studies.

Imaging interpretation and results

The relationship between ONSD and ICP is complex. The width and dynamics of ONSD changes are affected not only by ICP, but probably also by age, patency of the anterior fontanelle and type of pathology. In children, the ONSD grows most during the first year of life [14]. Kerscher et al. showed that children >1 year had a better correlation between ICP and ONSD ($r = 0.63$; $p < 0.01$) and those ≤ 1 year a worse correlation ($r = 0.21$) [21]. Therefore, ONSD to detect ICP should be used with caution in children ≤ 1 year. In addition, no correlation has been reported in infants with an open fontanelle [21]. Similarly, normal ICP values vary according to age, and in general are <10–15 mmHg for adults and older children, 3–7 mmHg for young children, and 1.5–6 mmHg for term infants [22]. The threshold above which the ICP level should be considered abnormal also varies depending on age. Therefore, the abnormal upper limit of ICP should not be strictly defined as 20 mmHg in children. Kerscher et al. reported the correlations between different cut-off values for ICP and ONSD. In their study, in children >1 year, the best ONSD cut-off values for detecting ICP ≥ 10 and ≥ 15 mmHg were 5.28 and 5.57 mm (odds ratio [OR] 5.3 and 9, area under the curve [AUC] 0.981 and 0.770), respectively, compared to 4.65 and 4.99 mm (OR 2.75 and 6.75, AUC 0.556 and 0.699), respectively, in children < 1 year [23]. In addition, they reported that other factors affected the width and dynamics of ONSD changes including the duration of ICP increase, intraocular pressure, and disturbed communication between optic and intracranial subarachnoid spaces [23].

At present, intensive care and emergency POCUS literature typically uses the following cutoff values, as measured inner-edge to inner-edge, for the upper limit of normal ONSD: 5.0 mm in adults (>15 years of age), 4.5 mm in children aged 1–15 years, and 4.0 mm in infants < 1 year of age [13–15,24–26].

Recognize specific pearls and pitfalls with ocular POCUS

It is important to recognize specific pearls and pitfalls with the use of ultrasound of ONSD in children. First, a small linear probe is better than a large linear probe as it may provide better contact with the globe. Second, measurement of the optic nerve sheath requires a scanning plane in the middle of the nerve (to avoid underestimation of the diameter). If there is trouble finding the nerve in one plane, try another orbital approach, or attempt a coronal approach which takes a cross-sectional cut through the optic nerve and nerve sheath which can mitigate this type of measurement error [18,19]. Third, images that are low in quality or resolution can lead to inaccurate measurements. The gain setting when performing the examination can cause a blooming effect, which means that decreasing the gain will cause the ONSD to appear enlarged. Fourth, an inexperienced clinician

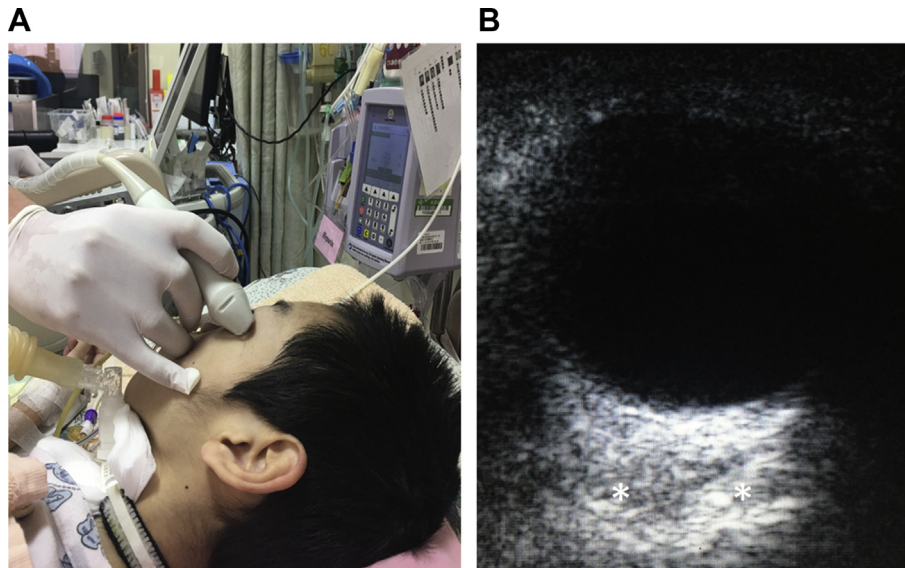


Fig. 3 Technique and representative ultrasound images for a coronal approach. (A) Linear array transducer placed inferior to the closed eye to obtain a coronal image. (B) B-mode image showing a cross sectional cut of the optic nerve. (*..* ONSD: optic nerve sheath diameter).

that starts using POCUS of ONSD in a clinical setting needs to be sure of accurate visualization of the anatomical structures and of the possibility of errors or artifacts [27,28]. Fifth, the optic nerve in children can be tortuous, and care should be taken to perform measurements perpendicular to the axis of the nerve. Since the central retinal artery and vein pass centrally through the optic nerve, color Doppler will help the examiner to correctly identify the optic nerve and avoid errors in interpreting the ONSD (Fig. 4) [27,29]. Sixth, in the anterior transbulbar approach, the artifact of lamina cribrosa increases the diameter of the optic nerve [27]. In addition, ocular muscles can be confused with the optic nerve,

although they are usually distinguishable from the optic nerve in that they are usually much thinner and arise laterally on the globe rather than centrally [30].

Relevant adult-specific literature

The correlation between POCUS of ONSD and ICP in adults

The correlation between POCUS of ONSD and ICP, either with invasive ICP monitoring, CT imaging or lumbar puncture, has been reported to be high in adults with brain injury. A

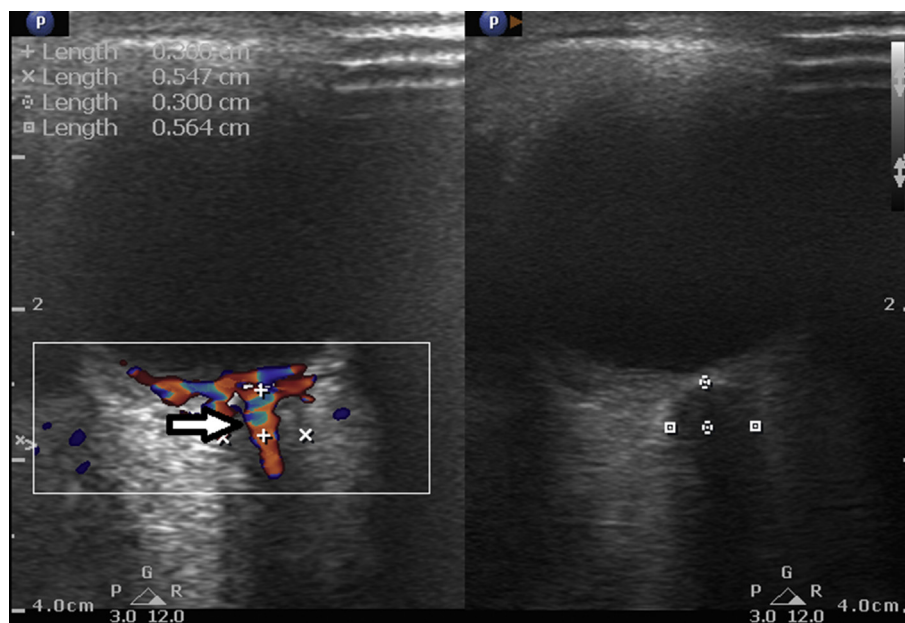


Fig. 4 Optic nerve in children can be tortuous. Since the central retinal artery (white arrow) passes centrally through the optic nerve, color Doppler will help the examiner to correctly identify the optic nerve and avoid errors in interpreting the ONSD.

systematic review compared POCUS of ONSD with invasive ICP monitoring (with an ONSD cut-off value ranging from >5.0 to 5.9 mm), and reported a pooled sensitivity of 90% (95% confidence interval [CI] 80–95%) and pooled specificity of 85% (95% CI 73–93%) [5]. A recent meta-analysis assessed the diagnostic accuracy of POCUS of ONSD (with a cut-off value of > 5 mm) compared with findings of increased ICP on CT imaging, and reported a pooled sensitivity of 95.6% (95% CI 87.7–98.5%) and specificity of 92.3% (95% CI 77.9–98.4%) [8]. A recent systematic review focused on the diagnostic accuracy of POCUS of ONSD to evaluate increased ICP in adults (defined as ICP > 20 mmHg or > 25 cm H₂O), and included seven prospective studies (320 patients). The pooled diagnostic OR, positive likelihood ratio and negative likelihood ratio were 67.5 (95% CI 29–135), 5.35 (95% CI 3.76–7.53) and 0.088 (95% CI 0.046–0.152), respectively, with an AUC of 0.938 [9]. Although two systematic reviews and one meta-analysis study have shown excellent sensitivity and specificity of POCUS of ONSD in the detection of increased ICP, the different cut-off value and relatively wide range of 95% CIs in the pooled diagnostic OR suggest that the data should be interpreted with caution.

POCUS of ONSD reflects immediate changes in ICP in adults

An important finding is that ONSD reflects immediate changes in ICP. Several adult studies have shown that POCUS of ONSD changes within minutes of pressure change, and demonstrated that the change in POCUS of ONSD is strongly correlated with changes in ICP ($r = 0.67$ to 0.90), implying that POCUS of ONSD could be used to dynamically detect real-time changes in ICP [31–35]. The median change in ONSD (Δ ONSD) and change in ICP (Δ ICP) were 0.11 mm and 30 mm H₂O, respectively [32]. The other study investigated the effect of osmotic therapy on POCUS of ONSD in patients with increased ICP [36]. The authors found a statistically significant correlation between ONSD and ICP before (median ICP and ONSD values of 35 mmHg and 6.3 mm) and after treatment with mannitol (median ICP and ONSD values of 25 mmHg and 5.7 mm) ($r^2 = 0.54$; $p < 0.002$). Although the technique does not seem to be accurate enough to be used as a replacement for invasive ICP measuring methods, it can potentially be used as a screening method for detecting increased ICP when invasive ICP monitoring is not indicated or available in neurocritically ill adults.

Relevant pediatric-specific literature

The correlation between POCUS of ONSD and ICP in children

Studies of POCUS of ONSD in children undergoing evaluations for increased ICP are limited to small prospective and retrospective case series [15,17,18,21,23–25,37–46]. These studies have compared POCUS of ONSD with clinical signs of increased ICP on CT imaging or direct ICP measurements by lumbar puncture or invasive intracranial monitoring devices. The causes of a suspected or truly increased ICP varied and were divided into traumatic or non-traumatic. A summary of the characteristics and outcomes of the studies assessing POCUS of

ONSD in children who were suspected of having an increased ICP is presented in Table 1 [15,17,18,21,23–25,37–46].

A large case-control study showed that POCUS of ONSD was significantly greater in pediatric patients with signs of increased ICP on CT compared with a control group (ICP group: 5.6 ± 0.6 mm vs control group: 3.3 ± 0.6 mm, $p < 0.001$) [38]. Kerscher et al. reported 28 ICP-monitored children who had a sustained increase in ICP with different etiologies [21]. The correlation between ICP and POCUS of ONSD was high ($r = 0.802$, $p < 0.01$), although with strongly differing individual regression curves. Therefore, even if there is a good overall ONSD-ICP correlation, every individual has their own distinctive and precise correlation line [21]. Intensive care and emergency POCUS typically uses the following cut-off values for the POCUS of ONSD to evaluate increased ICP in children: upper limit of normal ONSD of 5.0 mm in adults (>15 years of age), 4.5 mm in children aged 1–15 years, and 4.0 mm in infants < 1 year of age [13–15,24–26]. Several publications have described the use of these measurements in the evaluation of children at risk of ICP in a clinical setting, and have shown wide ranges of sensitivity (11%–83%) and specificity (18–97%) of POCUS of ONSD in the detection of increased ICP [15,18,41–43]. A recent summary of the evidence showed that POCUS of ONSD in pediatric emergency medicine demonstrated variable results in predicting increased ICP. Further studies are needed to evaluate the role of POCUS of ONSD in the assessment of increased ICP in children [47].

POCUS of ONSD reflects immediate changes in ICP in children

The real-time detection of ICP is an important issue for the diagnosis and management of ICP in neurocritically ill children. Kerscher et al. studied 30 ICP-monitored patients who had increased ICP [23], and after treatment for the increased ICP, all POCUS of ONSD values decreased significantly (5.7 ± 0.69 mm versus 5.0 ± 0.58 mm, $p < 0.01$), although there was no correlation between Δ ICP (10.3 ± 6.8 mmHg) and Δ ONSD (0.7 ± 0.33 mm) ($r = 0.16$, $p > 0.05$). However, this indicated that strong decreases in ICP can lead to smaller changes in ONSD and vice versa. Therefore, we do not think that POCUS of ONSD should replace invasive ICP monitoring, but that POCUS of ONSD may be considered as a screening tool in the intensive care unit for intermittent monitoring of ICP when invasive methods are unavailable.

Limitations and further direction

The accurate dynamic evaluation of ICP is particularly crucial since fluctuations are common in children with acute brain injury. In addition, patients who receive treatment need to be monitored and evaluated continuously. POCUS of ONSD can be used as an accurate and quick method to monitor changes in ICP [34]. However, there are several limitations with POCUS of ONSD to detect increased ICP in current practice.

First, although previous studies have established cut-off values for POCUS of ONSD to evaluate increased ICP in

Table 1 Characteristics and outcomes of studies assessing ultrasound measurements of optical nerve sheath diameter in children with suspected increased intracranial pressure.

	Author and year	Study design	Study population and clinical setting	Ultrasound probe	Reference standard	Cut-off value of ONSD (mm)	Sensitivity and specificity of US-ONSD ^a
1	Helmke et al., 1996 [37]	Prospective observational study	24 patients who were suspected of having an increased ICP/ICU	7.5 MHz linear probe	NE, CT, ICP monitoring	ICP \geq 20 mmHg: 5.3 mm	NM
2	Newman et al., 2002 [15]	Retrospectively study	23 children with shunted hydrocephalus/NM	7 MHz linear probe	NE, CT and Shunt revised	>1 year old: 4.5 mm \leq 1 year old: 4.0 mm	NM
3	Malayeri et al., 2005 [38]	Case-control study	156 patients who were suspected of having an increased ICP/non-ICU+ICU	7.5 MHz linear probe	CT, brain sonography, funduscopy	ICP group: 5.6 \pm 0.6 mm Control group: 3.3 \pm 0.6 mm	NM
4	Körber et al., 2005 [25]	Retrospectively study	483 patients who were suspected of having an increased ICP/NM	5 MHz linear probe	NE, EEG, CT and/or MRI	4.5 mm	NM
5	Tsung et al., 2005 [39]	Case series	3 children with head trauma/ED	7 MHz linear probe	NE, CT and Shunt revised	Age >15 years: 5.0 mm Age 1–15 years: 4.5 mm \leq 1 year old: 4.0 mm	NM
6	Beare et al., 2008 [40]	Prospective observational study	14 patients who were suspected of having an increased ICP/NM	7 MHz linear probe	NE, CT	4.2	Sensitivity: 100% Specificity: 86%
7	Le et al., 2009 [41]	Prospective observational study	64 patients who were suspected of having an increased ICP/ED+ICU	8 to 5 MHz linear probe	CT, ICP monitoring, LP	>1 year old: 4.5 mm \leq 1 year old: 4.0 mm	Sensitivity: 83% Specificity: 38%
8	McAuley et al., 2009 [42]	Retrospectively study	160 children with shunted hydrocephalus/NM	8–13 MHz linear probe	Clinical history	>1 year old: 4.5 mm \leq 1 year old: 4.0 mm	NM
9	Driessen et al., 2011 [43]	Prospective observational study	128 patients with syndromic craniosynostosis/NM	8.5 MHz linear probe	Funduscopy	>4 years old: 4.5 mm \leq 4 years:> 4.0 mm	Sensitivity: 11% Specificity: 97%
10	Hall et al., 2013 [17]	Prospective observational study	39 patients who were suspected of having ventriculoperitoneal shunt failure/ED	14 MHz linear probe	Neurosurgical decision to revise the shunt within 2 weeks	5.0 mm	Sensitivity: 61.1% Specificity: 22.2%
11	Marchese et al., 2015 [18]	Case series	4 children who were suspected of having an increased ICP/ED	14 MHz linear probe	Invasive ICP Monitoring, LP and Funduscopy	Age >15 years: 5.0 mm Age 1–15 years: 4.5 mm \leq 1 year old: 4.0 mm	NM
12	Padayachy et al., 2016 [44]	Prospective observational study	174 children who required invasive ICP monitoring/ICU+OR	7–15 MHz linear probe	Invasive ICP Monitoring	ICP \geq 15 mmHg: 5.49 mm ICP \geq 20 mmHg: 5.75 mm	ICP \geq 15 mmHg: Sensitivity: 93.7% Specificity: 74.4% ICP \geq 20 mmHg: Sensitivity: 88.9% Specificity: 84.2%

13	Lin et al., 2019 [45]	Prospective observational study	32 patients who were suspected of having ventriculoperitoneal shunt failure/ED	5–13 MHz linear probe	CT/MRI, Neurosurgical impression	>4 years old: 4.5 mm ≤4 years: 4.0 mm	Compared to CT/MRI: Sensitivity: 60% Specificity: 66.7% Compared to neurosurgical impression: Sensitivity: 75% Specificity: 67.9% NM
14	Kendir et al., 2019 [46]	Prospective observational study	36 children who were suspected of having an increased ICP/ED	6–15 MHz linear probe	Clinical criteria	4.5 mm	
15	Kerscher et al., 2020 [21]	Prospective observational study	72 children who were suspected of having an increased ICP/ICU+OR	12 MHz linear probe	Invasive ICP Monitoring, LP	ICP ≥ 15 mmHg: 5.28 mm ICP ≥ 20 mmHg: 5.57 mm	ICP ≥ 15 mmHg: Sensitivity: 90.9% Specificity: 69.2% ICP ≥ 20 mmHg: Sensitivity: 81.3% Specificity: 62.5%

Abbreviations: NE: neurological examination; CT: computed tomography; ICP: intracranial pressure; LP: lumbar puncture; NM: not mentioned. ONSD: optical nerve sheath diameter; US: ultrasound; ED: emergency department; ICU: intensive care unit; OR: operation room.
^a Sensitivity and specificity by a given cutoff value for detection of a raised ICP (ICP > 20 H₂O) seen on invasive ICP measurements or in cranial CT imaging.

children, there is no consensus regarding the optimal cut-off values of ICP according to age in children. Second, our literature review of POCUS of ONSD in children found marked variability in ONSD. These pediatric studies included different patient populations (e.g. those with traumatic brain injuries, shunted hydrocephalus or all possible causes of increased ICP) and different reference standards (e.g. CT imaging, lumbar puncture or invasive ICP monitoring), and also different sizes of study populations and methodological approaches. Therefore, more data on POCUS of ONSD in children are needed in order to establish both normal and optimal cut-off values of ONSD.

Third, the image quality and equipment requirements of ultrasound to measure ONSD correctly should be standardized. Because most ultrasound probes have a smallest measurable distance of 0.1 mm, accurate measurement of ONSD with satisfactory image quality is important. Sonographic quality criteria for optimizing ONSD measurements in critical care settings have been suggested as mentioned in [Ultrasound technique and the relevant anatomy of ocular sonography](#), and applying them in future studies may help to standardize ONSD calculations [16,48,49].

Fourth, the limitations of variability in how the optic nerve sheath is measured, even from one study to the next which makes it hard to know true cut-off values for normal or abnormal [27,50]. Fifth, the POCUS of ONSD in adults is usually measured at 3 mm behind the globe. When measuring ONSD in pediatric patients (and even in infants), the maximal distensible part of the optic nerve sheath may be much more proximal than in adults. Future research should focus on the different location of ONSD with increased ICP in children [48]. Sixth, a model which could determine an accurate value of ICP by measuring the change in ONSD is needed. We suggest that future research should focus on defining the threshold of POCUS of ONSD with different levels of ICP in children.

Summary

Increased ICP is a frequent complication in neurocritically ill children. Current standard diagnostic methods are invasive and have many drawbacks. Clinicians should also be aware that the time from hospital admission to the placement of invasive ICP monitoring is often greater than 1 h [5]. POCUS of ONSD may fill this gap as it is a safe, noninvasive bedside tool that allows for the real-time assessment of increased ICP and the earlier initiation of management. Although not a new procedure, it appears to have an underutilized application in pediatric neurocritical care. For now, the biggest limitation is the marked variability in POCUS of ONSD reported across pediatric studies in normal healthy children and children with pathological conditions. However, we still suggest that POCUS of ONSD may serve as an alternative qualitative rather than quantitative modality to screen patients with suspected increased ICP in neurocritical care. Furthermore, we suggest that assessments of increased ICP values should not be done with POCUS of ONSD alone, and should always be assessed together with available data from clinical examinations and other diagnostic modalities.

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Conflicts of interest

The authors declare no conflicts of interest.

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