Point of Care Ultrasound of the Optic Nerve

Subjects: Emergency Medicine

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Point of care ultrasound (POCUS) of the optic nerve is easy to learn and has great diagnostic potential. Within emergency medicine, research has primarily focused on its use for the assessment of increased intracranial pressure, but many other applications exist, though the literature is heterogeneous and largely observational. In many of these applications, sonographic optic nerve sheath diameter (ONSD) has moderately high sensitivity and specificity, but the supporting studies are heterogeneous.

Keywords: ultrasound ; point of care ultrasound (POCUS) ; optic nerve ; optic nerve sheath diameter (ONSD)

1. Introduction

Point of care ultrasound (POCUS) is an essential diagnostic and evaluative tool in emergency medicine (EM). While applications such as focused assessment with sonography for trauma (FAST) and focused echocardiography are well established, other applications such as ultrasound assessment of the optic nerve may be less familiar to the average emergency physician (EP). Like other POCUS applications, the advantage of ultrasonography is the ability to perform rapid bedside assessment using a relatively inexpensive, portable, and non-invasive device. It does not require transportation of critically ill patients out of a monitored setting for conventional neuroimaging such as computed tomography (CT) and magnetic resonance imaging (MRI) [1][2]. Further, its use can evaluate the eye in challenging patient populations, such as in pediatrics or in the setting of trauma where swelling of the eyelid can interfere with conventional examination and direct ophthalmoscopy of the eye [3].

Ultrasonography of the optic nerve is best described in the literature for the evaluation of elevated intracranial pressure (ICP), but other applications exist. These include its use in idiopathic intracranial hypertension (IIH), optic neuritis, acute mountain sickness (AMS), and ventriculoperitoneal (VP) shunt assessment [2]. POCUS of the optic nerve may assist EPs in identifying critically ill patients, facilitating advanced imaging, or expediting transportation to appropriate referral centers if advanced neuroimaging capabilities are not available locally [2].

2. Clinical Applications: Increased Intracranial Pressure

The most prominent clinical application of optic nerve POCUS is its diagnostic ability to detect elevated ICP. Kim et al. conducted a prospective observational study in 2021, comparing ultrasound assessment of ONSD with CT of the brain performed within 30 min in patients suspected of raised ICP in the ED [4]. From a total of 199 enrolled patients, 57 were found to have signs of raised ICP on CT scan. The median ONSD on ultrasound in the raised ICP group was significantly higher compared with the normal ICP group (5.7 mm vs. 4.3 mm, $p < 0.001$). These results confirm the findings of another prospective observational study from 2019 by Hanafi et al. where 62 trauma patients were compared with 50 healthy controls [5]. Of the 55 trauma patients with increased ICP on CT scan, sonographic ONSD was 6.06 mm in these patients compared to 4.02 mm in healthy controls.

Ohle et al. published a systematic review and meta-analysis in 2015 comparing trials assessing sonographic ONSD to diagnose elevated ICP compared to CT as the reference standard [6]. They included 12 studies with 478 study subjects in ED and ICU settings and found that ONSD had a sensitivity of 96% (95% CI, 88–99%), specificity 92% (95% CI, 78–98%), diagnostic odds ratio (DOR) 319 (95% CI 79–1290), positive likelihood ratio (+LR) 12.5 (95% CI 4.2–37.5), and negative likelihood ratio (–LR) 0.05 (95% CI 0.02–0.14). The major limitation of this meta-analysis was the moderate-to-high heterogeneity of the included studies.

Recognizing that invasive monitoring is more accurate than CT to detect raised ICP, Robba et al. performed a meta-analysis in 2018 that only included studies using invasive ICP measurement (intraparenchymal, intraventricular, or lumbar puncture [LP]) as the reference standard [7]. Raised ICP was defined as >20 mmHg or >25 cmH_2O. They included seven studies with a total of 320 patients and found a pooled DOR of 68 (95% CI 29–135), +LR 5.4 (95% CI 3.8–7.5) and −LR

0.09 (95% CI 0.05–0.15). Their results are more modest compared to Ohle's systematic review, but this likely relates to a more robust reference standard, fewer included studies, and lower heterogeneity. An updated meta-analysis by Aletreby et al. in 2022 assessed ONSD compared to invasive ICP measurement as the reference standard [8]. They included nine additional studies compared to Robba's systematic review for a total of 619 patients. Their results were similar: pooled sensitivity of 90% (95% CI 85–94%), specificity 85% (95% CI 80–89%), DOR 47 (95% CI 26–83), +LR 6.1 (95% CI 4.4–8.5), and −LR 0.11 (95% CI 0.07–0.18).

The largest meta-analysis of optic nerve POCUS was published by Koziarz et al. in 2019 and included trials with participants in all age groups, sonographers of any training level, and used any reference standard as the comparator [9]. Their analysis included 71 studies with a total of 4551 patients and found a sensitivity and specificity in the traumatic brain injury subgroup of 97% (95% CI 92–99%) and 86% (95% CI 74–93%), respectively. In non-traumatic brain injury, sensitivity was mildly reduced at 92% (95% CI 86–96%) while specificity was similar at 86% (95% CI 77–92%).

Most studies used differing ONSD thresholds to diagnose increased ICP [4][8]. In 2019, Kim et al. attempted to establish a single sonographic ONSD cut point to detect elevated ICP [10]. They included six studies with 352 participants in their final analysis, all utilizing 5 mm as a cut point. They found this cut point provided a pooled sensitivity of 99% (95% CI 96–100%), specificity 73% (95% CI 65–80%), DOR 178 (95% CI 53–599), +LR 4.6 (95% CI 2.0–10.9), and −LR 0.05 (95% CI 0.02–0.14).

In comparison, the physical exam is generally poorly sensitive and specific for elevated ICP. Fernando et al. compared multiple modalities to diagnose elevated ICP, including physical exam and sonographic ONSD. Their meta-analysis found pupillary dilation was insensitive at 28% but moderately specific at 86%. Motor posturing had poor sensitivity and specificity at 54% and 64%, respectively. Decreased level of consciousness was more sensitive at 76% but less specific at 40% [11]. In comparison, sonographic ONSD measurement had a pooled area under the receiver operating characteristic (ROC) curve of 0.94. These authors did not calculate pooled sensitivity and specificity as the included studies used many different optimal cut points for elevated ICP. Finally, while direct ophthalmoscopy can detect elevated ICP based on the presence of papilledema, it is infrequently and poorly performed by EPs [12].

Based on the literature, optic nerve POCUS using an ONSD threshold of 5 mm appears to be a clinically useful and accurate tool to detect elevated ICP in the emergency setting. In general, it seems to be more sensitive than specific, which is clinically appropriate given that it would be undesirable to miss a case of high ICP. However, the lack of large randomized controlled studies limits the widespread use of this tool. POCUS assessment of ONSD cannot replace CT or invasive monitoring to diagnose elevated ICP, but it can be used in an appropriate clinical context to monitor at-risk patients, in patients too unstable to leave a monitored setting, or as a supplementary test in settings where access to advanced neuroimaging is limited.

3. Clinical Applications: Idiopathic Intracranial Hypertension

IIH is a neurologic disorder characterized by diffuse headache, visual abnormalities, and papilledema, most commonly affecting young females with increased body mass index (BMI) [13]. Physicians who are not ophthalmologists may have difficulty performing ophthalmoscopy for a variety of reasons, including limited equipment, lack of experience, or patient factors [14]. Therefore, POCUS of the optic nerve can be an effective alternative means to assess for elevated ICP and assist with the diagnosis of IIH.

Case-control studies have assessed the diagnostic accuracy of sonographic ONSD to detect elevated ICP to diagnose IIH, generally finding good sensitivity and specificity with varying diagnostic thresholds. Dağdelen et al. measured ONSD in 47 subjects with IIH and 50 healthy controls. They found the mean ONSD in IIH patients was increased at 6.4 mm compared with 4.9 mm in controls ($p < 0.001$). They identified an optimal cut point of 5.7 mm, yielding a sensitivity of 100% and specificity of 98% [15]. However, Kishk et al. found more modest results when they compared 99 females with both clinically definite and probable IIH to 35 healthy controls. All cases had both neurologic and ophthalmologic assessment including neuroimaging to rule out other diagnoses. ONSD measurement was performed prior to diagnostic LP. Mean sonographic ONSD was higher in cases than controls (6.57 mm vs. 5.50 mm, $p < 0.001$). Using a cut point of 6.05 mm, sonographic ONSD had only modest sensitivity but good specificity at 73% and 91%, respectively [16]. Their more modest results may be due to the inclusion of nine cases with probable IIH. Smaller studies have demonstrated good diagnostic utility for ONSD measurement. Del Saz-Saucedo et al. studied 30 subjects with suspected IIH, of which 19 were diagnosed with a positive LP. Using a higher cut point of 6.3 mm, sonographic ONSD had a sensitivity of 95% (95% CI 82–100%) and specificity of 91% (95% CI 69–100%) [17]. Finally, Ebraheim et al. studied 24 patients with

suspected IIH, of which 20 were diagnosed with a positive LP. Sonographic ONSD had a sensitivity of 88% and specificity of 100% using a cut point of 6.2 mm [18].

Multiple studies have demonstrated dynamic changes in sonographic ONSD after LP. Jeub et al. found that removal of 30 mL of CSF by LP led to a reduction in ONSD by 0.4 mm and 0.5 mm in the right and left eyes, respectively [13]. In another study, Del Sez-Saucedo found that ONSD decreased by a mean of 0.9 mm after therapeutic LP achieved a CSF pressure of <15 cmH_2O [17]. Even without therapeutic LP, Ebraheim found that after 4 weeks of treatment with acetazolamide alone, ONSD decreased by a mean of 0.4 mm [18].

ONSD appears to have good sensitivity and specificity to diagnose IIH. Further, it can be used to monitor the response to treatment. However, no standardized cut points currently exist, limiting its use as a diagnostic tool. Ultimately, more studies are required to establish a standard cut point to serve as a diagnostic threshold for IIH.

4. Clinical Applications: Optic Neuritis

Optic neuritis is an acute inflammatory disorder of the eye that causes vision disturbance or loss and ocular pain. It is most commonly idiopathic but may be secondary to other disease states, most notably multiple sclerosis [19]. Diagnosis is largely clinical and is aided by MRI [19][20]. Numerous case reports describe increased ONSD when measured by POCUS in patients with optic neuritis, leading to observational studies to research its potential as a diagnostic tool [21][22][23].

Lochner et al. studied 21 patients with first-episode demyelinating unilateral optic neuritis and 21 matched controls. All patients underwent MRI imaging to rule out other causes for their symptoms. They determined that sonographic ONSD was significantly increased compared to the unaffected eye, median 6.3 mm vs. 5.5 mm, respectively, and ONSD was larger in affected eyes than in controls. ONSD of the unaffected eye was similar to controls [24]. Kwon et al. studied 17 patients with new-onset unilateral optic neuritis and found median ONSD to be modestly higher in affected eyes than in unaffected eyes, measuring 5.51 mm and 5.05 mm, respectively [25]. While their findings are modest, they are supportive of the findings from Lochner's study. As only two studies exist, more research is required to establish sonographic ONSD as a useful tool to diagnose optic neuritis.

5. Clinical Applications: Acute Mountain Sickness

Optic nerve sheath sonography has also been explored as a portable and non-invasive surrogate measure for increased ICP in acute altitude illnesses. Although causality is not clearly established, increased ICP has been reported in patients with AMS and high-altitude cerebral edema (HACE). Both entities often overlap with high altitude pulmonary edema (HAPE) [26][27].

Analysis of trekkers at high altitude has demonstrated positive correlation between ONSD and AMS. Fagenholz et al. studied travelers at 4240 m and found the mean ONSD in 69 patients with AMS was significantly larger than 218 patients without AMS. They also identified a positive correlation between ONSD and the Lake Louise Score (LLS) used to diagnose AMS [28]. Similarly, Sutherland et al. followed 13 mountaineers and took serial measurements from sea level to 6400 m, finding a positive correlation between increasing altitude, ONSD, and LLS [29].

However, analysis of healthy volunteers with non-exertional ascent to high altitude has shown conflicting results. Lawley et al. measured ONSD in 23 subjects at sea level and then at 3777 m via cable car ascent. They found ONSD increased significantly with altitude compared to baseline, but the increase was similar in those with and without symptoms of altitude illness [30]. Keyes et al. measured ONSD in a cohort of healthy patients at 1400 m, after rapid ascent to 4300 m via vehicle, and again after oxygen therapy. They found a small increase in mean ONSD in patients with AMS compared to patients without AMS [31]. However, the association was weak, and the majority of ONSD measurements were <5 mm, which is below the typical cut point for elevated ICP.

In contrast, Strapazzon et al. followed a cohort of 19 healthy volunteers and measured ONSD at baseline (262 m) and after helicopter ascent to 3830 m. They found that ONSD increased with altitude in all participants with a peak at 24 h and remained increased at 8 days [32]. In particular, the increase was more pronounced in patients who developed AMS, although this only comprised three participants. Kanaan et al. followed a cohort of 86 healthy adults who drove from 1240 m to 3545 m and then hiked up to 3810 m. All their subjects had an increase in ONSD with ascent that was not statistically significant, regardless of AMS diagnosis [33]. However, the degree of increase was higher in patients with AMS than patients without AMS. This suggests individual variability, so changes in an individual's ONSD from baseline may be more important for the diagnosis of AMS compared to a standardized cut point.

The discrepant results are best summarized by Lochner's systematic review. They included six studies with 436 patients but found considerable clinical and methodological heterogeneity across the studies that prevented them from performing a meta-analysis. The studies varied with respect to variables such as ascent time, confounding factors related to method of transport to altitude, interval measurements, and scanning protocol. With regards to ONSD, there was a significant degree of individual variability across the studies and within each study, limiting ONSD as a diagnostic tool for AMS [34].

Further research is necessary to clearly establish whether there is a correlation between ONSD and AMS. Ideally, there needs to be a large longitudinal cohort study measuring ONSD at baseline followed by a range of altitudes at consistent time intervals, using a standardized scanning protocol with assessment of interobserver reliability, and controlling for confounding factors such as medication use (such as acetazolamide and dexamethasone), ascent time, and acclimatization periods.

6. Clinical Applications: Pediatrics

There is particular interest in POCUS of the optic nerve in pediatric populations where radiation exposure for diagnostic imaging and invasive procedures are ideally avoided if reasonably possible. However, the measurement of ONSD in children is more complicated than in adults. ONSD increases with age, most rapidly in the first year of life [35]. Furthermore, ONSD may be affected by the patency of the anterior fontanelle and head circumference [36][37][38][39]. Because of these factors, no standardized ONSD normal value exists, though numerous diagnostic cut points for raised ICP have been suggested. One commonly cited ONSD cut point is 4 mm in children ≤1 year old, 4.5 mm in children 1 to 15 years old, and 5 mm in children >15 years old [35][37].

Bhargava et al. performed a systematic review and meta-analysis of 11 publications to investigate the performance of sonographic ONSD to detect increased ICP in a pediatric population. Their study included patients with acute or chronic causes of elevated ICP. When compared to any reference standard, they found a pooled sensitivity of 93% (95% CI 74–99%), specificity 74% (95% CI 52–88%), +LR 3.55 (95% CI 1.67–7.54), −LR 0.10 (95% CI 0.02–0.46), and DOR 39 (95% CI 4.16–365) with moderate-to-high heterogeneity when compared to any reference standard. When limited to an invasive reference standard, sensitivity was 89% (95% CI 63–97%), specificity 74% (95% CI 47–90%), +LR 3.36 (95% CI 1.36–8.31), −LR 0.15 (95% CI 0.04–0.68), and DOR 22 (95% CI 2–192) with minimal heterogeneity [40].

Şik et al. studied 147 children presenting to the ED with head trauma requiring a CT head. ONSD ultrasound was performed by a pediatric EM fellow who was blinded to clinical and radiologic findings. When compared to CT as the reference standard, they found a high sensitivity of 93% and specificity of 94% when using a cut point of 5.1 mm amongst all age groups [41]. However, others found sonographic ONSD to have lower diagnostic performance consistent with the results of Bhargava's systematic review. Padayachy et al. performed a relatively large observational study comparing sonographic ONSD to invasive ICP measurements. They included 56 children ≤1 year old and 118 children >1 year of age. In children ≤1 year old using a cut point of 5.16 mm to detect ICP above 20 mmHg, sonographic ONSD had a sensitivity of 80% (95% CI 44–98%) and specificity of 76% (95% CI 61–87%), while in children >1 year, a cut point of 5.75 mm produced a sensitivity of 86% (95% CI 75–93%) and specificity of 70% (95% CI 56–82%). They found children with an open anterior fontanelle had the poorest correlation between sonographic ONSD measurements and the reference standard [36]. Ultimately, ONSD appears to have high sensitivity and only modest specificity to detect raised ICP in pediatric populations, but further research is required, especially to determine age-appropriate cut points.

There has been increasing interest in utilizing sonographic ONSD to detect VP shunt failure. While VP shunt malfunction results in raised ICP, children often present with non-specific symptoms overlapping with benign childhood ailments [42]. While imaging is heavily relied upon to diagnose VP shunt failure, CT and MRI are insensitive and children often require repeat CT imaging, thereby raising the risk of malignancy due to cumulative radiation exposure [43]. Lin et al. studied 32 patients with suspected VP shunt failure and compared sonographic ONSD measured by pediatric EPs against neuroimaging and a neurosurgical clinical diagnosis as reference standards. When compared to neuroimaging, sonographic ONSD had a sensitivity of 60% (95% CI 23–88%) and specificity of 67% (95% CI 48–81%). When compared to neurosurgical opinion, sensitivity rose to 75% (95% CI 30–95%) and specificity to 68% (95% CI 49–82%) [44]. Hall et al. studied 39 encounters suspicious for VP shunt failure and compared sonographic ONSD by pediatric EPs with neurosurgical diagnosis. They found sensitivity to be 61% (95% CI 36–83%) and specificity to be 22% (95% CI 6–48%) [45]. Unfortunately, sonographic ONSD appears to have poor diagnostic value in VP shunt failure, though larger studies in the future may provide clarity in this emerging area of interest.

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