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Original Research Article

CSF flowmetry: an innovative technique in diagnosing normal pressure hydrocephalus

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ABSTRACT

Background: Normal pressure hydrocephalus is a very gloomy entity. The objective of this study is to analyse aqueductal velocity parameters by phase contrast MRI CSF flowmetry in Idiopathic Normal pressure hydrocephalus patients (NPH).
Methods: This study consists of 72 participants which included 36 patients and 36 matched healthy controls. The study stretched over three years in multicentre tertiary research hospitals using 3T MRI scanner. Both normal MRI sequences and phase contrast CSF flowmetry was done for both group of patients and result analysed using SPSS 17 software.
Results: Mean age of patients in our study is 61.07 years. The most common clinical symptom was gait unsteadiness in our study. Most common conventional MRI finding was ventriculomegaly with transependymal seepage of CSF. Amongst CSF flowmetry parameters Aqueductal stroke volume, peak systolic velocity, mean systolic velocity, forward flow volume and backward flow volume were statistically significant in differentiating cases from controls.
Conclusions: MRI CSF flowmetry using phase contrast method is an advanced imaging parameter which can non-invasively and reliably detect NPH. Also, it can be used to follow the response to treatment following shunting and can act as a prognostic marker.

Keywords: CSF flowmetry, Hydrocephalus, NPH, Phase contrast MRI

INTRODUCTION

Normal pressure hydrocephalus (NPH) is a gloomy entity with no definite cause know till date. There are various theories of NPH: One theory is related to reduced CSF absorption while the other is based on periventricular ischemic changes which tends to slow CSF outflow through extracellular spaces resulting in back pressure effect causing ventricular enlargement.[1]

This entity is first described by Hakin and Adams. The classical clinical trial of gait apraxia, urinary incontinence and dementia is not seen in all patients. Not all patients of NPH have dementia but it is one of the treatable causes of dementia.

The majority of cases of normal pressure hydrocephalus (NPH) are idiopathic. The incidence is much higher in elderly populations. There are several MRI features like ventriculometry, periventricular hyperintensity, crowding of gyri at the vertex and several other signs which point towards NPH. Over a period of time need was felt to evaluate CSF dynamics in patients of hydrocephalus. Phase contrast MRI (PC-MRI) is the most commonly used amongst MRI techniques to evaluate CSF flow dynamics in real time. By using this technique CSF flow is coupled with cardiac cycle and CSF flow dynamics is evaluated using various parameters. Quencer et al was one of the first researcher to evaluate CSF flow dynamics by cine magnitude imaging.[2] Following this phase contrast MRI came into picture which is capable of determining CSF flow velocity (quantitative) in addition to qualitative assessment.

PC-MRI has wide clinical applications ranging from NPH evaluation, follow up, surgical decision and post-surgery and post shunting status, Chairi malformation, syringomyelic cyst, posterior cystic malformation, etc. With more and more research being accumulated, NPH which was initially thought of as an idiopathic entity is now being increasingly recognized as a chronic communicating hydrocephalus with a potential benefit to patients of this group from VP shunting. The incidence of NPH as quoted in literature by Brean and Eide is 5.5 per 100000 and prevalence is 21.9 per 100000.[3]

Despite several studies investigators have failed to reach at a conclusion regarding NPH etiology and benefit of shunting in these patients. So far, no study has established clear cut off of CSF flow parameters for the definite diagnosis of NPH.

In view of the above this study has been undertaken to assess if PCMRI is a sensitive, accurate and effective method for diagnosis and evaluation of NPH.

METHODS

The aim of this study is to evaluate the diagnostic utility of CSF flowmetry using its various flow indices in patients of NPH. Objective of this study is to calculate aqueductal stroke volume (ASV), peak systolic velocity (PSV), forward flow (FF) and backward flow (BF) by PCMRI in patients of NPH and controls and to evaluate utility of these parameters in diagnosing NPH.

After taking ethical clearance from institutional ethics committee the study was conducted for a period of three years in two different tertiary care hospitals with an aggregated sample size of 77 patients out of which five patients were excluded from study (two patients of claustrophobia and two patients with pacemakers and one patient with metallic foreign body in eye).

After excluding the five patients our final sample size was 72 which included 36 patients of idiopathic NPH and 36 controls. This is an observational study with cross sectional case control study design. The age group of patients was between 41 to 83 years with mean age of 57 years. 36 patients as cases were referred by neurology department with clinical suspicion of NPH and 36 healthy volunteers are patients with minor complaints and found to have normal MRI brain on routine brain sequences.

Inclusion Criteria

- Patients clinically diagnosed as NPH.
- Patients with features of NPH on MRI.

Exclusion criteria

- Patients with contraindications for MRI
- Claustrophobic patients
- Patients having secondary cause for NPH on imaging

The study was conducted using 3T Siemens Magnetom Trio, Germany. Multichannel head coils and ultra-fast gradients were used. First routine brain sequences T1WI, T2W1, GRE, DWI were done and this is followed by PCMRI.

PCMRI Images are typically presented in sets of 3 for each plane and VENC obtained, similar to susceptibility weighted images (SWI). The set comprises of:

- Re-phased image (magnitude of flow compensated signal): flow is of high signal, background is visible
- Magnitude image (magnitude of difference signal): flow is of high signal (regardless of direction), background is suppressed
- Phase image (phase of difference signal): signal is dependent on direction: forward flow is of high signal; reverse flow is of low signal, background is mid-grey Quantification of flow is done by defining a region of interest (cross-sectional area of the aqueduct of Sylvius) and charting velocity versus time, which is typically pulsatile i.e. forwards during systole and backwards during diastole. The area under the curve for each cardiac phase generates values of flow forwards and flow backwards.

The slice thickness was kept at the minimum as aqueduct of sylvius measures 2-3mm, so slice thickness more than this will cause volume averaging of static tissue within the voxel. Data was collected and analysed using statistical software SPSS 17. The categorical data was presented in percentages.

RESULTS

Mean age of patients in our study is 61.07 years with mean age of 63 years in cases and 61 years in controls. Total no of males were 40 and females 32. Amongst cases 21 were males and 15 were females. Amongst controls 19 were males and 17 females. Most common clinical symptom in our cases was gait unsteadiness, followed by urinary incontinence and lastly dementia.

Amongst MRI findings the most common finding was ventriculomegaly with trans ependymal seepage of CSF followed by superior bowing of corpus callosum (Table 1).

Table 1: Prevalence (%) of various conventional MRI criteria in our study population.

MRI findings	Percentage
Ventriculomegaly	95
Trans ependymal seepage of CSF	92
Superior bowing of corpus callosum	67
Crowding of gyri at vertex	61
Corpus callosum thinning	61
Flow void at cerebral auqeduct	62

CSF flow study takes into account following variables:

- Increased aqueductal stroke volume.
- Aqueductal stroke volume is the average volume of CSF moving through the cerebral aqueduct.
- Calculated by summing the absolute values of stroke volume in systole and diastole and dividing by 2.
- (Forward stroke volume + reverse stroke volume)/2.
- Increased aqueductal peak velocity.
- Various publications have set various normal and abnormal ranges.
- Flow rate of > 24.5mL/min 95% specific for NPH.[4,5]
- Stroke volume of >42 microL shown on one paper to predict good response from shunting.
- Upper limit of stroke volume is variable between institutions due to intrinsic scanner differences, thus each centre should obtain their own "normal values", with the upper limit being suggested as two times the normal value.[7]
- Studies have shown that aqueductal stroke volume decreases later in the disease process despite clinical progression.
- This is attributed to cerebral atrophy, which indicates that the patient is unlikely to respond to shunt surgery.[8]

In present sample of 72 patients which includes 36 cases and 36 controls we have calculated CSF flowmetry parameters which included ASV, PSV, MSV, FF and BF (Table 2). Mean value of ASV for control was .0321 ml std deviation of 0.0123 ml, while for cases mean value of ASV was 0.152ml, standard deviation 0.0490 ml. P value of 0.0001. Mean value of PSV for controls was 3.99 cm/s standard deviation of 1.56 cm/s, while for the cases mean value of PSV was 8.12 cm/s standard deviation of 2.53 cm/s, P value of 0.0002.

Table 2: Combined study parameters of control and study groups with p values.

	Category	Counts	Mean	Std deviation	P value (<0.05 significant)
ASV(ml)	Control	36	0.0321 ml	0.0123 ml	0.0001
	Cases	36	0.152ml	0.0490 ml	
PSV(cm/s)	Control	36	3.99 cm/s	1.56 cm/s	0.0002
	Cases	36	8.12 cm/s	2.53 cm/s	
MSV(cm/s)	Control	36	3.19 cm/s	1.34 cm/s	0.0003
	Cases	36	5.17 cm/s	1.69 cm/s	
FF(ml)	Control	36	0.0312 ml	0.0134 ml	0.003
	Cases	36	0.0692 ml	0.0321 ml	
BF(ml)	Control	36	0.0247 ml	0.0102 ml	0.023
	Cases	36	0.0883 ml	0.0217 ml	

Mean of MSV for controls was 3.19 cm/s standard deviation of 1.34 cm/s while for cases mean MSV was 5.17 cm/s standard deviation of 1.69 cm/s. P value of 0.0003. Mean of FF for controls was 0.0312 ml standard deviation of 0.0134 ml for cases mean FF was 0.0692 ml standard deviation of 0.0321ml. P value of 0.003. Mean of BF for controls was 0.0247 ml standard deviation of 0.0102 ml for cases mean FF was 0.0883 ml standard deviation of 0.0217 ml. P value of 0.023

DISCUSSION

CSF is present in all ventricles, CSF subarachnoid spaces, such as cisterns and sulci, and the central canal of the spinal cord. The rate of CSF formation in humans is about 0.3-0.4 ml min^{-1} (about 500 ml day^{-1}). Total CSF volume is 90-150 ml in adults and 10-60 ml in neonates and it is undergoes resorption and reformation of its entire volume at least three times a day. Potential sites of CSF origin include the choroid plexus, parenchyma of the brain and the spinal cord, and ependymal lining of the ventricles.[9]

Two components can be distinguished in CSF circulation: (i) bulk flow (circulation) and (ii) pulsatile flow (back and forth motion). In bulk flow theory, CSF is produced by choroid plexus and absorbed by arachnoid granulations. The force, which provides CSF movement from the ventricular system to arachnoid granulation and CSF absorption, is caused by a hydrostatic pressure gradient between the site of its formation (slightly high pressure) and its site of absorption (slightly low pressure). In pulsatile flow theory, movement of the CSF is pulsatile and results from pulsations related to cardiac cycle of the choroid plexus and the subarachnoid portion of the cerebral arteries.[10] Because very little CSF water truly circulates through the subarachnoid space, pulsatile flow, rather than bulk flow, can be measured and demonstrated by PC MRI.

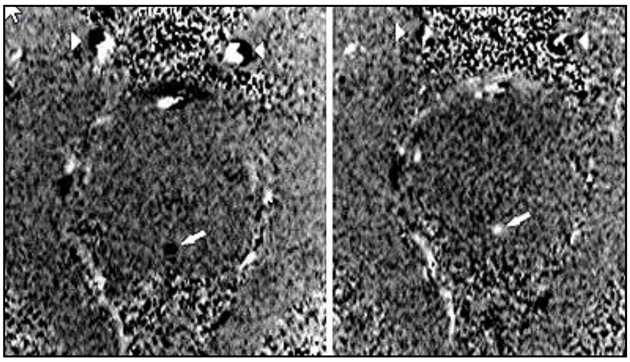

Figure 1: Phase-contrast images obtained perpendicular to the aqueduct; left: hypo intense signal within the aqueduct (arrow) indicating cranial flow (CSF diastole); right: hyper intense signal within the aqueduct (arrow) indicating caudal flow (CSF systole).

The PC MRI generates signal contrast between flowing and stationary nuclei by sensitising the phase of the transverse magnetisation to the velocity of motion.[11] Before PC MRI data are acquired, the anticipated maximum CSF flow velocity must be entered into the pulse sequence protocol (velocity encoding (VENC).[12] To obtain the optimal signal, the CSF flow velocity should be the same as, or slightly less than, the selected VENC. CSF flow velocities greater than VENC can produce aliasing artefacts, whereas velocities much smaller than VENC result in a weak signal. The mean VENC value is 5-8 cm s^{-1} for standard CSF flow imaging.

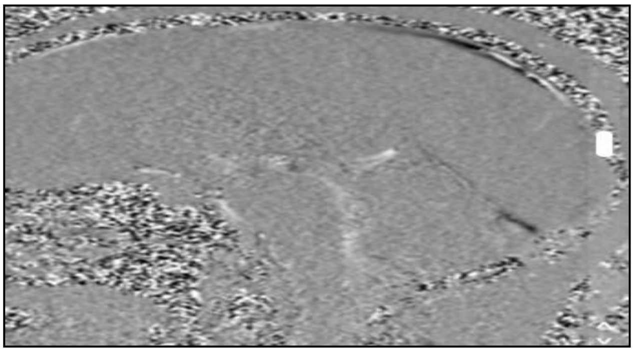

Figure 2: Phase-contrast images obtained in sagittal plane to the aqueduct; left: hypo intense signal within the aqueduct (arrow) indicating cranial flow (csf diastole); right: hyper intense signal within the aqueduct (arrow) indicating caudal flow (CSF systole).

Low VENC values (2-4 cm s^{-1}) can be helpful in the discrimination of communicating and non-communicating arachnoid cysts, and in the assessment of the ventriculoperitoneal shunt patency. In normal pressure hydrocephalus, significantly higher VENC values (20-25 cm s^{-1}) should be chosen owing to hyperdynamic CSF flow within the cerebral aqueduct.[12]

The signal initially contains phase and magnitude information. Magnitude and phase images can be generated for anatomy and velocity information, respectively. The result is that the greyscale intensity of each pixel is directly related to the velocity of CSF. Caudal flow of CSF is conventionally represented as shades of white on phase images, whereas cranial flow is by shades of black.

Since it reflects the phase shifts, PC velocity image is far more sensitive to CSF flow than is the magnitude image. Two series of PC imaging techniques are applied in the evaluation of CSF flow, one in the axial plane, with through-plane velocity encoding in the craniocaudal direction for flow quantification, and one in the sagittal plane, with in-plane velocity encoding in the craniocaudal direction for qualitative assessment.

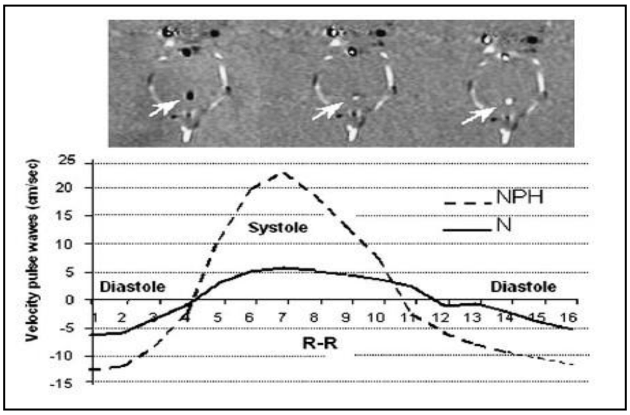

Figure 3: Aqueductal cerebrospinal fluid (CSF) flow velocity in a patient of normal pressure hydrocephalus (NPH). a, the 3-phase contrast images demonstrate CSF flow in the aqueduct (arrows) during diastole (caudocranial flow), at the time of inversion of the flow, and during systole (craniocaudal flow), respectively.

CSF flow is pulsatile and synchronous with the cardiac cycle, therefore cardiac gating can be used to provide increased sensitivity.[13] More accurate results can be obtained with retrospective gating when compared with prospective gating.[14] Normal pressure hydrocephalus (NPH) is a state of chronic hydrocephalus in which the CSF pressure is in physiological range, but a slight pressure gradient persists between the ventricles and the brain parenchyma.

The diagnosis of NPH is supported by the radiological findings of ventricular dilatation: out of proportion cortical sulcal enlargement, upward bowing of corpus callosum, flattening of the gyri against the calvarium and increased or normal CSF flow void. In properly selected patients, ventricular shunting results in resolution of symptoms and slows progressive deterioration. The aim of ventriculoperitoneal shunting is not to decrease mean pressure, but to dampen the pulse pressure by providing extra capacitance to the ventricular system.[15,16]

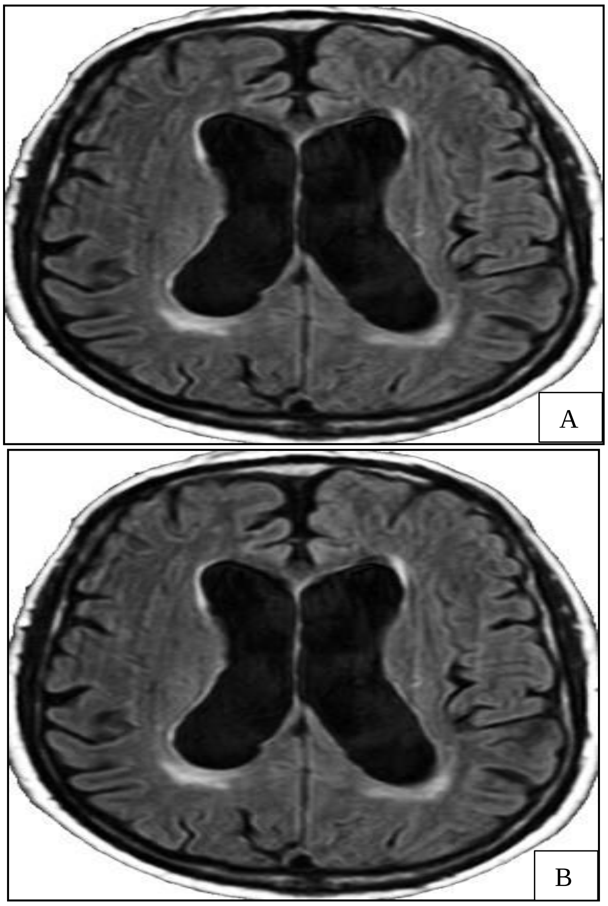

Figure 4: FLAIR images in a 62-year patient with NPH shows bilateral lateral ventricular dilatation with hyper intensity around frontal and peritrigonal deep white matter suggestive of trans ependymal seepage of CSF.

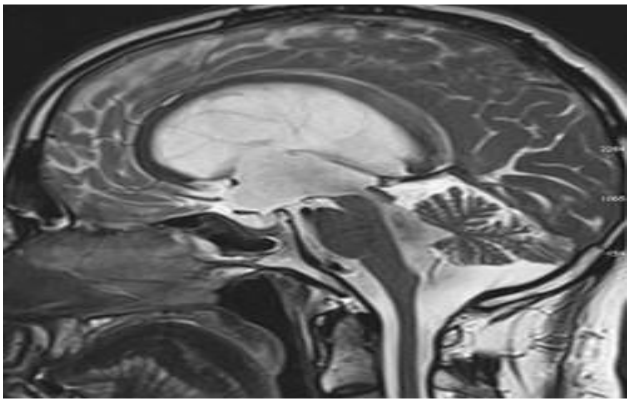

Figure 5: T2WI sagittal image of same patient in mid sagittal plane shows superior bowing of corpus callosum and crowding of gyri at the vertex.

PC MRI is useful in selection of patients for shunt placing. Caudal and rostral peak aqueduct CSF flow was significantly increased in patients with NPH. While a CSF flow measurement of less than 18 ml $min^{-1}$with a sinusoidal flow pattern is normal, a flow of greater than 18 ml min^{-1} suggests idiopathic NPH at the cerebral aqueduct.

Demonstration of increased pulsatility throughout the cerebral aqueduct has been correlated with a favourable response to shunting.

CSF velocity imaging is the most sensitive method for detecting symptomatic patients with a shunt responsive NPH on the basis of hyperdynamic CSF flow. In present study, we have taken VENC of 5 cm s^{-1} for controls and VENC of 20 cm s^{-1} for cases.

Mean value of ASV for cases in our study was 0.152ml, with standard deviation 0.0490 ml and for control was 0.0321 ml std deviation of 0.0123 ml. P value of 0.0001is highly significant establishing a strong statistical correlation. So ASV is one of the parameters for establishing NPH in patients. ASV value of this study is in close agreement with the study done by Schoder et al and Bradley et al. Mean value of PSV for the cases was 8.12 cm/s standard deviation of 2.53 cm/s.

Mean value of PSV for controls was 3.99 cm/s standard deviation of 1.56 cm/s. The values were statistically significant with P value of 0.0002. Present study was in agreement with study done by Yousef et al. The study by Marco G, et al studied PSV in NPH and the radings were different from present study with the mean PSV of 6.71 cm/s with a standard deviation of 2.84 cm/s. Mean of MSV for controls was 3.19 cm/s standard deviation of 1.34 cm/s while for cases mean MSV was 5.17 cm/s standard deviation of 1.69 cm/s.

P value of 0.0003 suggesting a strong statistical significance. Our study was in agreement with study done by Yousef et al. Mean of FF for controls was 0.0312 ml standard deviation of 0.0134 ml for cases mean FF was 0.0692 ml standard deviation of 0.0321ml. (P value of 0.003). Mean of BF for controls was 0.0247 ml standard deviation of 0.0102 ml for cases mean FF was 0.0883 ml standard deviation of 0.0217 ml. (P value of 0.023). Both these values are statistically significant.

CONCLUSION

PC cine MR is a useful imaging technique in evaluating CSF dynamics that affects various disease processes. In evaluation, follow-up, surgical decision and post-operative survey of these disease processes, PC cine MR can provide valuable additional information to conventional MRI. CSF pulsatility and stroke volume through the aqueduct has been correlated with a positive response to shunting in patients with normal pressure hydrocephalus.

Limitation of the present study was all the measurements were taken at a single point of time with no subsequent interval follow up evaluation.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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