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Prognostic Value of MRI-CSF Flowmetry for Shunt Responsiveness in Patients with Idiopathic Normal Pressure Hydrocephalus

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Abstract

Background: Idiopathic normal pressure hydrocephalus (iNPH) is considered a treatable cause of dementia. MRI-CSF flow study is a non-invasive investigation for qualitative and quantitative CSF flow analysis to be used for the diagnosis of normal pressure hydrocephalus (NPH). The degree of clinical improvement of NPH symptoms post CSF diversion and shunting; was better in patients with higher pre-operative CSF stroke volume; allowing MR-CSF flowmetry to be a promising prognostic tool.

Aim of Study: To evaluate the prognostic value of MRI-CSF flowmetry for shunt responsiveness in patients with idiopathic normal pressure hydrocephalus and its usefulness as a predictor of post CSF diversion favorable outcome.

Patients and Methods: Our study is prospective. 38 patients with clinical diagnosis of iNPH, ventriculomegaly and hyper dynamic CSF flow on PC MRI were included in our study. We used two protocols of PC MRI-CSF flowmetry examination; one assessing CSF flow dynamics qualitatively using a sagittal plane and one quantitatively using an axial plane perpendicular to the aqueduct. All patients underwent ventriculo-peitoneal shunt (VPS). Patients were followed up after shunting surgery for average 10 months at neurology and neurosurgery outpatient clinics for improvement of clinical symptoms & categorized into well responsive to shunt or not.

Results: We found that aqueductal CSF stroke volume (>42 microL) shows sensitivity of about (93.4%) & specificity of about (75.1%) with total accuracy of about (89.6%) in predicting shunt responsiveness and favorable outcome in iNPH patients.

Conclusion: MRI-CSF flowmetry is a promising non-invasive prognostic tool for iNPH. It had a high predictive value for shunt responsiveness. Our study enhances the utility of PC MRI-CSF flowmetry in selection of iNPH patients who are likely to benefit from VPS (shunt responsive); thus reducing the rate of unnecessary previously used invasive procedures as external lumbar drainage.

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Key Words: *NPH – ventriculomegaly – CSF Flowmetry – Phase contrast MRI – shunt responsive – prognostic.*

Introduction

IDIOPATHIC normal pressure hydrocephalus (iNPH) was first described by Hakim and Adams in 1965 as a syndrome of gait disturbance (apraxia), cognitive deterioration (dementia) and urinary incontinence associated with normal opening CSF pressure and dilated ventricles **[1]**.

The incidence of NPH is much higher in elderly populations. The majority of cases are idiopathic **[2]**.

On imaging; it could be characterized both on CT and MRI by enlarged lateral and third ventricles out of proportion to the degree of enlargement of cortical sulci with Evans' index value (more than 0.3); yet not diagnostic for NPH **[3]**.

MRI-CSF flow studies using cine phase contrast MRI (PC MRI) is a promising, safe and non-invasive investigation for both qualitative and quantitative CSF flow analysis; to be used for diagnosis of NPH especially in those cases where differentiation from age related involution brain changes and brain atrophy is difficult on clinical and conventional imaging basis. Increased CSF stroke volume (SV) across aqueduct was seen in NPH population **[4]**.

iNPH is considered a treatable cause of dementia. Preoperative aqueductal CSF stroke volume was noted to be higher in NPH patients with favorable post shunting response; allowing MR-CSF flowmetry to have a prognostic role in selection of shunt responder patients **[5]**.

Patients and Methods

The aim of our study was to evaluate the prognostic value of MRI-CSF flowmetry for shunt responsiveness in patients with idiopathic normal pressure hydrocephalus and its usefulness as a predictor of post CSF diversion favorable outcome.

This study is a single-center prospective study; enrolled a total of 38 patients (26 males, 12 females; mean age 61.5±8.3 years) referred from the neurology outpatient clinic with clinical diagnosis of suspected iNPH and ventriculomegaly as well as hyper dynamic CSF flow on PC MRI. From the original cohort of 50 patients with clinically suspected iNPH and ventriculomegaly; 12 patients proved to be brain atrophy with hypo dynamic CSF circulation across cerebral aqueduct and were excluded from the study with the final population enrolled a total of 38 patients.

Our study was conducted between December 2019 and August 2021 after approval of local ethical committee with written informed consent was taken. We used two protocols of PC MRI-CSF flowmetry examination; one assessing CSF flow dynamics qualitatively using a sagittal plane and one quantitatively using an axial plane perpendicular to the aqueduct. All patients underwent ventriculo-peitoneal shunt surgery (VPS). Patients were followed-up after shunting surgery for average 10 months at neurology and neurosurgery outpatient clinics for improvement of clinical symptoms & categorized into well responsive to shunt or not.

Inclusion criteria:

- Clinically suspected iNPH (gait apraxia, dementia with or without urinary incontinence).
- Ventriculomegaly (Evan's index >0.3).
- Normal CSF pressure at lumbar puncture.

Exclusion criteria:

- Presence of other cofounding diagnoses (neurodegenerative disorders).
- Presence of previous disorders (e.g. meningitis, subarachnoid hemorrhage, cranial traumas or intra-cranial surgery) that can be related to secondary NPH.
- Routine MRI contraindications as claustrophobic patients and pacemaker.

All patients were subjected to:

- Full history taking.
- 1.5 T MR unit (Toshiba Vantage Titan closed machine) was used; with the scan carried out using standard circular polarized head-array coils in the neutral supine position without any patient preparation. The patients were asked to avoid deep breathing during the exam. Initially; routine conventional MRI sequences were obtained before CSF measurements: - Axial T1WI (TR=500, TE=10), axial and sagittal T2WI (TR=3700, TE=100) and axial FLAIR images (TR=6300, TE=100).
- For PC MR-CSF flowmetry; sagittal images were obtained for qualitative analysis and axial images for quantification of CSF flow indices. Cardiac gating was performed in all cases with MR compatible electrodes.
- Sagittal 2D cine phase-contrast MRI (2D cine PC-MRI) done for all patients using the following parameters:-
  - TR=21ms, TE=10ms, flip angle= 15°.
  - Matrix: 256 x 265 pixels.
  - Slice thickness: 5mm.
  - Field of view: 180mm.
  - Number of acquisitions: 2
- Mid sagittal PC images were obtained and displayed on a gray scale; where hypo intense signal represents caudal flow in CSF systole and hyper intense signal represents cranial flow in CSF diastole. These phase grey scale images were displayed in a continuously repeated cine format allowing visualization of CSF circulation across the cerebral aqueduct and subarachnoid CSF spaces; the change of flow across the cerebral aqueduct during systole and diastole ruled out the presence of any aqueductal obstruction.
- Axial images for quantitative analysis of CSF flow: In the mid-sagittal image; a localizer was placed on cerebral aqueduct perpendicular to its proximal one third (ampullary region). High resolution axial PC image was then obtained. A circular ROI was drawn manually to include all pixels that reflected CSF flow signals across the cerebral aqueduct on the axial PC image after magnification of the image to clarify the flow. Thereafter; CSF flow wave form and corresponding table showing CSF velocity and flow values were automatically generated.
- On the CSF flow wave form; CSF moves craniocaudally during CSF systole and caudo-cranially during CSF diastole.
- Post-processing calculations including peak systolic velocity (cm/s), end diastolic velocity (cm/s) and aqueductal stroke volume (SV) defined as mean volume of CSF passing across the cerebral aqueduct during systole = mean systolic flux x duration of CSF systole (microL).

- The estimated duration of the procedure was about 25-30 minutes.
- All patients underwent ventriculo-peitoneal shunt (VPS).
- Patients were followed-up after shunting surgery for average 10 months at neurology and neurosurgery outpatient clinics for improvement of clinical symptoms & categorized into well responsive to shunt or not.

Statistical analysis:

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Standard diagnostic indices including sensitivity, specificity and diagnostic accuracy were calculated. Mann Whitney U test was used to test the difference in PSV and aqueductal stroke volume (SV) in relation to shunt responsiveness. Chi-square test was used as a test of significance. *p*-value less than 0.05 was considered as statistically significant.

Rersults

The study population included 38 iNPH patients (26 males, 12 females; mean age was 61.5 ±8.3 years).

Regarding NPH symptomatology: 34 patients (89.4%) had dementia as a presenting symptom, 29 patients (76.3%) had gait apraxia as a presenting symptom or associated with other symptoms of Hakim's clinical triad and 10 patients (26.3%) had urinary incontinence accompanied with gait apraxia or dementia in most of cases as urinary incontinence is considered a late symptom of iNPH.

Regarding conventional MRI findings: All patients had dilated lateral and third ventricles (100%), 29 patients (76.3%) had evident CSF flow void across cerebral aqueduct ±3rd & 4th ventricles.

The included iNPH patients in our study show mean PSV=10.3±3.7cm/s and mean stroke volume (SV)=109.5±68.4 microliter/cycle (Table 1).

Table (1): PSV and Aqueductal SV in the study group.

	Mean	SD
PSV	10.3	3.7
Aqueductal SV	109.5	68.4

30 patients out of the study population had well response to VP shunt (78.9%) with improvement of the clinical symptoms.

PSV in relation to shunt responsiveness: The 30 patients who had well response to shunt had mean PSV of (11.6±3.6cm/s); the other 8 shunt non-responsive cases had mean PSV of (6.7±1.7cm/s).

Aqueductal stroke volume (SV) in relation to shunt responsiveness: The 30 patients who had well response to shunt had mean aqueductal SV of (115.8±65.7 microliter/cycle); the other 8 shunt non-responsive cases had mean aqueductal SV of about (34±11.3 microliter/cycle. There is significant correlation between increased PSV & aqueductal SV and symptoms improvement post shunting (*p*-value 0.008) (Table 2).

Table (2): PSV and Aqueductal SV in the study group.

	Shunt Responsiveness				*p*-value#
	Well-Responsive (N=30)		Non-Responsive (N=8)		
	Mean	SD	Mean	SD	
PSV	11.6	3.6	6.7	1.7	0.007 (S)
Aqueductal SV	115.8	65.7	34	11.3	0.008 (S)

Aqueductal stroke volume (> 42 microliter/cycle) in relation to shunt responsiveness in NPH patients: 28 out of 30 patients who had well response to CSF shunt surgery (93.4%) had aqueductal SV >42.6 out of 8 patients who had not responded to CSF shunt surgery (75%) had aqueductal SV between 28-42 microliter/cycle (Table 3).

Table (3): Relation between aqueductal SV (> 42microL/cycle) and shunt responsiveness.

Variable	Shunt Responsiveness				*p*-value#
	Well-Responsive (N=30)		Not-Responsive (N=8)		
	N	%	N	%	
Aqueductal SV:					
>42	28	93.4	2	25.0	0.014 (S)
Between 28-42	2	6.6	6	75.0	

Prognostic significance of aqueductal stroke volume (> 42microL/cyscle) in predicting shunt responsiveness and symptoms improvement in iNPH patients: There is statistically significant

relation between aqueductal SV (>42 microL) and favorable response post shunting (*p*-value=0.014). Aqueductal CSF stroke volume (>42 microliter/cycle) shows sensitivity of about (93.4%) & specificity of about (75%) with total accuracy of about (89.6%) in predicting shunt responsiveness and favorable outcome in iNPH patients post CSF diversion surgeries (Table 4) (Figs. 1,2).

Table (4): Prognostic significance of aqueductal SV >42 microL in predicting shunt responsiveness in iNPH patients.

Aqueductal SV (>42)	%
Sensitivity	93.4
Specificity	75
Total accuracy	89.6

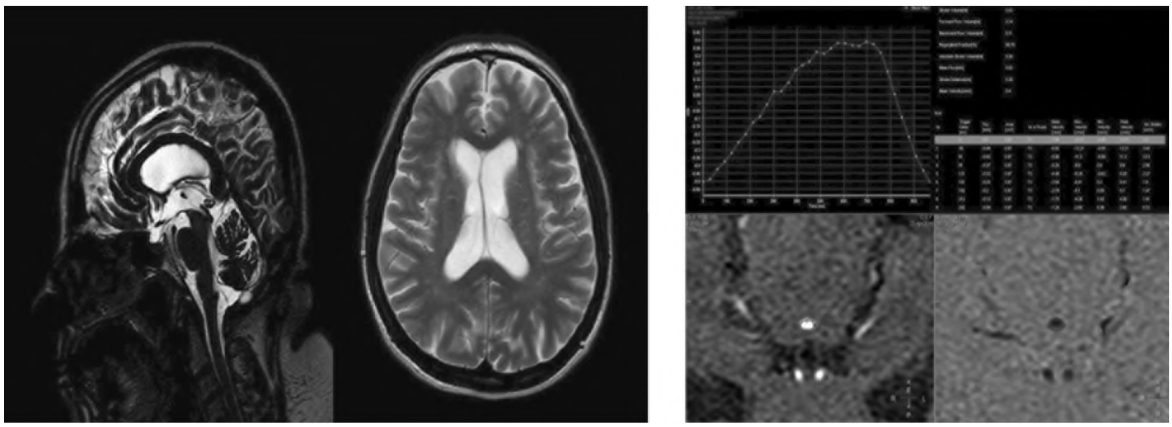

Fig. (1): Female patient aged 62 years presented with dementia and gait disturbance. Axial T2 and sagittal T2 CISS WIs showing ventriculomegaly out of proportion to sulcal prominence and prominent aqueductal CSF flow void detected through the aqueduct of sylvius & 4th ventricle in CISS sequence denoting hyper dynamic CSF circulation. CSF flow study showing free aqueductal CSF flow as a cranial flow during CSF diastole (hyperintense signal) and caudal flow during systole (hypointense signal). Systolic peak velocity=10.76cm/s. Estimated systolic stroke volume=115 microlitre/cycle. The patient underwent ventriculo-peritoneal shunt and was well responsiveness with significant improvement of symptoms.

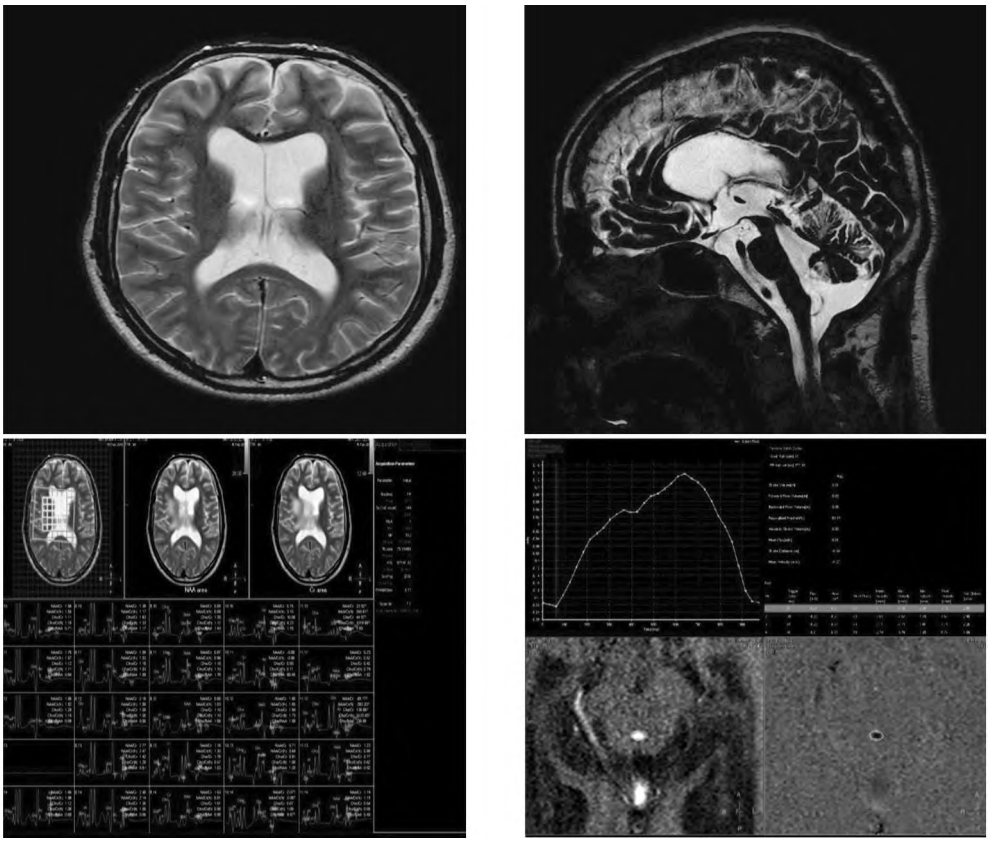

Fig. (2): Female 59 year old patient presenting with gait disturbance. Axial T2 and sagittal T2 CISS WIs showing evident ventriculomegaly out of proportion to sulcal prominence, marked corpus callosal thinning and prominent aqueductal CSF flow void detected through the aqueduct of sylvius in CISS sequence. MR Spectroscopy showing intra-ventricular lactate peak with no peri-ventricular significant NAA/Choline ratio reduction (suggesting reversible ischemia & predicting well response to shunt). CSF flow study showing free aqueductal CSF flow as a cranial flow during CSF diastole (hyperintense signal) and caudal flow during systole (hypointense signal). Systolic peak velocity = 5.7cm/s. Estimated systolic stroke volume =38 microliter/cycle suggestive of early stage of the disease. The patient underwent ventriculo-peritoneal shunt and was well responsive.

Two iNPH shunt responsive patients had aqueductal SV between 28-42 microliter/cycle compatible with mild hyper dynamic CSF circulation & early NPH. This denotes that aqueductal SV > 42 microliter/cycle favors good outcome after CSF diversion surgery; yet mild hyper dynamic CSF circulation with SV between 28-42 microliter/cycle is not an absolute exclusion criteria for shunt responsiveness.

Two iNPH shunt non-responsive patients had aqueductal stroke volume > 42 microliter/cycle which could be explained by the companion extensive white matter brain ischemic changes in these two cases.

Discussion

Idiopathic normal pressure hydrocephalus (iNPH) is considered the first treatable cause of dementia ever described; with its symptoms can show clinical regression and improvement with CSF shunting [6].

MRI-CSF flow studies using cine phase contrast MRI (PC MRI) is a promising, safe and non-invasive investigation used for diagnosis of NPH especially in those cases where the differentiation from brain atrophy on clinical and routine imaging basis is equivocal [4].

Once the diagnosis of iNPH is established; a CSF shunting procedure usually ventriculo-peritoneal adjustable shunt valves are considered. Therefore; identification of useful criteria for selection of ideal patients who will benefit from shunting procedure is crucial [7].

The aim of our study was to evaluate the prognostic value of MRI-CSF flowmetry for shunt responsiveness in patients with idiopathic normal pressure hydrocephalus and its usefulness as a predictor of post CSF diversion favorable outcome.

A total of 38 patients referred from the neurology outpatient clinic with clinical diagnosis of suspected iNPH and ventriculomegaly as well as hyper dynamic CSF flow on PC MRI were included in this study (mean age was 61.5±8.3 years). The patients were examined by MRI-CSF flowmetry with qualitative and quantitative analysis. All patients underwent ventriculo-peitoneal shunt surgery (VPS) and followed-up after shunting surgery for average 10 months at neurology and neurosurgery outpatient clinics for improvement of clinical symptoms & categorized into well responsive to shunt or not.

In our study; dementia was the leading presenting symptom in the study population (89.4%).

We found obvious increase of the PSV and aqueductal SV in the iNPH patients with mean PSV= 10.3±3.7cm/s and mean stroke volume (SV)= 109.5±68.4 microliter/cycle. Abdallah A.E.A et al., 2015 [8] reported that mean PSV & aqueductal stroke volume in the healthy volunteers to be of about (2.27±0.94cm/s & 27.26±2.05 microliter/cycle) respectively. He also reported markedly elevated mean PSV and aqueductal SV values in iNPH patients with mean values of about (9.1±3.1cm/s & 141±83 microliter/cycle) respectively; which agreed with our study.

30 patients out of the study population had well response to VP shunt (78.9%) with improvement of their clinical symptoms.

In our study; we found that 28 out of 30 patients who had well response to CSF diversion surgery (93.4%) had aqueductal SV >42 microliter/cycle; while 6 out of 8 patients who had not responded to the shunt surgery (75%) had aqueductal SV between 28-42 microliter/cycle. Aqueductal SV>42 microliter/cycle was found to have sensitivity of about (93.4%) & specificity of about (75%) with total accuracy of about (89.6%) in predicting shunt responsiveness and favorable outcome in iNPH patients post CSF diversion surgeries.

In our study; two NPH shunt responsive patients had aqueductal SV between 28-42 microliter/cycle compatible with mild hyper dynamic CSF circulation. This emphasized that aqueductal SV >42 microliter/cycle is a valuable predictor of favorable outcome after CSF diversion surgery; yet mild hyper dynamic CSF circulation with SV between 28-42 microliter/cycle is not an absolute exclusion criteria for shunt responsiveness; but more precisely patients with aqueductal SV between 28-42 microliter/cycle are less likely responding but still had the opportunity of clinical improvement after CSF diversion and still have a chance with VP shunting.

Kahlon B et al., 2008 [9] and Bradley W.G. 2020 [10] stated that patients who responded well to CSF diversion surgeries for iNPH had at least twice the aqueductal SV of healthy elderly patients; with increased aqueductal systolic SV >42 microliter/cycle was set as a threshold value for patients who benefited from surgery which is matching with our study.

Ginera et al., 2013 [11] emphasized PC-MRI CSF flow study as a useful prognostic tool for prediction of shunt responsiveness in iNPH patients.

Senger KPS et al., 2020 [12] also reported that stroke volume of >42 microL/cycle is shown to predict good response after CSF shunting.

Conclusion:

MRI-CSF flowmetry is a promising non-invasive prognostic tool for iNPH. It had a high predictive value for shunt responsiveness. Our study enhances the utility of PC MRI-CSF flowmetry in selection of iNPH patients who are likely to benefit from VPS (shunt responsive); thus reducing the rate of unnecessary previously used invasive procedures as external lumbar drainage.

References

1- HAKIM S., VENEGAS J.G. and BURTON J.D.: The physics of the cranial cavity, hydrocephalus and normal pressure hydrocephalus: Mechanical interpretation and mathematical model. Surg. Neurol., 5: 187–210, 1976.

2- FASANO A., ESPAY A.J., TANG-WAI D.F., et al.: Reply to: "gaps, controversies, and proposed roadmap for research in normal pressure hydrocephalus". Mov. Disord, 36: 1043–4. doi: 10.1002/mds. 28573, 2021.

3- QUATTRONE A., SARICA A., LA TORRE D., et al.: Magnetic resonance imaging biomarkers distinguish normal pressure hydrocephalus from progressive supranuclear palsy. Mov. Disord, 35: 1406-15. doi: 10.1002/mds. 28087, 2020.

4- PETERSON K.A., MOLE T.B., KEONG N.C.H., et al.: Structural correlates of cognitive impairment in normal pressure hydrocephalus. Acta Neurol Scand, 139: 305-12. doi: 10.1111/ane. 13052, 2019.

5- CAPONE P.M., BERTELSON J.A. and AJTAI B.: Neuroimaging of normal pressure hydrocephalus and hydrocephalus. Neurol Clin, 38: 171–83. doi: 10. 1016 / j.ncl. 2019.09.003, 2020.

6- SARICA A., QUATTRONE A., QUARANTELLI M., et al.: Reduced striatal DAT uptake normalizes after shunt in normal-pressure hydrocephalus. Mov. Disord, 36: 261-2. doi: 10.1002/mds. 28336, 2021.

7- LEMCKE J. and MEIER U.: Improved outcome in shunted iNPH with a combination of a Codman Hakim programmable valve and an Aesculap-Miethke Shunt Assistant. Cen. Eur. Neurosurg, 71 (3): 113-6, 2010.

8- ABDALLAH A.E.A., SHAABAN M.H., HASSAN M.A. et al.: The role of MRI-CSF flowmetry in differentiation between NPH and Involutional brain changes, 10. 1594/ecr/C-0117, 2015.

9- KAHLON B., ANNERTZ M., STÅHLBERG F., et al.: Is aqueductal stroke volume, measured with cine phase-contrast MRI scans useful in predicting outcome of shunt surgery in suspected normal pressure hydrocephalus? Neurosurgery, 60 (1): 124-9; discussion 9-30, 2008.

10- BRADLEY W.G.J.r.: CSF flow in the brain in the context of normal pressure hydrocephalus. AJNR Am. J. Neuroradiol., 36: 831-838, 2020.

11- GINERA J.F., SANZ-REQUENA R., FLÓREZ N., et al.: Quantitative phase contrast MRI study of cerebrospinal fluid flow: A method for identifying patients with normal-pressure hydrocephalus. Neurología, 2013.

12- SENGER K.P.S., SINGH K.R., SINGH A.K., et al.: CSF flowmetry: An innovative technique in diagnosing normal pressure hydrocephalus. Int. J. Adv. Med., 4: 682-7, 2020.

تقييم دور قياس تدفق سائل النخاع الشوكى عن طريق الرنين المغناطيسى فى توقع استجابة مرضى استقاء الراس متساوى الضغط لعمليات البزل

مرض استسقاء الراس متساوى الضغط هو مرض يصيب غالبا كبار السن، تشمل أعراضه اضطراب المشى، سلس البول والخرف.

تشخيص استسقاء الرأس متساوى الضغط عادة يتم بطرق مختلفة مثل تصوير الدماغ سواء بالطبقى المحورى أو الرنين المغناطيسى ثم تتبع بالبزل القطنى للسائل الدماغ الشوكى.

قياس تدفق سائل النخاع الشوكى عن طريق الرنين المغناطيسى من أكثر طرق التشخيص شيوعاً وغيرمؤذية للمريض وكذلك له قيمة تنبؤية عالية لنجاح عملية تركيب تحويلة لسائل النخاع الشوكى.

ولقد هدفت هذه الرسالة إلى دراسة دور قياس تدفق سائل النخاع الشوكى عن طريق الرنين المغناطيسى فى توقع استجابة مرضى استقاء الرأس متساوى الضغط لعميات البزل.

وقد وجدنا انه عند النقطة الفاصلة = ٤٢ ميكروليتر، كان فحص تدفق سائل النخاع الشوكى عن طريق الرنين المغناطيسى له قيمة تنبؤية عالية بنجاح عملية تركيب التحويلة فهو تقنية بسيطة وسريعة وغير غارية رفعت منالدقة الكلية لفحص الرنين المغناطيسى مما أدى إلى زيادة الثقة فى التشخيص وتقليص معدل المضاعفات من الطرق التداخلية والغازية.