Non-invasive assessment of ICP in children: Advances in Ultrasound-based techniques

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Introduction

Assessing intracranial pressure (ICP) remains a cornerstone of decision making in neurosurgery. In children the value of repeat measures to establish whether ICP has changed is perhaps even more pertinent when planning treatment strategies.

Monitoring and treatment of ICP are still widely recommended in the management of severely head injured patients. [1] Invasive ICP monitoring through an intraparenchymal microtransducer or intraventricular catheter remains the gold standard, but usually requires admission to an intensive or high care unit and are further limited by complications including infection or haemorrhage. [2,3]

While there is still no ideal method for evaluating ICP, the benefit of continuous, real-time monitoring provided by invasive techniques is counter balanced by distinct limitations. The need for reliable non-invasive ICP monitoring techniques especially when invasive ICP monitoring is contraindicated or not available, is an obvious priority. The additional benefit of being able to screen patients with raised ICP at a primary health care level, especially in children would be a major stride toward early detection and improved outcomes, especially in diseases like brain tumors and hydrocephalus. [4,5,6] The benefits of such techniques are certainly not limited to neurosurgery but have diagnostic value in medical emergency units, ophthalmology assessment, anesthesiology as well as certain contact sports and aeronautical health assessments. [7]

Currently, most non-invasive techniques of assessing ICP in children evaluate physiological or anatomical characteristics influenced by increases in ICP. There are a

variety of techniques which include both clinical and technological assessment with varying degrees of diagnostic accuracy and requiring different levels of technical expertise. [8,9,10] In children this situation is more complex, given their physiological and anatomical heterogeneity. [11]

The non-invasive profile of brain ultrasonography, together with its safety, portability, ease-of-use and relatively low cost as a neuromonitoring tool has determined its applicability in the non-invasive evaluation of ICP in a number of settings, these include neuro- and general intensive care, the emergency department and the operating room. Different methods and combinations of techniques have been studied to non-invasively assess ICP with contrasting results. [4,7,12] This review describes some of the emerging ultrasound-based techniques reported to improve on or advance the diagnostic accuracy and the applicability of these techniques in children.

TCD waveform analysis has been widely investigated and reported on as a technique for non-invasive ICP estimation; as increased ICP could affect the waveform of blood flow velocity in major cerebral vessels. [13] Rasulo et al. demonstrated excellent sensitivity utilising a method based on the flow velocity diastolic formula. The authors recommended this method as a good option to exclude intracranial hypertension. (The accuracy of transcranial Doppler in excluding intracranial hypertension following acute brain injury: a multicenter prospective pilot study. [14]

The measurement of the optic nerve sheath diameter (ONSD) by transorbital ultrasonography is another well reported technique. The optic nerve sheath is an extension of the dura which contains cerebrospinal fluid (CSF); in conditions of increased ICP, volume changes in the intracranial compartment pressure shift CSF into the optic nerve sheath.

Due to its elasticity, the optic nerve sheath (ONS) dilates as the pressure increases, which can be seen as an increase in the ONSD using suitable imaging modalities such as ultrasound or magnetic resonance imaging (MRI). [19,20] presented an autopsy study demonstrating the largest diameters measured three millimetres behind the globe, with a baseline diameter ranging from 2.1 to 4.8 mm. [20] By volume injection into the perineural space, all sheaths were enlarged, with a maximum observed ONSD of 6.5 mm. A later study reported that the ONSD increased up to 140% of baseline value, with a decline within a few minutes after subsequent decompression. Hysteresis was observed, suggesting a viscoelastic material model for the ONS. With pressure loads of around 50 mmHg, the ONSD did however not completely reach the baseline value after decompression, suggesting that some plastic deformation may occur at high pressure values. [20]

ONSD measurement has shown strong correlation with ICP assessed invasively in TBI patients. The hypothesis that raised ICP is transmitted to the perineural subarachnoid space surrounding the optic nerves is well established in adults and children. [15,16,17,18]

A recent case report described the successful management of a patient with suspected meningitis presenting with potentially raised ICP for whom invasive monitoring was contraindicated due to the risk of bleeding. The use of both ONSD and TCD assessments for non-invasively assessing ICP were applied in a clinical protocol for intracranial hypertension. [21]

A less developed method for ICP assessment evaluates the relationship between ICP and cerebral venous sinus pressure; increasing ICP leads to venous hemodynamic changes at the level of the subarachnoid bridging veins with a volume compensatory mechanism within the intracranial system. [23,24]

In a recent prospective study in 64 brain injury patients [25], different ultrasound-based methods to assess ICP were compared; these methods included measurement of the ONSD, arterial TCD-derived indices and the insonation of the straight sinus.

The regression analysis revealed good correlation between ICP and ONSD (R=0.76), averaged per patient (N=64. The regression formulas described in this work for ONSD was:

$nICP_{ONSD} = 4.7 \times ONSD - 12.35$ (mmHg) (Adjusted R^2=0.57)

The authors also demonstrated that the systolic flow velocity in the straight sinus (FVsv) had a good correlation with ICP (r=0.72). Non-invasive ICP was calculated as $0.38 \times FV_{sv} + 0.0005$ (mmHg) with an area under the curve of 0.81 for a threshold of 20 mmHg of ICP.

Moreover, the combination of FVsv and the optic nerve sheath diameter resulted in an even higher accuracy to assess ICP (r = 0.81):

nICP = 4.23 x optic nerve sheath diameter + 0.14 x FVsv – 14.51 (mmHg)

The method based on the combination of ONSD and FV_{sv} demonstrated a statistically significant improvement of AUC values compared with $nICP_{ONSD}$ method alone (0.93; 95% CI=0.90-0.97), with sensitivity of 0.98 and specificity of 0.58, positive predictive value of 0.91 and negative predictive value of 0.89. The combination of ONSD ultrasonography and venous TCD as described by the authors provides an accurate technique for non-invasively assessing ICP, that is safe and low-cost. [26,27]

Considering that raised ICP influences the state of the ONS, it has been suggested that not only does the diameter increase, but the mechanical properties of the optic nerve complex may also be altered. Specifically, with increased pressure within the perineural space and subsequent distention of the optic nerve sheath, the tissue becomes less compliant, and therefore less deformable when subject to dynamic forces. These dynamic forces may arise from physiological sources such as cardiovascular pulsation transmitted either through cerebrospinal fluid (CSF) within the sheath or induced by nearby arteries. In an exploratory study, it was shown that ultrasound images could be used to extract tissue displacements on opposite sides of the optic nerve, and further used to obtain a measure of deformability. (Fig 1). The authors introduced the Deformability Index (DI) [D1 – D2 / D1 + D2] and found that the value of this index was significantly reduced in patients with high ICP compared to patients with normal ICP. [28]

In a follow-up study, including 28 paediatric patients of varying etiology (19 high ICP), DI was again significantly lower in the high ICP group (0.105 vs 0.28, p=0.001). A cut-off value of DI ≤ 0.18 (average between left and right eye) indicated ICP ≥ 20 mmHg with both sensitivity and specificity just below 90%. [29] By further combining DI with ONSD, a sensitivity was increased to almost 95% without compromising specificity. Using multivariable regression, a Pearson correlation coefficient of 0.82 was reported between invasive ICP and the combination of ONSD and DI.

$$ICP = 4 + 4.3 \cdot ONSD\text{-}42 \cdot DI$$ [29]

Despite a limited sample size, and the fact that the studies included only paediatric patients, the results seem promising. More clinical studies are necessary however, addressing the intra- and inter- user variablity of the method, validity in an adult populations and the potential confounding effect of various demographic, physiological parameters (e.g. age, blood pressure,) and etiologic factors.

Ragauskas et al described a modified TCD technique, Two Depth Transorbital Doppler (TDTD) flowmetry. [30] This method measures flow in the ophthalmic artery, which has an intra- and extra- cranial segment. Progressively increased pressure is applied to the globe using specialized goggles, until the flow velocity in the intra- and extra-cranial segments of the ophthalmic artery are the same, a similar physiological principle to using a blood pressure cuff when measuring arterial blood pressure. The authors describe a good agreement between this method and invasively measured ICP, with a measurement error of 0.12 mmHg (98% CI). [30] In a study aimed at verifying the accuracy of this method, however Bershad et al demonstrated fair agreement with lumbar CSF measurement, concluding that the wide limits of agreement would preclude use of the device as a stand-alone method for ICP determination, but may be useful if combined with other ICP screening techniques, and with certain improvements in the technology [31]

The goal of improving the diagnostic accuracy of these non-invasive techniques remains a worthy, yet formidable task. The value of combining some of the established techniques, such as TCD and ONSD with dynamic, physiological parameters, and also expanding on the traditional methods of acquisition, appears to be a useful approach [4,10,30]

Behmanesh et al performed a prospective study on infants undergoing craniosynostosis surgery. [32] The authors describe a novel technique of using a standard intraparenchymal probe which they secured to the anterior fontanelle using a wooden tongue depressor and medical tape. The readings obtained from this noninvasive epicutaneous transfontanelle technique were then compared to simultaneous invasive ICP readings, revealed no significant difference between the mean values from the two readings, transfontanelle, 13.10 mmHg [SEM 6.68 mmHg]; epidural, 12.46 mmHg [SEM6.45 mmHg], p = 0.4643.

A recent study in adults with TBI and subarachnoid hemorrhage describes a novel noninvasive technique for assessing ICP using advanced signal analysis algorithms to measure the acoustic signals propagating through the cranium. The authors report a strong positive relationship between the invasive ICP measurement and the noninvasive method, with differential pressure between the two techniques within ± 3 mmHg in 63% and within ± 5 mmHg in 85%, with an AUROC 0.895. [33]

Several other standalone techniques for non-invasively assessing ICP have been described, these include techniques involving the auditory canal, such as the tympanic membrane displacement (TMD) [34], and the distortion product autoacoustic emissions (DPOAE), a technique based on measuring the change in perilymphatic pressure as a marker of associated change in ICP [31] both of which have some applicability in children.

The quest to develop a portable, reproducible, accurate and cost-effective technique for noninvasively assessing ICP both in adults and in children, ideally with the capability of continuous ICP recording remains an ongoing quest for neurosurgeons. The ability to noninvasively screen patients with subtle symptoms of raised ICP earlier as well as monitor patients in the intensive care unit certainly justifies the efforts made to refine

some of the described techniques. While no standalone noninvasive technique provides adequate diagnostic accuracy, the combination of certain static and dynamic parameters as described by some of the methods in this paper will likely contribute towards improving the widespread use of noninvasive techniques of ICP assessment.

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