THE RELIABILITY OF VENOUS SINUS STENOSIS USING NON CONTRAST 3D MRV IN PREDICTION OF THE DIAGNOSIS OF IDIOPATHIC INTRACRANIAL HYPERTENSION, A CASE CONTROL STUDY

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ABSTRACT

Idiopathic intracranial hypertension, or shorty IIH, refers to a clinical syndrome in which there is elevated CSF pressure and papilledema in the lack of any focal neurological signs. It is largely a diagnosis of exclusion, but imaging workup is undertaken routinely in order to rule out other pathologies. In this study we tried to evaluate the prevalence of venous sinus abnormalities using the simpler and less invasive non contrast enhanced 3D TOF MRV in group of patients with IIH, using the combined stenosis score, and compare this score with a group of controls, to assess the accuracy of MRV alone as an individual test in predicting the diagnosis of IIH. The study sample included 44 patients and 25 control subjects, following MRV analysis it was found that a combined severity score of cut of value of 4.5 for the combined conduit score (CCS) was associated with 79% sensitivity and 88.6 specificity for the diagnosis of IIH, and a cut off value of 5.5 for the adjusted score method gives a 83% sensitivity and 88.6 % specificity for the diagnosis. MRV is a valuable in the diagnosis of IIH; non contrast 3D MRV is an efficient test and gives valuable diagnostic information.

Keywords: *3D MRV, idiopathic intracranial hypertension.*

INTRODUCTION

Idiopathic intracranial hypertension, or shorty IIH, also termed primary pseudotumor cerebri, refers to a clinical syndrome in which there is elevated CSF pressure and papilledema in the lack of any focal neurological signs. It is largely a diagnosis of exclusion, but imaging workup is undertaken routinely in order to rule out other pathologies that my lead to intracranial hypertension, such as obstructive hydrocephalus, masses, meningitis, vascular malformations and fistulae, or dural venous sinus (1–6).

The importance of this condition is that if left untreated, visual deterioration and even blindness may ensues (1,3).

With routine use of MRI and MRV to exclude other causes of raised intracranial pressure, a significant proportion of patients were noted to have non-thrombotic venous sinus abnormalities (1,7–9).

The most frequent MRV finding is bilateral lateral sinus stenosis, with some working groups showing that nearly all patients showing venous sinus flow abnormalities that are non-thrombotic in nature, namely, bilateral significant focal venous sinus stenosis (6,8,10).

However, venous sinus abnormalities like narrowing and hypoplasia are not infrequent findings noted routinely in MRI imaging including studies on healthy subjects (9); older research have questioned the value of MRV for diagnosis of IIH stating that venous sinus abnormalities may are prevalent in controls, making the diagnostic contribution of MRV limited in cases of IIH, suggesting that MRI and MRV makes no important contribution in confirming or refuting a diagnosis of IIH (11,12).

Moreover, most of the radiological workup of IIH patients with MRI used contrast enhanced MRV, stating higher sensitivity and accuracy in evaluation of sinovenous stenosis , and for this purpose some researchers used a quantitative scoring system that combine the findings from both lateral sinuses to assess the combined stenosis score (8,9,13).

THE AIM OF THE PAPER

In this study, we tried to evaluate the prevalence of venous sinus abnormalities using the simpler and less invasive non contrast enhanced 3D TOF MRV in group of patients with IIH, using the combined stenosis score, and compare this score with a group of controls, to assess the accuracy of MRV in predicting the diagnosis of IIH.

PATIENTS AND METHODS

Patients

In the time from March 2019 to December 2020, cases clinically suspected to have IIH by the hospital's neuromedicnie specialists, were referred to the MRI unit at our hospital, examination by MRI and MRV was done, the MR study was followed by CSF pressure assessment by LP done 24-72 hours by the clinical team and only cases proved to have raised ICP were selected for the patient group; therefore, the inclusion criteria included cases clinically suspected as IIH, with neuroimaging showing no alternate pathology , and confirmed by CSF manometry done in the neuromedicine ward.

The local ethics committee approved the study.

Written informed consent was obtained from all the patients prior to inclusion.

Exclusion criteria for cases were when the MRI showed abnormalities such as mass, infection, intracranial hypotension, patients with previous surgical interventions, cases with venous sinus thrombosis, hydrocephalus, or any abnormality that would label the patient a diagnosis other than Idiopathic intracranial hypertension .

Controls

All MRV studies performed from March 2019 to December 2020 at the MRI unit at our hospital were reviewed and a control group of subjects was identified based on the availability of a brain MRI reported as normal by a single neuroradiologist and with no feature of venous sinus thrombosis on MRV. Patients were not excluded from the control based on MRV abnormalities other than thrombosis.

Unfortunately, no clinical data for the presenting symptoms of the control group was available.

Image acquisition

MR imaging was performed with a Philips healthcare Achieva 3T TX 32CH.

Standard neurovascular coil (8-channel). Routine coronal, axial, and sagittal T2-weighted images (TR=3440–4100 ms; TE=84–88 ms; field of view 23 cm; slice thickness 5mm; interslice gap1mm; echo train length, 16; matrix, 352×256; number of average=2) and 3DPCA MRV (TR=15ms, TE=35 ms; field of view 22cm; slice thickness 1.4 mm; number of average 1; echo train length 1; matrix 256*256; flip angle10°) source, and maximum intensity projection (MIP) images were evaluated. Two radiologists with 10 years of experience in neuroimaging evaluated the radiological images.

Image analysis

For assessment of the venous diameter for both patients and control, we used the combined conduit score method, CCS, which is the method originally adopted by Frab et al

(13), were assessment of the lumen of each transverse sinus was measured and compared to the diameter of the of the distal superior sagittal sinus , regardless of the length of the segment , then graded as: 0 for lack of flow or total aplasia, 1 for severe >75% narrowing; 2 for moderate 50-75% narrowing; 3 for narrowing less than 25-50%; and 4 for normal or very mild less than 25% stenosis (13).

Interpretation of the findings was done by two radiologists with more than 7 years' experience in neuroimaging, and consensus result was recorded, the radiologists were not blinded to the diagnosis of patients and controls.

Based on our belief that venous sinus hypoplasia is a common benign finding that is seen frequently in asymptomatic subjects, and in order not to overcall stenosis, we proposed an additional adjusted score method, in this method , whenever venous sinus hypoplasia was encountered, we used the grade for the better opposite side, and multiplied it by two to calculate the combined score, if the opposite side is worse, we would keep the hypoplastic side score as it is, we tried to examine whether this method would give more accuracy in diagnosis of IIH.

Statistical analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences, version 23.0 (SPSS, Chicago, Illinois).

ROC curves were used to assess the sensitivity, specificity, and cut of values.

RESULTS

Our study sample included a total of 44 patients, 38 of whom are females (86.4%), the control group included 24 subjects, 15 of which (62%) are female (table 1).

Table 1. Demographic data of both groups.

Parameter		Patients	Control	P value
		N=44	N=24	
Age (yr)		29.61±1.13	32.25±3.7	**0.502**
Gender	Female	38 (86.4)	15 (62.5)	**0.033**
	Male	6 (13.6)	9 (37.5)	

Age presented by mean±; standard error of mean, gender presented by frequency and percentage, p value for age by unpaired t-test, p value for gender by Fisher exact test.

For the MRV results, using unpaired t-test, both of the combined score and the adjusted score showed statistically significant difference between patients and controls, with P value less than 0.0001 for both, table (2).

Table 2. Comparison of scores between patients and control by unpaired t-test.

Parameter	Patients	Control	P value
	N=44	N=24	
Combined score	2.09±0.31	6.0±0.34	**<0.001**
Adjusted score for hypoplasia	2.23±0.35	7.08±0.32	**<0.001**

Data presented by mean± standard error of mean

For the Combined score method, ROC curve analysis showed that a cut of value of 4.5 was associated with 79.2% sensitivity and 88.6% specificity between IIH cases and controls (figure 1), table (3).

Figure 1. ROC curve for combined score between patients and controls

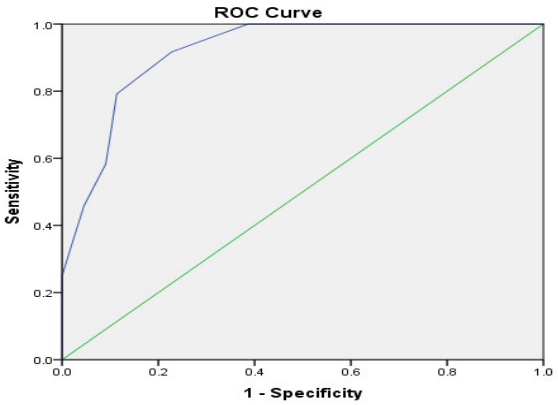


Table 3. Area under curve, sensitivity, specificity and cutoff value for combined score between patients and controls.

Parameter	Area under curve	Sensitivity	Specificity	Cutoff value
Combined score	0.919	79.2%	88.6%	**4.5**

Using CCS, five of our control showed values less than the cutoff, and 5 of the patient showed values higher than the cutoff.

Adopting the adjusted score, a cut of value of 5 was associated with improved sensitivity of 83.3% , without compromising specificity (88.6% as well); (figure 2, table 4).

Figure 2. ROC curve for adjusted score for hypoplasia between patients and controls

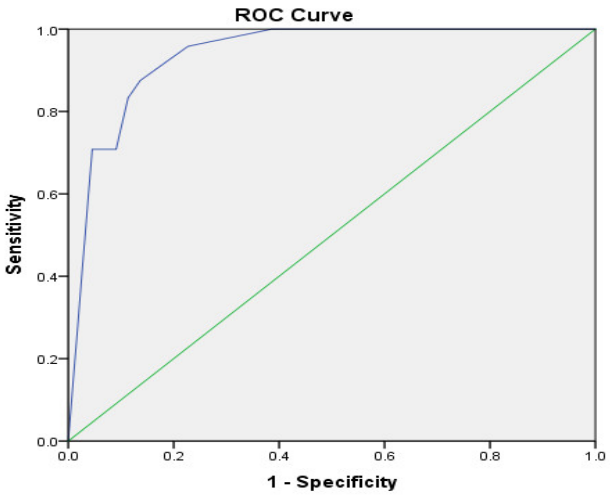


Table 4. Area under curve, sensitivity, specificity and cutoff value for adjusted score between patients and controls.

Parameter	Area under curve	Sensitivity	Specificity	Cutoff value
Adjusted score for hypoplasia	0.938	83.3%	88.6%	**5.5**

Using adjusted scores, four of controls showed values less than the cutoff, and five patients showed values more than the cutoff.

Therefore, in the majority of the cases, MRV did show venous sinus abnormalities in comparison to controls, most bilateral stenosis, as shown in figures 3 and 4.

Figure 3. MIP coronal (A) and axial (B) images MRV showing bilateral occlusions of the lateral segment of both transverse sinuses in patient with pseudotumor cerebri.

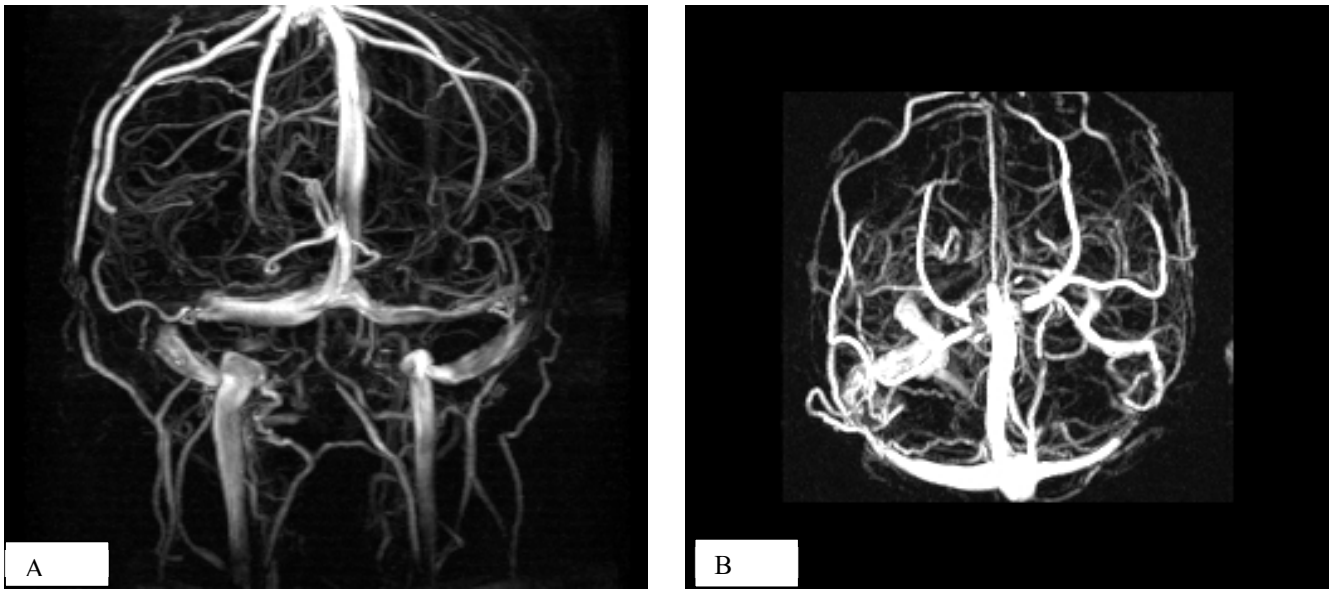
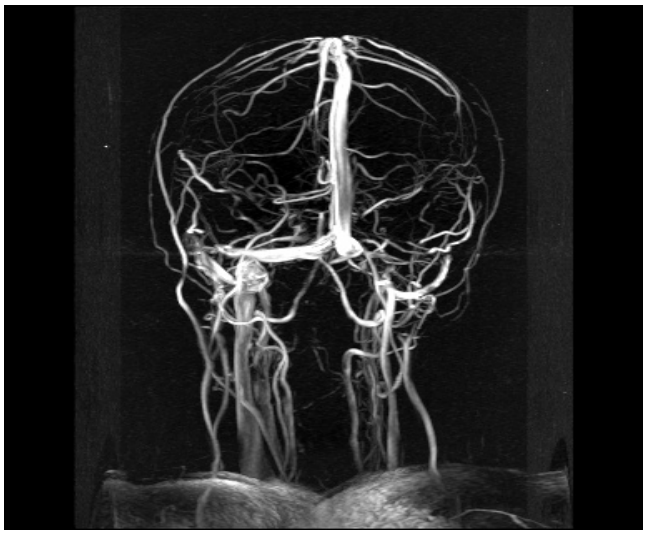


Figure 4. Coronal MIP MRV image shows bilateral transverse sinus occlusions; the patient was diagnosed with IIH clinically.



DISCUSSION

The diagnosis of IIH is supported by multiple radiological findings, and while most of them are variable and may be observed in healthy controls, with no single MRI feature being consistently reported in patients with IIH, but the addition of MRV is frequently reported to raise diagnostic accuracy of MRI (6–8,12,14–17).

We did not attempt to assess the conventional MRI signs for predicting their accuracy alone or in combination with MRV, as this study was mainly targeted at the MRV value in IIH.

Most of the studies used combination of conventional MRI signs such as empty sella turcica and perioptic nerve sheath fullness etc. with MRV, and most of the available studies on the subject used contrast enhanced venography, and concluded that MRV show bilateral venous sinus stenosis in very high percentage of patient with IIH (13,15–17).

In our study, we used our routine non contrast 3 D TOF MRV which is readily available noninvasive technique, and we observed that venous sinus stenosis was far more frequent in patients with idiopathic intracranial hypertension than our control group, and that a combined severity score of cut of value of 4.5 for the CCS was associated with 79% sensitivity and 88.6 specificity, figure 1 table 3, and 5.5 for the adjusted score method gives a 83% sensitivity and 88.6 % specificity figure 2 table 4.

Our use of adjusted scores for hypoplasia has resulted in mild improvement in sensitivity (from 79% to 83%) after adjusting the cutoff point from 4.5 to 5, this method, would prevent overestimation of the score in cases of simple hypoplasia, and while not affecting the specificity, allowed for better sensitivity because of the higher cutoff value of 5.

This result is consistent with the study done by Maralani et at (10) (8), they adopted contrast enhanced MRV, and found that CCS of less than 4 is very specific , nearly 100% but with sensitivity of 62% , and they concluded that finding CCS less than 4, with or without other MRI conventional signs for IIH on MRI, would greatly increase the diagnostic certainty of the test, from 18-46 folds as given in the results (8), however, their results showed sensitivity of 62%, so they concluded also that absence of MRV findings should not dismiss the diagnosis of IIH.

Our data showed overall improved sensitivity in comparison to Maralani et al, this could have been resulted from the higher cut off values for our results, however, the specificity is significantly better in their study , i.e. 100% , our figure of 88.6 % may also have resulted from difference in the calculated cut off, but may also be the result of the technique itself with higher proportion of controls showing venous narrowing that may be artefactual in nature related to slower flow, reflecting the inherently less accurate nature of the non-contrast MRV as compared to contrast studies, but this should not, nonetheless, abandon the value of unenhanced MRV with good sensitivity and specificity, with the advantage of ease of use and lack of contrast medium administration , with its well-known limitations and clinical implications.

Morris et al (16) also found that transverse sinus stenosis was identified on MRV in 94% of patients with idiopathic intracranial hypertension and in 3% of controls and they concluded that MRV is the most sensitive test for IIH (16), these studies were also conducted using contrast MRV. Their data show higher sensitivity than ours, but this may have been largely related to the image analysis they adopted, they regarded unilateral venous sinus stenosis of less than 50% as a positive result, not calculating scores as in our study, which would result in higher positive results, therefore, higher sensitivity.

The variability of MRV findings in normal subjects is well known, and the fact that venous sinus hypoplasia or narrowing may be seen in normal subjects may cast doubt on the significance of MRV findings when IIH is suspected, and earlier research on the topic has even refuted a significant association between IIH and venous sinus abnormalities, stating that they are no more common than in control subjects (12), however, and similar to our results, a study by Kelly et al (9) investigated the prevalence of venous sinus abnormalities in a retrospective study excluding with IIH , their study, with imaging protocol using contrast MRV, indicated that while bilateral significant venous sinus narrowing may exist in subjects without IIH, but this observation is not common, and therefore, finding bilateral lateral sinus narrowing should prompt a thorough search for papilledema (9).

Higgins et al. (18) and similar to our experiment, relied on non-contrast 3D and 2D MRV, and their work on 20 patients with IIH and 40 control subjects, their control group was a group of healthy adult subjects, rather than studies reported as normal, their patients were asymptomatic for headache or any other neurologic complaint, they found that MRV showed significant value in diagnosis of IIH, with 13 out of 20 patients showing bilateral venous sinus stenosis, Higgins et al found that none out of 40 healthy controls were showing significant bilateral transverse sinus narrowing, but 13 of them did show unilateral sinus narrowing, but the study did not attempt to quantitatively assess the degree of stenosis, to enable comparison between patients and controls, or to enable comparison with our work, however, they are obviously in disagreement with the studies refuting the value of non-contrast MRV in the diagnosis of IIH. Higgins et al suggested that image artefacts and poor choice of control may contribute to failure to recognize typical IIH pattern in MRV by the other workers.

The most significant limitation was the nature of the control group, being recruited retrospectively from the radiology department archive using cases with consensus reporting as normal, and not from a group of healthy volunteers.

Also the radiologist was not blinded to the diagnosis, but adapting a score system rather than visual interpretation would have eliminated the potential reading bias.

CONCLUSION

MRV is a valuable in the diagnosis of IIH. Non contrast 3D MRV is an efficient test and gives valuable diagnostic information.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2013. Voluntary written and informed consent was obtained from each participant prior to enrollment in the study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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