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MRI measurement of optic nerve sheath diameter using 3D driven equilibrium sequence as a non-invasive tool for the diagnosis of idiopathic intracranial hypertension

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Abstract

Background: The idiopathic intracranial hypertension is a disease that is represented by high intracranial pressure of unknown reason. The visual disturbance presents the main medical problem of this syndrome. This study was conducted to assess the diagnostic value of the optic nerve sheath diameter (ONSD) measured using MRI 3D DRIVE in the diagnosis of idiopathic intracranial hypertension.

Results: The mean value of the ONSD measured using 3D DRIVE sequence in the patient group (5.81 ± 0.33) was significantly higher than the mean value of the normal control group (4.95 ± 0.45) ($p < 0.001$). The optimal optic nerve sheath diameter cut-off value for diagnosing idiopathic intracranial hypertension was > 5.31 mm, with 94.12% sensitivity and 93.3% negative predictive value.

Conclusion: The high resolution of 3D DRIVE provides an accurate measurement of ONSD which correlated with elevated cerebrospinal fluid pressure and hence the diagnosis of idiopathic intracranial hypertension.

Keywords: Optic nerve sheath diameter, Intracranial hypertension, 3D DRIVE, MRI, CSF

Background

The idiopathic intracranial hypertension syndrome (IIH) is a disease that is characterized by high intracranial pressure with no known cause, and it predominantly affects young females [1]. Headache, nausea, and vomiting as well as visual disturbance are the presenting symptoms of this disease with associated papilledema on ocular examination [2].

The diagnosis of idiopathic intracranial hypertension is based on the revised modified Dandy criteria, which is based on the raised opening pressure of lumbar puncture more than 20 mmHg, with exclusion of any ventricular dilatation or intracranial mass lesion, the other criteria also include normal spinal fluid composition and normal examination of the nervous system rather than presence of papilledema [3].

The early detection and treatment of increased IIH is an important condition as the early diagnosis and treatment can preserve patients vision, but it is often challenging condition, because intracranial pressure (ICP) monitoring is not usually done in many patients, yet the magnetic resonance imaging (MRI) is often performed in such patients to exclude other cause of intracranial hypertension and therefore provides a non-invasive tool for diagnosing IIH [4].

The cerebrospinal fluid (CSF) accumulates in the retrobulbar optic nerve sheath due to raised CSF pressure, and the direct measurement of such CSF accumulation may provide an earlier tool for diagnosing and measurement of intracranial hypertension. The measurement of optic nerve sheath diameter could, therefore, be a more sensitive sign of elevated ICP [4]. High-

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resolution MRI can be used as a tool for measuring optic nerve sheath diameter (ONSD) adding in diagnosis of raised intracranial pressure [5, 6]. A positive correlation was found between the measurement of optic nerve sheath diameter and the intracranial pressure value, so the optic nerve sheath diameter value can be used as an additional criterion for the diagnosis of increased intracranial pressure [7].

The 3D DRIVE is a fast spin-echo sequence which provides an image with high spatial and contrast resolution with good cisternographic effect [8], so it gives more precise discrimination of the optic nerve sheath, with subsequent more accurate measurement of optic nerve sheath diameter.

The aim of this study was to evaluate the diagnostic value of measuring optic nerve sheath diameter using MRI 3D DRIVE in diagnosing idiopathic intracranial hypertension.

Methods

Patients

Our prospective study was performed in El-Demerdash hospital from October 2019 till November 2019, 34 participants participated in this study, and they were divided into two groups. The first control group included 17 normal volunteers (17 females and three males) with an average age of 40.06 ± 9.61 years (range of 27–57 years); all of them have no neurological symptom or clinical sign of increased intracranial tension. The second group included 17 patients (three males and 14 females) with an average age 37.94 ± 8.40 years (range, 26–57 years); all are referred to the radiology department, El-Demerdash hospital, with a diagnosis of intracranial hypertension according to revised modified Dandy criteria [3]. The MRI study was done for all control and patient group participants, after a written consent was taken from all participants, according to the rules of our ethical committee.

Exclusion criteria

- Patient with secondary cause of intracranial hypertension as intracranial mass, dilated ventricular system, and cerebral venous thrombosis
- Patient with any intracranial pathology as subarachnoid hemorrhage, meningitis, and congenital cranial malformation
- Patients with a history of intracranial surgery or trauma
- Participant with contraindication to MRI such as non-MRI compatible pacemaker
- Volunteers with history or MRI finding of intracranial mass, cranial operation or deformity, or orbital/optic abnormalities

Technique of MRI examination

- A routine MRI examination was done for all participants using 1.5-T Philips Achieva MRI unit with 16-channel sensitivity-encoding head coil; then, an additional axial sequence on the orbit was performed using the 3D DRIVE technique.
- The 3D DRIVE parameters were TR = 1500 ms, TE = 250 ms, flip angle 90°, matrix 256 × 204, field of view 15 × 15 cm, slice thickness and gap = 1.4/0.7 mm, and the parameters of axial T2 WI turbo spine echo were TR = 5282 ms, TE = 110, matrix 244 × 147, field of view 21 × 21 cm, and slice thickness and gap 5/6
- The optic nerve sheath diameter was measured on the 3D DRIVE sequence and it was visualized as a linear low signal band between the CSF bright signal in the optic nerve sheath and the bright intraconal fat, the ONSD was also measured in the axial T2 WI sequence.
- The orbital retrobulbar region was zoomed and the axial slice which gave the best imaging view of the ONSD was chosen; then, the optic nerve sheath diameter was measured 3 mm behind the posterior sclera of the eye globe in plan perpendicular to the optic nerve.
- An average value of the right and left ONSD measurement was taken. Then, a comparison between the ONSD average value and ICP measurements was performed; a comparison between the measurement of the 3D DRIVE ONSD and T2 WI ONSD was also performed.
- The interobserver variability in measuring ONSD was measured by comparing the value of ONSD in both patient and control groups, and it was tested on 34 ONSD (17 patients and 17 normal volunteers); then, a comparison between the measurement of the two readers in both 3D DRIVE and T2 WI sequences was performed.

Analysis of data

- The data analysis was performed using IBM SPSS statistics (V. 25.0, IBM Corp, USA, 2017). For quantitative parametric measurements, the data were expressed as mean ± SD. The paired *t* test was used to compare the paired numerical data. A receiver operating characteristic (ROC) curve was performed to assess the diagnostic accuracy of the measured ONSD for diagnosing raised ICP using diagnostic validity tests which included sensitivity and specificity. The *P* value < 0.05 was considered a statistically significant value. The *P* value < 0.001 was considered a highly statistically significant value.

Results

This study included 34 participants divided into control group which included 17 normal volunteers and patient group which included also 17 patients, each group included 14 females (82.4%) and three males (17.6%). The mean age of the control and patient groups was 40.06 ± 9.61 and 37.94 ± 8.40, respectively (Table 1).

In the 3D DRIVE sequence, the mean value of ONSD diameter measured by the first and the second readers in the patient group was 5.81 ± 0.33 and 5.90 ± 0.30, respectively, and it was significantly higher than the mean value of the normal control group measured by first and second readers which was 4.95 ± 0.45 and 4.74 ± 0.31, respectively (*P* value < 0.001) (Table 2).

Based on the area under ROC curve of 0.929 (CI 95% = 0.786 to 0.989), the estimated optimal ONSD cut-off value measured in the 3D DRIVE sequence for detecting raised ICP more than 20 mmHg was > 5.31 mm, with sensitivity of 94.12%, specificity of 82.53%, negative predictive value of 93.3%, and 84.2% positive predictive value and overall accuracy of 88.24% (Table 3) (Fig. 1), and at this cut-off value there was only one false-negative case in which the ONSD was 5.2 mm, yet the lumbar puncture revealed high opening CSF pressure, and three normal volunteers who were diagnosed as false-positive cases, as the ONSD was high measuring 5.61, 5.66, and 5.73 mm, yet they did not suffer from any sign or symptom of intracranial hypertension. On the other hand, the overall accuracy of the ONSD measured in the T2 WI was of less value measuring 76.47%, at the optimal cut-off point of ONSD > 5.6 mm, with 88.2% sensitivity, 64.71% specificity, 71.43% positive predictive value, and 84.62% negative predictive value (five false-positive cases and four false-negative cases), and at lower cut-off value of ONSD > 5.31 mm, the sensitivity was increased to reach 94.12% yet with remarkable reduction in the specificity down to 52.94% (Figs. 2 and 3).

In T2WI, the mean value of ONSD in the patient group was significantly greater than in the control group (mean = 6.14 ± 0.41 and 5.22 ± 0.55, respectively, *P* value < 0.001), and it was also significantly higher than the mean value of ONSD measured in patient group using the 3D DRIVE sequence (mean = 6.14 ± 0.41 and 5.81 ± 0.33 in T2 WI and 3D DRIVE sequences, respectively, *P* value < 0.001).

Table 1 Demographic data of the study participants

		Control group No. = 17	Patients group No. = 17	*P* value	Sig.
Sex	Females	14 (82.4%)	14 (82.4%)	1.000	NS
	Males	3 (17.6%)	3 (17.6%)		
Age	Mean ± SD	40.06 ± 9.61	37.94 ± 8.40	0.499	NS
	Range	27–57	26–57		

The mean difference of the measured ONSD between the two observers was significantly higher in T2 WI sequence (mean = 0.08 mm ± 0.1) compared to 3D DRIVE sequence (mean = 0.01 ± 0.08 mm, *P* value < 0.001) (Table 4).

Discussion

An idiopathic increase of intracerebral tension is a clinical setting of unknown etiology which is characterized by elevated CSF pressure more than 20 mmHg in the absence of underlying neurological abnormalities or cranial structural lesion [3]. The disease should be diagnosed early to avoid serious permanent changes in vision which may end up to blindness [9].

The gold standard for diagnosis of IIH is monitoring and measurement of the opening CSF pressure through the lumbar puncture technique, yet it is an invasive method with variable complications. Moreover, the different sites of insertion and different types of devices make it difficult to accurately diagnose and monitor idiopathic increase of intracranial tension (ICT) [10]. Several studies used the CSF pressure cut-off value of 20 mmHg (25 cm CSF fluid) for the diagnosis of raised ICP [11].

Empty sella turcica, distension of the optic nerve sheath, posterior globe flattening, and optic nerve tortuosity were significantly associated with IIH [12].

This study revealed that there was a strong correlation between the measured ONSD in the 3D DRIVE and the increased ICP more than 20 mmHg which is a cornerstone for diagnosing IIH, with a significant difference between the mean ONSD in the patients with increased ICP and the control healthy volunteers (mean = 5.81 ± 0.33 mm and 4.95 ± 0.45 mm, respectively, *P* value < 0.001).

To our knowledge, this was the first study which used axial thin cut 3D DRIVE sequence in measuring the ONSD, and we used 3D DRIVE as the inherited high image quality of this sequence with higher spatial and contrast resolution to allow better assessment of fluid-filled structures or those surrounded by the CSF, which gives a more accurate measurement of the ONSD, and as the ONSD measurement was of low value (in millimeters), the 3D DRIVE will be more specific for the diagnosis of increased intracranial hypertension; another advantage of the 3D DRIVE sequence is the availability of the sagittal reformatted images which allow visualization of the posterior eye globe flatting and optic nerve head protrusion in a second plan in addition to the axial plan.

Other studies also concluded a positive relationship between the ONSD and the increased ICP of more than 20 mmHg, either using an MRI technique or through US or CT techniques [4, 13–20].

A study done by Geeraerts et al. [4] also used MRI in the measurement of ONSD, yet an axial fat-suppressed

Table 2 ONSD mean value measured by the first and the second reader in the 3D DRIVE sequence in the control and patient group

		Control group	Patients group	*P* value	Sig.
		No. = 17	No. = 17		
First reader	Mean ± SD (mm)	4.95 ± 0.45	5.81 ± 0.33	< 0.001	HS
	Range (mm)	4.31–5.73	5.21–6.4		
Second reader	Mean ± SD (mm)	4.74 ± 0.31	5.90 ± 0.30	< 0.001	HS
	Range (mm)	4.3–5.26	5.44–6.46		

T2 WI turbo spin-echo sequence was obtained on a 3-T MRI unit with relatively large slice thickness (4 mm) and interslice spacing (5 mm), yet in our study, the use of thin cut 3D DRIVE sequence with 1.4/0.7-mm slice thickness and gap allowed better demarcation of the optic nerve sheath and more accurate assessment of ONSD.

Lim et al. [13] used CT for the measurement of ONSD, yet the main disadvantage of this study was the radiation exposure.

Many studies used US for measuring the ONSD catching the advantage of US as a bedside test with less cost [15–20]. However, the main disadvantage of US is that the US is an operator-dependent technique so its measurement may be affected by the inexperience of the examiner, the other disadvantages are the poor penetration of US beam, the artifacts from the tissues under observation, the bad cutting plane, and the low spatial resolution, all these disadvantages may explain the difference in ONSD value using the MRI and the ultrasound.

The optic nerve sheath diameter was measured 3 mm behind the posterior aspect of the ocular globe, with the axis of measurement perpendicular to the nerve axis. Several studies used the same method of measurement [4, 13, 17, 18], yet the ONSD was measured 1 cm anterior to the optic foramen on an axial T2 MRI sequence in a study done by Shofty et al. [20] who compared the ONSD with IIP in pediatric patients with an idiopathic increase of intracerebral tension.

In our study, two operators, with 5 years head and neck experience, used to measure optic nerve sheath diameter in both 3D DRIVE and T2 WI sequences, the 3D DRIVE showed significantly less interobserver variability (mean of difference in 3D DRIVE and T2 WI sequences was 0.01 ± 0.08 mm versus 0.08 mm ± 0.1, respectively, *P* value < 0.001), and this low interobserver variably was attributed to the inherited high image quality of 3D DRIVE sequence with higher spatial and contrast resolution allowing better assessment of fluid-filled structures which give a more accurate measurement of the ONSD with higher confidence. This value was also better than the value stated by Geeraerts et al. [4] who showed that the interobserver variability mean difference was 0.11 ± 0.17 mm, yet in Geeraerts et al.'s [4] study the interobserver variability was analyzed on 22 out of 74 participants (12 out of 36 normal volunteers and ten out of 38 patients with elevated ICP) and axial proton density/T2-weighted fat-suppressed sequence was used for measuring the ONSD.

In our study, the optimal ONSD cut-off value for diagnosing high ICP more than 20 mmHg in 3D DRIVE sequence was > 5.31 mm, with 94.12% sensitivity, 82.35% specificity, and 88.24% accuracy; on the other hand, the optimal cut-off value of the ONSD measured in the T2 WI sequence was of higher value (> 5.6 mm), yet with less sensitivity, specificity, and accuracy (88.2%, 64.71%, and 76.47%, respectively), and at lower cut-off value of > 5.31 mm, the sensitivity was increased to become similar to that of ONSD cut-off value measured in 3D DRIVE sequence yet with significant reduction of specificity down to 52.94%. The better accuracy of 3D DRIVE contributed to the cisternographic effect of the 3D DRIVE sequence and its higher contrast resolution which allow more precise discrimination and more accurate measurement of ONSD, as it avoids the optic nerve sheath blurring seen in the T2 WI sequence which becomes more apparent when image zooming was performed during ONSD measurement.

A higher yet comparable cut-off value was also noted in different studies. Geeraerts et al. [4], who compared

Table 3 The cut-off value of ONSD measured in 3D DRIVE and T2 WI sequences for diagnosing idiopathic intracranial hypertension

	Cut-off value (mm)	Sensitivity (%)	Specificity (%)	+PV (%)	-PV (%)	Accuracy (%)
3D DRIVE ONSD	> 5.21	94.12	70.59	76.2	92.3	82.35
	> 5.31	94.12	82.35	84.2	93.3	88.24
	> 5.6	76.47	82.35	81.2	77.8	79.41
T2 WI ONSD	> 5.31	94.12	52.94	66.67	90	73.53
	> 5.6	88.2	64.71	71.43	84.62	76.47
	> 5.8	76.47	70.59	72.22	75	73.6

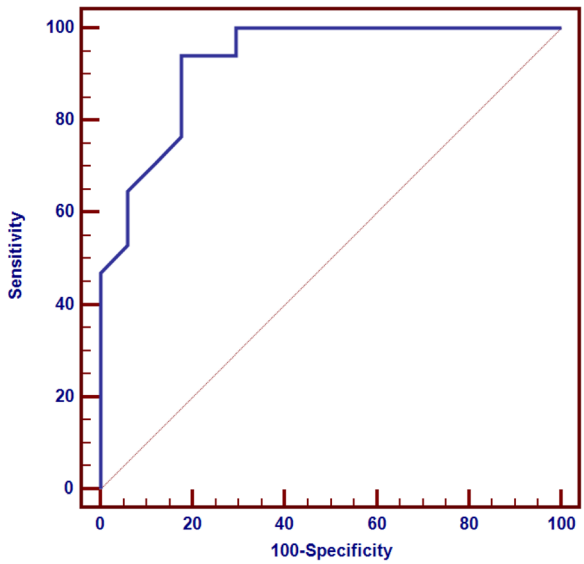

Fig. 1 ROC curves for ONSD measured in 3D DRIVE sequence in relation to raised ICP. AUC = 0.929, CI 95% = 0.786 to 0.989

patients with post-traumatic intracranial hypertension with healthy volunteers, revealed that optimal ONSD cut-off value was 5.82 with sensitivity of 90%, which increased at lower cut-off value of 5.3 mm to become 100% at the cost of reduced specificity reaching 50%; the difference in the cut-off values between our studies was attributed to the different MRI sequence and magnet strength as well as the studied patients' pathologies, as Geeraerts et al. [4] measured the ONSD in patients who suffered from traumatic brain injury with elevated ICP rather than patients with IIH; also, he measured ONSD on a 3-T MRI unit using fat-suppressed T2 WI turbo spin-echo sequence instead of 3D DRIVE sequence. Lim et al. [13] reported 89.9% sensitivity and 80% specificity of ONSD cut-off value of 5.5 mm yet the ONSD was measured in post-traumatic adults with high ICP using CT rather than an MRI scan.

Many studies using ultrasonographic examination were also used to measure the cut-off value for diagnosing intracranial hypertension. Jeon et al. [14] who used ultrasound to measure ONSD in patients requiring external ventricular drainage concluded that the best

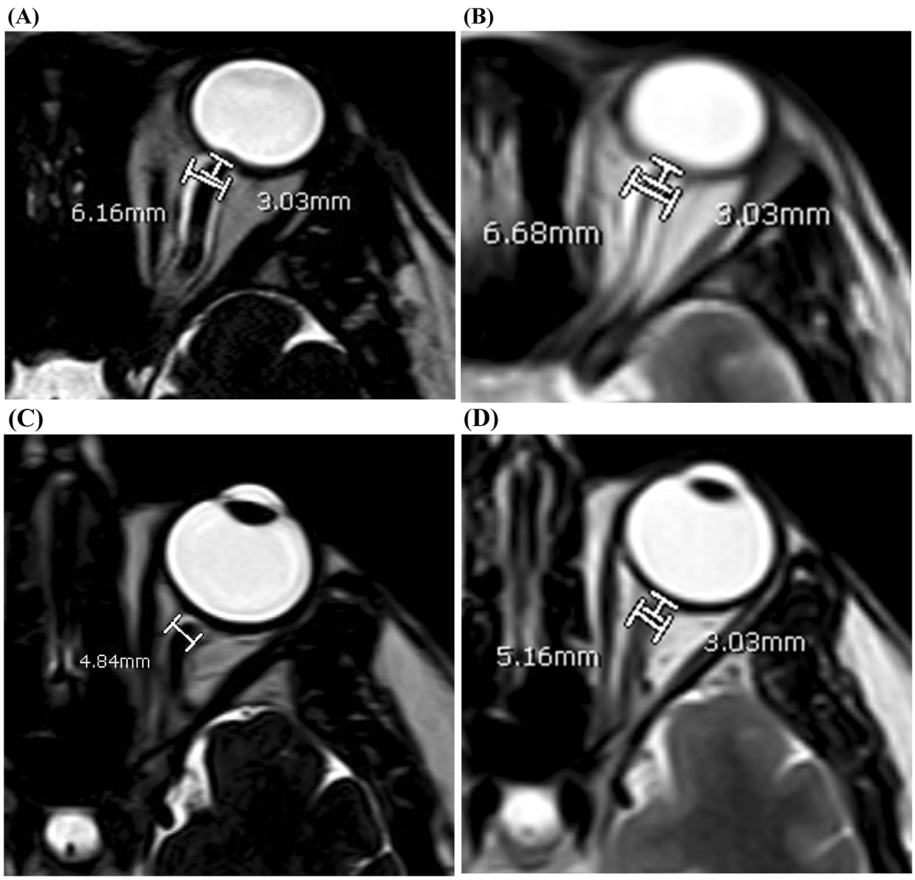

Fig. 2 3D DRIVE and T2 WI sequences show ONSD measured 3 mm behind eye globe. **a**, **b** 3D DRIVE and T2 WI sequences in a 35-year-old female patient with a diagnosis of IIH showing high ONSD measuring 6.16 mm in 3D DRIVE and 6.68 in T2 WI sequence. **c**, **d** 3D DRIVE and T2 WI sequences in 38 years female volunteer with normal ONSD measuring 4.84 mm in 3D DRIVE and 5.16 in T2 WI sequence

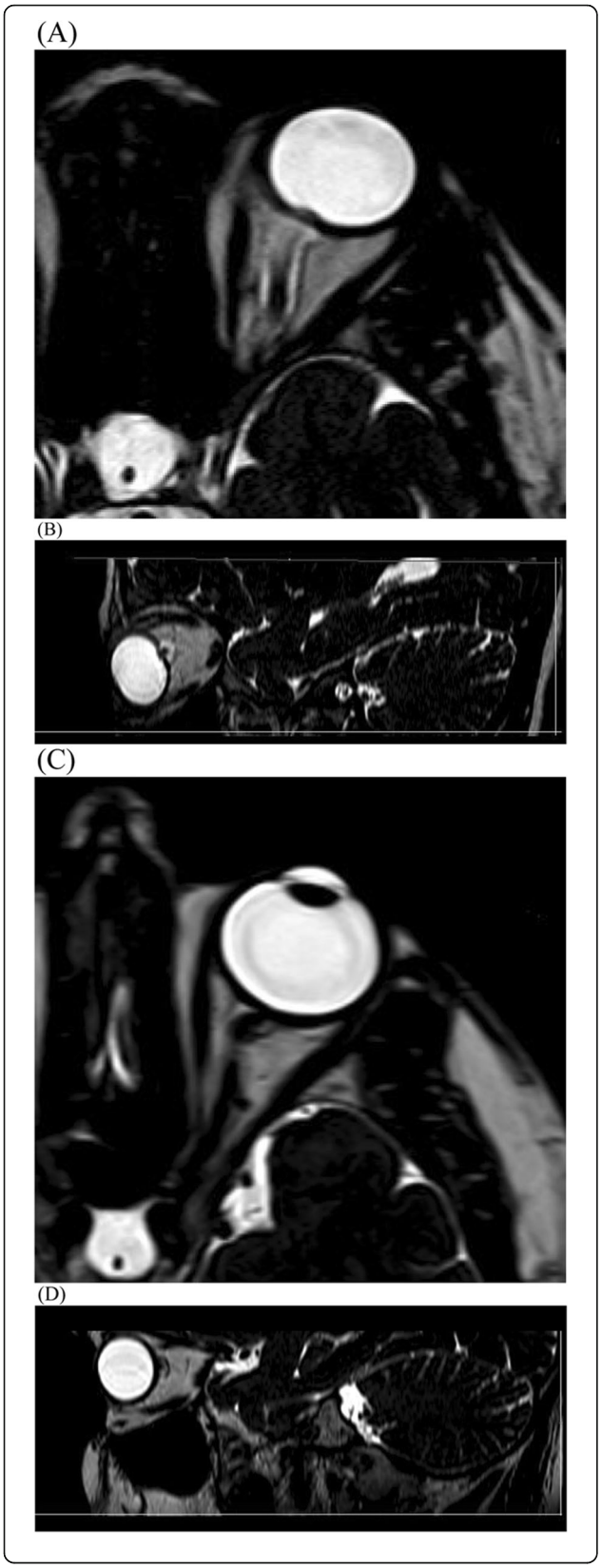

Fig. 3 axial (**a**, **c**) and sagittal reconstructed (**b**, **d**) 3D DRIVE sequence in the patient and volunteer of Fig. 2, showing posterior eye globe in the patient (**a**, **b**) and volunteer (**c**, **d**). **a**, **b** Posterior eye globe flattening and optic nerve head protrusion is seen in patient suffering from IIH. **c**, **d** Normal posterior eye globe in normal healthy volunteer

ONSD cut-off value for diagnosing intracranial hypertension was ONSD more than 5.6 mm with a sensitivity of 93.75% and a specificity of 86.67%. Robba et al. [15] also showed that the ONSD more than 5.85 is the best cut-off value for diagnosing intracranial hypertension in post-traumatic brain injury patients. A lower cut-off value for diagnosing high ICP was concluded in other studies measuring the ONSD by ultrasound technique in patients suffering from various brain pathology including intracerebral hemorrhage or subarachnoid hemorrhage; Rajajee et al. [16] showed that best ONSD cut-off value was 4.8 mm or more with 96% sensitivity and 94% specificity and with higher cut-off value of 5.2 mm the sensitivity was reduced down to 67% with minimal increase of specificity up to 98%. Moretti and Pizzi [17] stated that the best ONSD cut-off value was 5.2 mm with a sensitivity of 94% and specificity of 76%. Kimberly et al. [18] showed that a cut-off value of 5 mm or more was the best predictor of increased intracerebral pressure with a sensitivity of 88% and specificity of 93%. The difference in the cut-off value among these studies was attributed to different techniques used for measuring the ONSD and the different pathology involved in the elevated ICP.

To our knowledge, there was only one previous study which was done by del Saz-Saucedo et al. [19] who correlated the ONSD with the elevated ICP in adult patients suffering from IIH, yet their study showed a higher cut-off value by 1 mm more than our study, where their optimal cut-off value was 6.3 mm, with 94.7% sensitivity and 90.9% specificity; the difference in our cut-off values may be attributed to different modality used in ONSD measurement as the ONSD was measured by ultrasound technique in his study, it may be also related to the difference of the medical status of patients suffering from IIH as both of us did not correlate the ONSD with the clinical status of patient, e.g., the patients received medication for lowering the ICP or not.

Table 4 The inter observed variability. The ONSD mean value and range of the difference between the first and the second reader in both 3D DRIVE and T2WI sequences

	T2 WI ONSD	3D DRIVE ONSD	*P* value	Sig.
Mean of difference ± SD	0.08 ± 0.1 mm	0.01 ± 0.08 mm	< 0.001	HS
Range of difference	0.12–0.5 mm	0.13–0.3 mm		

The limitation of this study was related to the limited number of patients and we did not study different age groups nor different values of increased ICP as we used only the cut-off value of increased ICP more than 20 mmHg. Furthermore, a limitation related to the cost, availability, and the contraindication of MRI examination which may be of little value as the brain MRI/MRV is usually done as a routine investigation in patients with suspicious or sure diagnosis of IIH to exclude underlying neurological abnormalities of venous thrombosis. Hence, the ONSD measurement can add important clinical data on the presence of intracranial hypertension, and it may help to identify those patients who require more invasive monitoring.

Conclusion

The 3D DRIVE MRI provides an image with high spatial and contrast resolution in which the ONSD can be measured with high confidence with interobserver variability of little value. The measured ONSD correlates with the high ICP which is one of the diagnostic criteria for diagnosing IIH, and in addition, the brain MRI examination excludes the structural or neurological abnormalities needed for diagnosing IIH. So the ONSD can provide accurate data for diagnosing idiopathic increased ICP and it can be used as a complementary or preliminary study before proceeding to the invasive lumbar puncture technique.

Abbreviations

CSF: Cerebrospinal fluid; ICP: Intracranial pressure; IIH: Idiopathic intracranial hypertension; MRI: Magnetic resonance imaging; ONSD: Optic nerve sheath diameter

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Not applicable

Authors' contributions

AA suggested and developed the research idea, data collection, and analysis; shared in statistical analysis; shared in manuscript writing, revising, and editing; prepared MRI cases and performed required measurements; and prepared figures and tables. MB contributed to the data collection and analysis and reviewing of literature, performed statistical analysis, shared in manuscript writing, prepared MRI cases, and performed required measurements. Both authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the Faculty of Medicine at Ain Shams University in Egypt on 2 October 2019, reference number of approval FWA 000017585. All patients included in this study gave written informed consent to participate in this research. If the patient was unconscious at the time of the study, written informed consent for their participation was given by their legal guardian.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study. If the patient was unconscious when consent for publication was requested, written informed consent for the publication of this data was given by their legal guardian.

Competing interests

The authors declare that they have no competing interest.

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