American Journal of Emergency Medicine 49 (2021) 18–23

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Pediatric point-of-care ultrasound of optic disc elevation for increased intracranial pressure: A pilot study☆

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ARTICLE INFO

Article history:
Received 13 November 2020
Received in revised form 17 May 2021
Accepted 17 May 2021

Keywords:
Papilledema
Pediatric
Point-of-care ultrasound
Increased intracranial pressure

ABSTRACT

Objective: Papilledema is often difficult to detect in children. Ocular point-of-care ultrasound (POCUS) measurement of the optic nerve sheath diameter (ONSD) is a non-invasive test for increased intracranial pressure (ICP), but no consensus exists on normal pediatric ONSD values. Detection of optic disc elevation (ODE, a component of papilledema) using POCUS has recently been qualitatively described. We sought to establish the diagnostic accuracy of different ODE cutoffs to detect increased ICP in children who underwent ocular POCUS in our pediatric emergency department (PED).

Methods: We retrospectively reviewed charts of patients ages 0–18 years who received ocular POCUS in our tertiary PED between 2011 and 2016. Patients were included if their archived POCUS examinations were deemed high-quality by a POCUS expert and they underwent ICP determination within 48 h after ocular POCUS. A blinded POCUS expert measured ODE, optic disc width at mid-height (ODWAMH), and ONSD. Receiver-operator curve analysis was performed for various cutoffs for these measurements in detecting increased ICP.

Results: 76 eyes from 40 patients met study criteria. 26 patients had increased ICP. The mean ODE of both eyes (ODE-B) generated the largest area under the curve (0.962, 95% CI 0.890–1). The optimal ODE-B cutoff was 0.66 mm, with a sensitivity of 96% (95% CI 79–100%) and a specificity of 93% (95% CI 79–100%). 1/40 (2.5%) of patients with ODE-B < 0.66 had increased ICP.

Conclusions: ODE-B may represent the optimal ocular POCUS measurement for detecting increased ICP in children, and future prospective studies could more accurately describe the diagnostic performance of different pediatric ODE-B cutoffs.

1. Introduction

Detection of increased intracranial pressure (ICP) can be life- and vision-saving [1,2], and often examination of the optic disc provides the only physical exam evidence of this dangerous condition [2]. Since its invention in 1850 [3], the direct ophthalmoscope has been the tool used by clinicians to evaluate the optic disc for papilledema, a constellation of optic nerve head changes that occur with increased ICP [4]. Severe papilledema produces easily detectable changes on direct ophthalmoscopy (DO), with anterior and coronal protrusion of the optic nerve head, engorged and tortuous retinal vessels that climb steeply and disappear as they cross the disc margin, peripapillary hemorrhages, and retinal exudates [4,5]. Less severe papilledema, however, is more subtle, with minimal optic disc elevation and slightly blurred disc margins that may only be appreciated by an experienced ophthalmologist [4,5].

Competent DO for papilledema is a duty of care for ophthalmologists, primary care physicians, pediatricians, internists, neurologists, neurosurgeons, and emergency physicians, and is frequently required in the emergency department [1,6-8]. There is international consensus that all graduating medical students should be competent in DO for assessment of papilledema [9]. In reality, however, non-ophthalmologist clinicians are neither confident [1,2,6,8,10-14] nor competent with DO [2,6,8,12,14-17]. This low DO skill persists despite multi-year improvement programs of education, training, and curriculum development [11,12,16]. It is thus not surprising that clinicians rarely perform DO [6,8,10,11,14,17,18], even on acute care patients being assessed for

☆ Meetings: Poster presented at Pediatric Academic Societies Meeting, May 2018, in Toronto, Canada.

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https://doi.org/10.1016/j.ajem.2021.05.051
0735-6757/

possible increased ICP [2,16,19,20]. Even when non-ophthalmologist clinicians do perform DO, they fail to detect most cases of papilledema [8,16,17,21], which can lead to high medicolegal costs due to poor ophthalmologic and neurologic outcomes from undiagnosed increased ICP [22,23]. Further barriers to DO in children include small pupillary diameters and lack of cooperation [24-27].

For decades, ophthalmologists have used ocular point-of-care ultrasound (POCUS) to assess the optic nerve, which has been adopted more recently by pediatricians [28,29], general and pediatric emergency physicians [30-36], obstetricians [37], neurosurgeons [38], and neurologists [39-42] to assess the optic nerve head for the optic disc elevation that accompanies all grades of papilledema [4]. This technique is safe, convenient, and easy to learn and perform [31,34,41,43], but it remains unclear which ultrasound characteristics of the optic nerve head perform best in detecting increased ICP in children.

We analyzed ocular POCUS images obtained from pediatric emergency department (PED) patients to determine the performance of optic nerve sheath diameter (ONSD), optic disc elevation (ODE), and optic disc width at mid-height (ODWAMH) in detecting increased ICP. ODWAMH is a novel parameter created for this study, meant to assess whether measuring an elevated optic disc in a perpendicular direction to ODE might prove diagnostically useful.

2. Methods

We performed a retrospective observational cohort study of patients presenting to our tertiary PED who received ocular POCUS by pediatric emergency medicine (PEM) physicians. The study was approved by the Research Ethics Board of The Hospital for Sick Children. Our PED hosts a POCUS fellowship and ocular POCUS didactic and hands-on teaching is part of the POCUS curriculum for PEM fellows and PEM attendings.

Patients were included if: they were less than 18 years old; presented to our PED between September 2011 and July 2016; our PED ocular POCUS archive contained at least one high-quality ocular POCUS video clip of at least one of their eyes; and their ICP was determined in the 48 h after POCUS.

A high-quality video was defined by demonstration of an optic nerve running parallel to the ultrasound beam and intersecting with the retina, and a surrounding optic nerve sheath with clear outer margins [44]. This video rating was assigned after review of each clip by a POCUS expert (M.O.T.) who had completed a fellowship in PEM POCUS and had subsequently performed and interpreted >1000 ocular POCUS examinations.

Patients were excluded if: they had a known ocular or neurologic condition that might affect ocular POCUS measurements (ventricular shunt, optic nerve pathway tumor, or optic atrophy); no high-quality ocular POCUS clips were present in the PED POCUS archive; or no ICP determination occurred within the 48 h following POCUS.

The POCUS expert performed measurements of the optic nerve head on each high-quality POCUS clip, while blinded to all patient information. Images were viewed and measurements performed using picture archiving and communication system (PACS) software (Horos version 3.3.5, Nimble Co LLC, Annapolis, MD). Images were magnified 2× for ONSD measurement, and 3× for ODE and ODWAMH measurement. The POCUS expert selected the three highest quality still images from the POCUS clips for a given eye and performed an ODE, ONSD, and ODWAMH measurement on each of these images. As per prior protocols, ONSD was measured 3 mm posterior to the retinal plane (Fig. 1A) [42,45-47], and ODE was measured from the retinal plane to the most elevated point of the optic disc (Fig. 1B) [30,33,34,48]. ODWAMH measured the coronal width of an elevated optic disc at the midpoint of its elevation, as described in Fig. 1C. For a given eye, the ODE, ONSD, and ODWAMH measurements were each performed 3 times and the results reported as the mean ODE, ONSD, and ODWAMH [30,33,34,42,45-48].

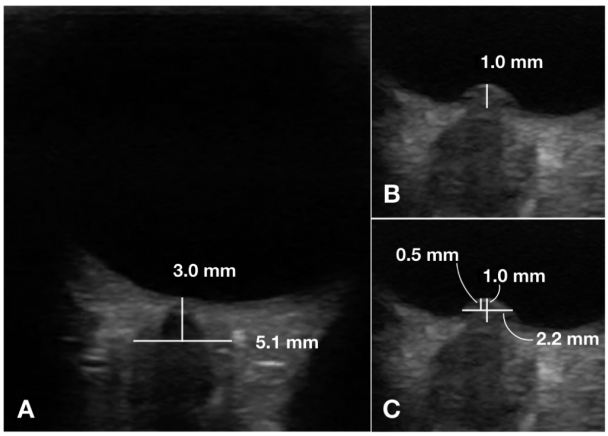

Fig. 1. Ocular POCUS images demonstrating measurements of ONSD, ODE, and ODWAMH. A. ONSD measurement. The vertical line runs parallel to the optic nerve, from the retina to a point 3 mm posterior. The horizontal line runs perpendicular to the vertical line at this point, and terminates at each boundary of the optic nerve sheath. The length of the horizontal line thus corresponds to the ONSD at a point 3 mm posterior to the retina. B. ODE measurement. The vertical line runs parallel to the optic nerve, from the point of most anterior protrusion of the optic disc to the point where the retina would be projected to continue across the optic nerve head. The length of this vertical line corresponds to the ODE. C. ODWAMH measurement. The long vertical line represents ODE measurement. The short vertical line runs parallel to the ODE measurement line, from the point of most anterior protrusion of the optic disc to the mid-point of the ODE measurement line. The horizontal line runs perpendicular to the ODE measurement line at its mid-point, and terminates at each boundary of the elevated optic disc. The length of the horizontal line thus corresponds to the width of the elevated optic disc at the mid-point of ODE.

A composite outcome of neuroimaging, lumbar puncture (with opening pressure), and/or findings during neurosurgery served as the reference standard for the determination of the presence or absence of increased ICP. Each chart was reviewed by 2 PEM physicians (F.A. and M.G.) who were blinded to ocular POCUS information and to each other's composite outcome result. A third PEM physician (N.F.) with the same blinding served as a tie-breaker in case of disagreements between the initial 2 chart review ratings. Increased ICP was considered present if any of the following conditions were met: a neuroimaging report indicating definitive signs of increased ICP; a lumbar puncture opening pressure of >28 cm H2O; or a neurosurgical operative report indicating signs of increased ICP. The absence of increased ICP was defined as a lumbar puncture opening pressure of ≤28 cm H2O or a neurosurgical operative report indicating no signs of increased ICP; normal neuroimaging alone was not sufficient for defining the absence of increased ICP.

Our primary outcome was the diagnostic accuracy of the mean ODE of both eyes of a patient (ODE-B) in detecting increased ICP. Secondary outcomes included the diagnostic accuracy of mean ONSD of both eyes (ONSD-B) and mean ODWAMH of both eyes (ODWAMH-B) measurements in detecting increased ICP, and the diagnostic accuracy of the highest value (from whichever eye of a patient produced the largest measurement) of ODE (ODE-H), ONSD (ONSD-H), and ODWAMH (ODWAMH-H) in detecting increased ICP. A further secondary outcome was the duration of ocular POCUS examinations (obtained from the time-stamps of the first and last image from each patient). The final secondary outcome was the inter-rater reliability of ODE, ONSD, and ODWAMH measurements, for which a second blinded PEM physician (A.D.) skilled in ocular POCUS (>100 exams performed) measured these parameters on a random selection of 10% of included eyes.

We analyzed the diagnostic accuracy of ODE-B, ODE-H, ONSD-B, ONSD-H, ODWAMH-B, and ODWAMH-H in detecting increased ICP using receiver-operator curves (ROCs) in SAS version 9.4 (SAS Institute Inc., Cary, NC). Optimal cutoffs for ROC curves were chosen using the Youden index, while bootstrapping was performed to generate 95%

confidence intervals. Interrater reliability was assessed with intraclass correlation (mixed effects, absolute agreement).

3. Results

3.1. Characteristics of study subjects

Our POCUS archive contained 899 ocular POCUS examinations during our study period, with 39 right eyes and 37 left eyes from 40 patients meeting study criteria (Fig. 2). Patient demographic variables are displayed in Table 1. The mean age of study subjects was 11.4 years and 26 subjects had increased ICP. There were no disagreements in reference standard ICP assignments between the physicians performing chart reviews. 20 of the included subjects had ocular POCUS performed by 12 different PEM POCUS fellows, 9 by 4 different PEM attendings, 6 by 5 different PEM fellows, and 5 by 3 different PEM attendings who had completed a PEM POCUS fellowship.

Table 1
Patient demographics

Age (y)	Mean 11.4 (SD 4.1)
Sex	
Male	21 (52.5%)
Female	19 (47.5%)
Eyes from patients without increased ICP	27 (1 left eye excluded)
Final diagnosis (number of eyes)	
Primary headache	11 (40.7%) – 1 left eye excluded
Optic nerve head drusen	4 (14.8%)
Optic neuritis	4 (14.8%)
Multiple cranial neuropathies	2 (7.4%)
Multiple sclerosis	2 (7.4%)
Neuromyelitis optica	2 (7.4%)
Meningitis	2 (7.4%)
Eyes from patients with increased ICP	49 (1 right eye and 2 left eyes excluded)
Final diagnosis (number of eyes)	
Space-occupying lesion	25 (51.0%) – 1 right eye and 2 left eyes excluded
Idiopathic intracranial hypertension	22 (44.9%)
Meningitis	2 (4.1%)

ICP – intracranial pressure.

3.2. Main results

The results of our diagnostic accuracy ROC analysis are presented in Table 2. ODE-B performed best out of all measurements, with an AUC of 0.962 (95% CI 0.890–1). The ODE-B cutoff that best maximized both sensitivity and specificity was 0.66 mm, with a sensitivity of 96% (95% CI 79–100%) and a specificity of 93% (95% CI 79–100%). The distribution of ODE-B measurements from subjects with and without increased ICP is presented in Fig. 3. The median duration of ocular POCUS was 4 min 8 s (range 30 s - 13 min 41 s). The intraclass correlation between the two raters on the random selection of 10% of POCUS examinations was 0.966 (95% CI 0.840–0.993), 0.949 (95% CI 0.756–0.990), and 0.959 (95%CI 0.814–0.992) for ODE-B, ONSD-B, and ODWAMH-B, respectively.

Two patients exhibited significant ODE discrepancy between right and left eyes. Both of these patients did not have increased ICP according to our reference standard. The first of these patients exhibited a right ODE of 1.15 mm and a left ODE of 0.412 mm, and was ultimately diagnosed with bilateral optic nerve head drusen. The second of these patients exhibited a right ODE of 0 mm and a left ODE of 0.65 mm, and was ultimately diagnosed with left optic neuritis.

4. Discussion

Ophthalmoscopy education is increasingly limited in undergraduate medical curricula across the world [19,49,50], and the majority of

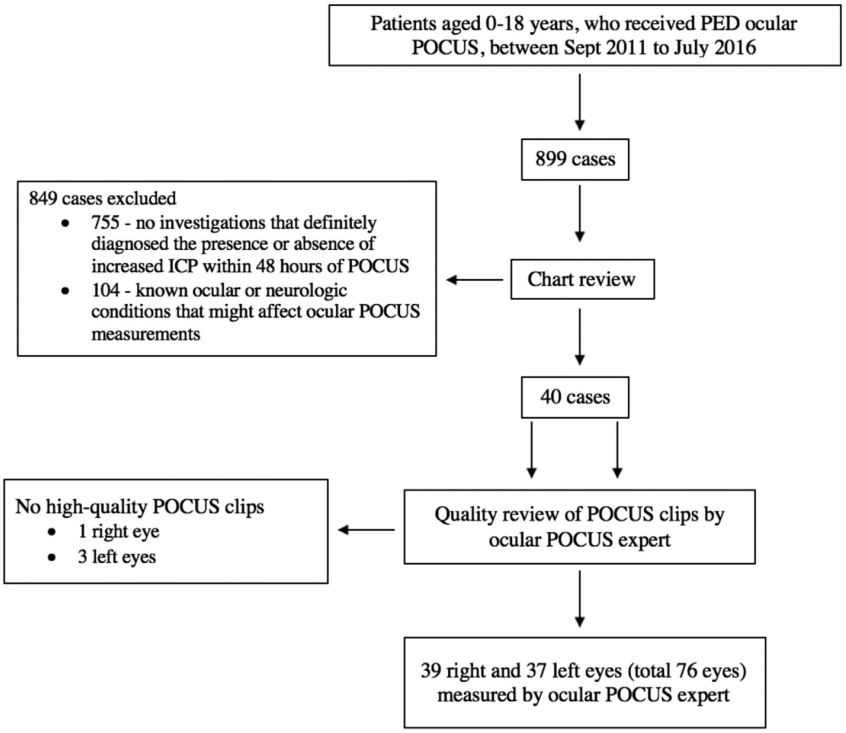

Fig. 2. Study flow diagram.

Table 2
AUC results from ROC analysis of ocular POCUS measurements and measurement ratios for the detection of increased ICP

Ocular POCUS Measurement or Measurement Ratio	AUC (95% CI)
ODE-B	0.962 (0.890–1)
ODE-H	0.923 (0.781–1)
ONSD-B	0.778 (0.610–0.923)
ONSD-H	0.805 (0.655–0.938)
ODWAMH-B	0.876 (0.758–0.969)
ODWAMH-H	0.789 (0.625–0.921)

POCUS – point-of-care ultrasound; AUC – area under the curve; ODE – optic disc elevation; ONSD – optic nerve sheath diameter; ODWAMH – optic disc width at mid-height.

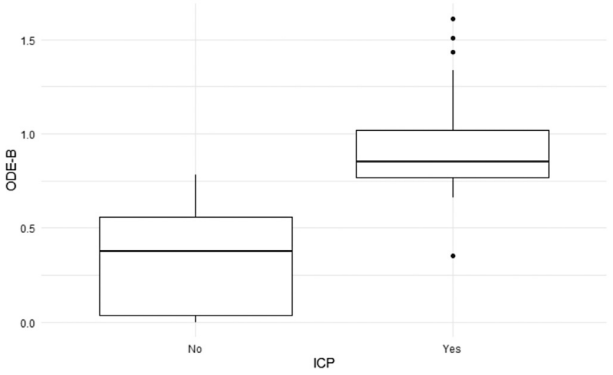

Fig. 3. Dot-and-whisker plot showing the distribution of ODE-B measurements between patients without increased ICP and with increased ICP. Boxes represent the interquartile range, while the line within each box represents the median. The whiskers from each box extend to the most extreme values within 1.5 interquartile ranges of the quartiles, while more extreme values are plotted individually.

graduating medical students and practicing generalists consider their DO training inadequate [6,8,17]. Many medical students never view an abnormal fundus via DO or receive DO technique feedback [13]. DO is considered one of the most difficult aspects of the pediatric physical examination, and generalists report low confidence in their pediatric DO skill [25,26,51,52]. Assessing for papilledema is the main purpose of pediatric DO [26], yet generalists often avoid performing DO on children with possible papilledema [8]. In emergent settings, time pressures and difficulty controlling room lighting are frequently cited as reasons for avoiding DO [1,17,53]. It is also difficult to objectively assess clinician DO competency, as an assessor cannot verify proper visualization of the fundus due to lack of a shared view [13].

A diagnostic test that is more feasible and accurate than DO in detecting pediatric papilledema could improve patient safety and appropriate use of cross-sectional neuroimaging resources [7,18]. Ocular POCUS is painless, safe, inexpensive, portable, does not require sedation, and can be used to serially monitor patients [42,54,55]. Our results suggest that the time required to perform ocular POCUS would not act as a barrier in clinical use. Ocular POCUS, in our experience, can also be performed and interpreted in either a lit or darkened patient room. Finally, ocular POCUS provides a shared view for a performing clinician and an assessor, which may make competency assessment easier than with DO.

ONSD measurements obtained from ocular POCUS were not more accurate than ODE measurement in our cohort. This is not surprising given the increased technical POCUS skill required for accurate ONSD capture and analysis [56-58], and the wide range of ONSD measurements reported for healthy children [59-64]. ODWAMH was also less accurate than ODE-B in detecting increased ICP, which is perhaps fortuitous as this measurement requires the most time spent performing caliper placements and calculations, which could act as a barrier to use in busy practice settings [1].

5. Limitations

There are limitations imposed by the retrospective nature of our study. Selection biases are possible in our study cohort compared to the typical pediatric cohort being assessed for possible increased ICP. Our inclusion and exclusion criteria were designed to ensure that study subjects had an accurate determination of the presence or absence of increased ICP, but this biased the study population towards one with a high prevalence (65%) of increased ICP. This represents a higher than typical true positive rate than in the typical PED cohort where fundus assessment is indicated. Study patients may also have exhibited distinct signs and symptoms leading the PEM physicians to perform ocular POCUS. It is also possible that patients excluded for low quality images may have exhibited unique characteristics. Patient positioning during ocular POCUS was also not recorded in charts, and variation in ONSD measurements is known to exist between supine and upright positions.

Several aspects of our study might affect the generalizability of our findings. Our study design involved images obtained by multiple ocular POCUS users and analyzed by a single POCUS expert. While this POCUS expert employed standard techniques for POCUS optic nerve head measurements, our results should be re-evaluated in studies in which the POCUS user also performs measurements. It is also possible that the quality of the ocular POCUS images obtained by our PEM physicians is higher than what would be obtained outside of our center, which has hosted a pediatric emergency medicine point-of-care ultrasound fellowship since 2011. The POCUS expert also performed measurements on images that had been magnified 2-3× on PACS software. This software was used to make the execution of the study more feasible. While most POCUS machines found in emergency departments have the ability to perform these magnifications, our results should be interpreted with this limitation in mind. While the interrater reliability was high between both raters, these raters were both experienced in ocular POCUS and lower reliability might exist between less experienced raters.

We acknowledge the relatively wide confidence intervals for the results of our AUC and diagnostic accuracy analyses, which reflects the relatively low numbers of patients included in this pilot study. Future work with larger sample sizes would better illuminate the true diagnostic performance of this technique. When interpreting the results of this study, it is also important to keep in mind that an optic disc can be elevated by processes other than increased ICP, such as optic neuritis, multiple sclerosis, and optic nerve head drusen. Future studies could investigate whether ODE detected by ocular POCUS in the conditions can be distinguished from ODE produced by increased ICP.

6. Conclusions

In our patient sample, PED ocular POCUS most accurately diagnosed increased ICP when the mean of the ODE measurements produced from both eyes (ODE-B) was used. Our results may prove useful in the design of future studies on larger patient cohorts, which could improve the predictive value of this technique by reducing the size of the diagnostic accuracy confidence intervals for different ODE cutoffs. Future prospective studies are also needed to validate the clinical performance of these cutoffs, explore the generalizability of this measurement technique, and investigate the potential of ocular POCUS as a screening test for increased ICP in children.

Funding

No external funding for this manuscript.

Author contributions

MOT, FA, and AD conceptualized and designed the study, and designed the data collection instruments. MOT coordinated and

supervised data collection. NF, FA, and MG collected data. NF drafted the initial manuscript. BM carried out the analyses. All authors.

all authors contributed substantially to revision of the manuscript. MOT takes responsibility for the paper as a whole.

Declaration of Competing Interest

All of the authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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