ORIGINAL ARTICLE

Utility of Transcranial Doppler in Idiopathic Intracranial Hypertension

Gary Hunter, Chris Voll, Michele Rajput

ABSTRACT: ***Introduction:*** Idiopathic intracranial hypertension (IIH) can be an elusive diagnosis, and poor visual outcomes may occur. Currently, the only means of accurately diagnosing and following these patients is with repeated lumbar puncture. Previous work has shown that transcranial doppler measurements of pulsatility correlate accurately with elevated intracranial pressure (ICP). This study is designed to assess whether pulsatility index (PI) correlates with ICP in patients newly diagnosed with IIH. ***Methods:*** Seven patients with clinical suspicion of IIH were included in this study. Clinical suspicion was based on history of recurrent headaches and papilledema. All patients had otherwise normal examinations and imaging. Middle cerebral arteries were insonated to obtain average PI values. Cerebrospinal fluid (CSF) was then withdrawn, and closing pressures were recorded. Pulsatility index values were then obtained again, within ten minutes after completing CSF withdrawal. PI values were correlated with ICP values, and pre and post CSF withdrawal values were compared. ***Results:*** All seven patients had elevated opening pressures (average 39 cm H_20, range 27-70). The average closing pressure after approximately 30 cc of CSF withdrawal was 11.9 cm H_20. The average PI before CSF withdrawal was 0.95, which dropped to 0.70 after CSF withdrawal ($p = 0.02$). The change in ICP was found to be correlated with a change in PI ($p = 0.004$). ***Conclusions:*** These findings suggest that PI may be useful for following patients with IIH non-invasively. Further study with larger groups and blinded assessments should be useful in better characterizing the accuracy of this technique.

RÉSUMÉ: Utilité du Doppler transcrânien dans l'hypertension intracrânienne idiopathique. ***Contexte :*** Le diagnostic de l'hypertension intracrânienne idiopathique (HII) peut être manqué, avec comme conséquence une altération de la vision. La ponction lombaire répétée est actuellement le seul moyen de poser un diagnostic exact et de suivre ces patients. Des études antérieures ont montré que la mesure de la pulsatilité par le Doppler transcrânien est corrélée exactement à l'augmentation de la pression intracrânienne (PIC). Cette étude a été conçue pour évaluer si l'indice de pulsatilité (IP) était corrélé à la PIC chez les patients chez qui un diagnostic d'HII vient d'être posé. ***Méthodes :*** Sept patients, chez qui on soupçonnait cliniquement la présence d'une HII à cause d'une histoire de céphalée récurrente et d'œdème papillaire, ont été inclus dans l'étude. L'examen et l'imagerie étaient par ailleurs normales chez tous les patients. Nous avons effectué une insonation de l'artère cérébrale moyenne (ACM) chez tous les patients pour obtenir des valeurs moyennes d'IP. Une ponction de LCR a ensuite été effectuée et les pressions de fermeture ont été enregistrées. Les valeurs d'IP ont été mesurées à nouveau en dedans de 10 minutes après la fin du retrait de LCR. Les valeurs d'IP ont été corrélées aux valeurs de PIC et les valeurs avant et après le retrait de LCR ont été comparées. ***Résultats :*** Les 7 patients avaient des pressions de départ élevées (moyenne 39 cm H2O, écart de 27 à 70). La pression moyenne de fermeture après la ponction d'environ 30 cm3 de LCR était de 11,9 cm H2O. L'IP moyen avant la ponction de LCR était de 0,95 et il a chuté à 0,70 après la ponction de LCR ($p = 0{,}02$). Le changement de la PIC était corrélé au changement de l'IP ($p = 0{,}004$). ***Conclusions :*** Ces observations sont en faveur de l'utilité de l'IP pour le suivi non effractif des patients atteints d'HII. Des études sur un nombre plus considérable de patients et effectuées à l'insu pourraient être utiles pour mieux définir la précision de cette technique.

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Idiopathic intracranial hypertension (IIH), formerly known as pseudotumor cerebri or benign intracranial hypertension, is a relatively common condition characterized by raised intracranial pressure without mass lesion or focal obstruction to cerebral venous flow. It is seen more commonly among women, with a prevalence estimated at 1/100,000, but up to 20/100,000 among those characterized as obese (20% above ideal body weight)[1].

The typical presentation includes frequent headaches, papilledema, pulsatile tinnitus, and visual disturbance. Less common symptoms include abducens palsy, while any other focal findings exclude the diagnosis. While some cases resolve spontaneously over months to years, most patients have persistent headache and visual deficits if untreated. Current standards for investigating IIH essentially consist of ruling out other disorders such as venous sinus thrombosis, which can closely mimic IIH. A lumbar puncture (LP) is also required to assess the opening pressure, and repeat LP is often required in order to follow cerebrospinal fluid (CSF) pressure while on treatment.

The etiology remains unknown, although various theories have been proposed and investigated, including increased CSF

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production or decreased resorption[2] and idiopathic venous hypertension[3]. Numerous medication associations have been described, including Vitamin A, glucocorticoids, and macrolide antibiotics[4], although causality has not been proven and a pathophysiologic mechanism remains to be demonstrated. Elevated body mass index is a fairly consistent feature[4], and weight loss is probably the single most effective strategy for preventing visual loss from IIH. Again, the pathophysiology of obesity as it relates to IIH is unknown, but could feasibly relate to diffusely elevated venous pressures and impaired CSF absorption. Another possibility is that a common unidentified mechanism causes both obesity and elevated intracranial pressure. Several authors have described transverse sinus stenosis in association with IIH, with some patients improving after stenting of the lesion[5,6]. Studies of venous pressures using direct manometry have shown that cerebral venous pressures may be universally elevated in patients with IIH[3,7].

Regardless of pathophysiology, techniques for non-invasive assessment of intracranial pressure (ICP) are needed, given the discomfort and invasiveness of repeated lumbar punctures. Visual field testing should always be employed as a means of following patients with IIH, but even formal perimetry is subject to significant false positives[8], and irreversible axonal loss may have occurred with preserved visual acuity[9]. The current method of repeated LP's is time consuming, painful for patients, and not without risk.

Transcranial doppler (TCD) measurement of the pulsatility index (PI) has been previously shown to accurately estimate ICP in comatose patients with various brain insults[10]. Pulsatility index is a ratio, calculated as the difference between the systolic and diastolic flow velocities (Vs - Vd) divided by the mean flow velocity (Vm). In the above mentioned study, Bellner et al found a high correlation between PI as measured with TCD and readings from intraventricular catheter manometry, with a correlation coefficient of 0.938 ($p < 0.0001$). However, only one patient in this study had been diagnosed with IIH, with the others representing a diverse set of etiologies including subarachnoid hemorrhage and head trauma. One previous study compared the PI of patients with IIH with controls and found no significant difference[11]. However, this study only sampled a single measurement of PI, as opposed to correlating changes in ICP with change in PI for each patient. Whether changes in PI accurately reflect changes in ICP in the setting of IIH therefore remains unknown. If this technique proves to accurately estimate changes in ICP, noninvasive testing could spare many patients

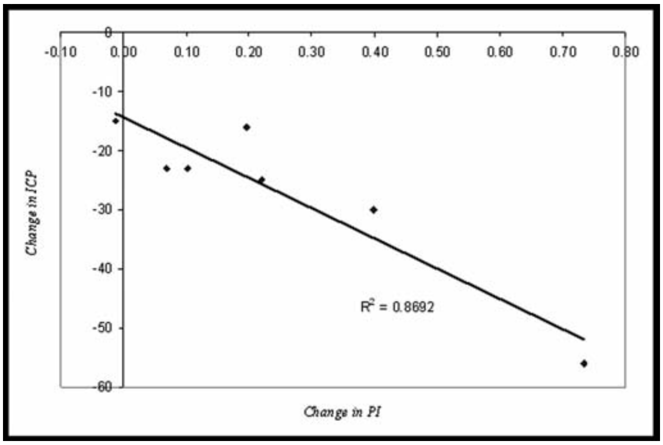

Figure 1: *Change in PI vs. Change in ICP (cm H2O).*

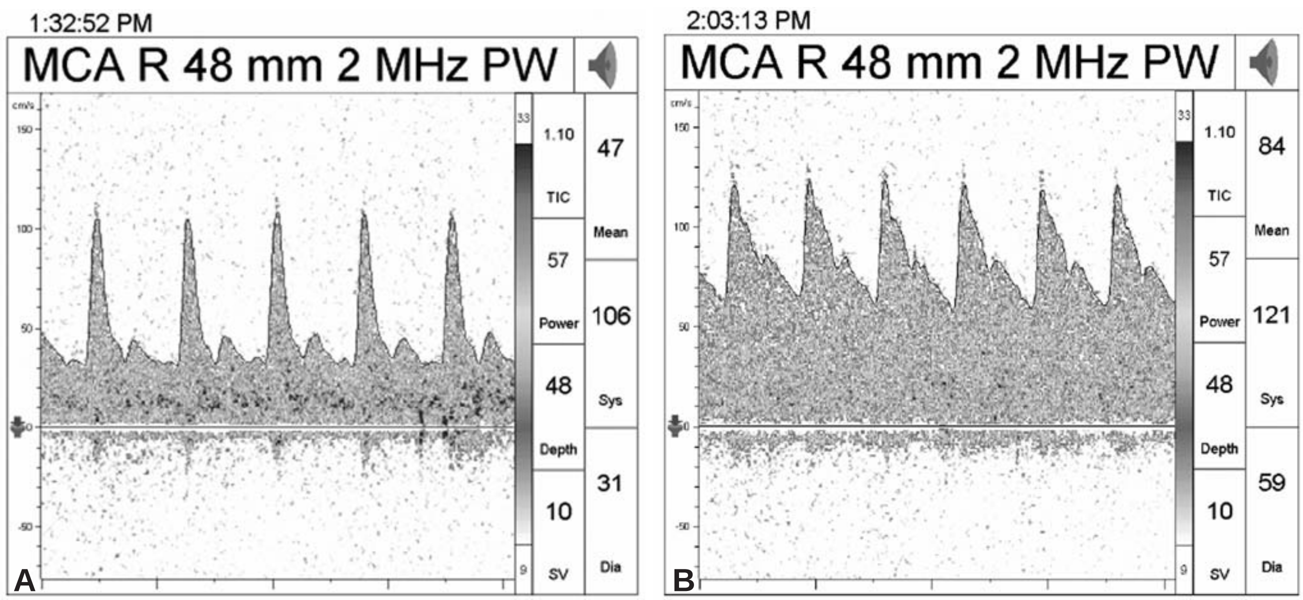

Figure 2: *Changes in TCD waveform morphology pre and post CSF withdrawal, Patient 5. Note the tall peaked systolic contour before CSF withdrawal, with a more gradual diastolic slope after normalization of CSF pressure.*

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the discomfort and anxiety associated with multiple lumbar punctures. It should be again emphasized that TCD measures of PI are not likely to replace LP as a means of diagnosing IIH, but rather as a means of following a given patient over time. The current study is a pilot study designed to assess whether PI correlates with opening and closing pressures in patients newly diagnosed with IIH.

Methods

Seven patients with clinical suspicion of IIH were included in this study. Clinical suspicion was based on history of recurrent headaches and papilledema, with otherwise normal physical examination (with the exception of abducens palsy). All patients had normal imaging, either with CT or MRI, including dedicated imaging of the venous system. All patients consented to undergoing TCD studies before and after lumbar puncture. Recordings were obtained using a Pioneer TC8080 Ultrasonic pulsed doppler imaging system with a 2 MHz transducer (Nicolet Vascular Division, Viasys Healthcare, Conshohocken, PA, USA). Subjects were in the supine position and the middle cerebral arteries were insonated through the temporal window, at a mean insonation depth of 50 mm. The principal investigator performed all recordings and was not blinded to the suspected diagnosis.

Background data regarding current complaints and past medical history were obtained using brief questionnaires. Transcranial doppler studies of middle cerebral arteries were obtained bilaterally to allow for calculations of PI. Three snapshots of waveforms and velocities were recorded from each side, and the highest velocities obtained were used for calculation of PI. The highest left and right PI values were then averaged to provide a single PI value. Lumbar punctures were then performed in the lateral decubitus position, with direct manometry to measure opening pressure. Approximately 30 ml of CSF were withdrawn, and closing pressures were recorded. Pulsatility index values were then obtained in the same fashion, within ten minutes after completing CSF withdrawal. Formal waveform analysis was not performed, but significant changes in waveform were noted and images were saved for review.

Pulsatility index values were correlated with ICP values using Pearson's correlation coefficient. Pre and post CSF withdrawal values were compared using a 2-tailed t-test, with significance assigned to $P < 0.05$.

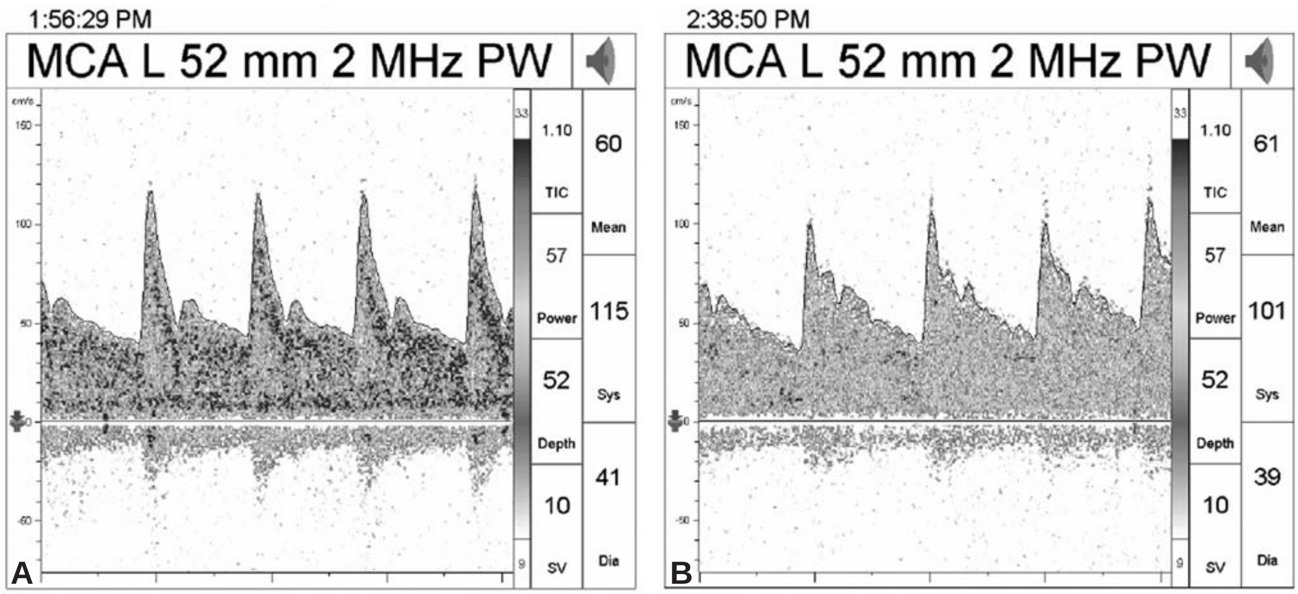

Figure 3: *Changes in TCD waveform morphology pre and post CSF withdrawal, Patient 7. Note the tall peaked systolic contour before CSF withdrawal, with a more gradual diastolic slope after normalization of CSF pressure.*

Results

Patient characteristics are shown in the Table. All seven patients had elevated opening pressures (average 39 cm H_20, range 27-70). The average closing pressure after approximately 30 cc of CSF withdrawal was 11.9 cm H_20. The average PI before CSF withdrawal was 0.95, which dropped to 0.70 after CSF withdrawal ($p = 0.02$). The Table also shows the raw data for all seven patients including pre and post CSF withdrawal PI and ICP values. The change in ICP was found to be correlated with a change in PI as shown in Figure 1, with an R^2 value of 0.832. The Pearson's correlation coefficient was 0.912 ($p = 0.004$).

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Table: Patient characteristics

Patient	Age (years)	BMI (kg/m^2)	Presenting Complaints	OP (cm H2O)	CP (cm H2O)	PI-1	PI-2	Comments
1	17	28.1	Headache, VO, tinnitus	27	11	0.79	0.59	
2	33	33	Papilledema	33	8	0.74	0.52	
3	45	32	Headache, tinnitus	29	14	0.65	0.66	Poor waveforms pre-withdrawal
4	34	33	Headache	37	14	0.71	0.65	
5	18	42.6	Headache, tinnitus, N/V, VO	>70	14	1.53	0.80	Patient returned within 1 week with elevated ICP, PI again very high
6	22	34.4	VO only	35	10	0.85	0.75	OP obtained with fluoroscopic guidance
7	21	29.5	Headache, VO	42	12	1.36	0.96	
Avg.	*27.1*	*33.2*		*39*	*11.9*	*0.95*	*0.7*	

BMI: Body mass index; OP: Opening Pressure; CP: Closing Pressure; PI-1: Pulsatility Index before CSF withdrawal; PI-2: Pulsatility Index after CSF withdrawal; VO: Visual Obscurations; N/V: Nausea and/or vomiting

While detailed analysis of waveforms was not performed, the slope of the waveforms changed dramatically in at least two cases (Figure 2). The morphology before withdrawal was peaked with a very steep systolic and diastolic component. After withdrawal of CSF and lowering the ICP, the diastolic component took on a much more gradual slope.

Discussion

These findings suggest that PI may be useful for following patients with IIH non-invasively, in an analogous fashion to following patients who have suffered a subarachnoid hemorrhage for evidence of vasospasm. In the setting of IIH, however, the clinician has the added advantage of having previously obtained baseline values in order to make direct comparisons for a given patient. The potential for prevention of patient discomfort are significant, and TCD measures of PI may serve as a useful adjunct to careful ophthalmologic follow-up for this patient population.

This study is not definitive, however, in demonstrating the usefulness of PI in IIH. First, the results may have been skewed by two of seven subjects who had very high ICP at baseline, very high PI values, and the greatest change in PI with withdrawal of CSF (Subjects 5 and 7). These patients also showed the greatest change in waveform morphology. While the results may not have achieved the same level of significance if these data were excluded, the overall small sample size makes such subgroup analysis less meaningful. In addition, these findings indicate that the sensitivity of PI measurements for detecting elevated ICP is greater with higher ICP, such that significantly elevated ICP is unlikely to be missed using this technique. Conversely, there may be potential for intermediate cases of elevated ICP to be missed. However, as mentioned, the utility of TCD would most likely apply to following a given patient over time and comparing PI values within patients, as opposed to screening for elevated ICP in patients with a suspected diagnosis of IIH. Whether PI changes correlate with ICP changes in a given patient remains to be determined, and a carefully conducted cohort study is required to address this question.

Other methods of analyzing TCD data may also contribute to estimating ICP, including computer models of waveform analysis. Aggarwal et al[12] performed a detailed retrospective analysis of TCD waveforms in patients with acute hepatic failure, and found that loss of the so-called Windkessel effect (which reflects arterial elasticity), and fraction of time spent in systole correlated well with ICP. The application of these techniques may supplement PI as a means of serially monitoring ICP in patients with IIH. The advantages of PI are that it is quick to obtain requiring only a few measurements of an easily accessible vessel, and that it is not dependent on angle of insonation, making the results highly reproducible and resistant to technician error.

Conclusions

The current study was conceived as a pilot study to assess the utility of PI in following patients with IIH non-invasively. Our findings add to the existing literature that TCD measurements

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can accurately reflect ICP, and this is the first study to assess this in patients with IIH. Questions remain as to whether PI or other TCD parameters (or combinations of TCD data) may increase the accuracy of ICP estimation, and whether these results apply to a given patient over time, such that they may be spared the discomfort of repeated painful testing without sacrificing accuracy.

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