

TYPE OF MANUSCRIPT- ORIGINAL RESEARCH ARTICLE

Cerebrospinal Fluid Flow Imaging To Differentiate Patients Of Communicating Hydrocephalus From Non-Communicating Hydrocephalus By Using Phase-Contrast Magnetic Resonance Imaging.

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ABSTRACT

Purpose-

To study cerebrospinal fluid flow by using phase contrast Magnetic Resonance Imaging to differentiate communicating hydrocephalus patients from non-communicating hydrocephalus patients.

Material and method

47 patients of hydrocephalus of all age group and gender were included for this prospective study, among those referred to the Department of Radiodiagnosis GRMC Gwalior for further evaluation with MRI. Patients giving informed consent were included in the study for 2 years.

Result

In communicating patients, mean PV at the level of aqueduct was found to be 7.26 ± 3.56 cm/s (range 2.07- 11.96), mean MV was 0.374 ± 0.495 cm/s (range 0.01- 2.18) and mean stroke volume to be 0.0189 ± 0.043 ml (range 0.001- 0.18) and mean absolute stroke volume to be 0.0595 ± 0.0628 (range 0.001- 0.25). In Non- communicating patients, mean PV at the level of aqueduct was found to be 8.47 ± 3.26 cm/s (range 1.25- 11.92), mean MV was 2.21 ± 2.3 cm/s (range .001- 6.09) and mean SV to be 0.1 ± 0.178 ml (range 0.001- 0.64). Between communicating and non-communicating patients, there is a significant difference in mean MV (P value 0.0001). ROC curve analysis was done for mean MV which showed cut-off value of 0.68 with sensitivity 58.3% and specificity 89% and mean ASV (P value 0.015). ROC curve analysis was done for mean ASV which showed cut-off value of 0.065 with sensitivity 91% and specificity 68% (Graph 2)

Conclusion

Among CSF flowmetry parameters absolute stroke volume and mean velocity were statistically significant in differentiating communicating and non-communicating hydrocephalus patients.

Key words: CSF flow, PCMRI, Hydrocephalus.

INTRODUCTION

Phase contrast MRI is a non-invasive method for measuring CSF flow dynamics. During the last two decades, flow-sensitive MRI techniques have been increasingly applied to assess cerebrospinal fluid (CSF) flow dynamics which provides quantitative and qualitative data regarding CSF circulation. Potentially with no need of contrast agents, the PC-MRI method is relatively simple for determining the level of obstruction and evaluating true CSF flow dynamics.

Hydrocephalus is an ambiguous diagnosis that may actually result from many different causes. In evaluation of the patients with hydrocephalus, the visualization of the cerebrospinal fluid (CSF) pathways is essential.

For MRI, the functional analyses of CSF flow dynamics and aqueductal patency primarily rely on the demonstration of flow void signal⁽¹⁾. Since cine PC-MRI is incapable of demonstrating CSF pathways anatomically, it should be used in conjunction with high-resolution two-dimensional (2D) T2-weighted (T2W) turbo spin echo (TSE) and three-dimensional (3D) heavily-T2W sequences (such as 3D-constructive interference steady state [CISS])⁽²⁻⁴⁾. PC-MRI also helps to discriminate the etiology of the disease additionally, it provides physiological information⁽⁵⁾. In this review, the role of PC-MRI used to discriminate between communicating hydrocephalus and non-communicating hydrocephalus patients.

PC-MRI is also used to study prognosis in patients of hydrocephalus, to discriminate between syringomyelia and cystic myelomalacia, to determine whether arachnoid cysts communicate with the subarachnoid space, to differentiate between arachnoid cysts and subarachnoid space, and to evaluate flow patterns of posterior fossa cystic malformations. The most used CSF flow parameters are aqueductal CSF stroke volume, peak velocity and mean velocity which will be recorded and compared in hydrocephalic patients⁽⁶⁾. We use encoding velocities of 6, 12, 20 cm/s to balance aliasing versus sensitivity. We use retrospective cardiac gating with either chest leads (electrocardiogram) or finger plethysmography (an MRI-compatible peripheral pulse transducer)⁽⁷⁾.

AIMS AND OBJECTIVES

- To study cerebrospinal fluid flow by using phase contrast Magnetic Resonance Imaging (MRI) to differentiate communicating hydrocephalus patients from non-communicating hydrocephalus patients.

MATERIAL AND METHOD

47 patients of hydrocephalus were included for this prospective study, amongst all age group and gender. The patients of hydrocephalus will be referred to the Department of Radiodiagnosis GRMC Gwalior for further evaluation with MRI. Patients of all ages of both sexes giving informed consent were included in the study from September 2019 to September 2021.

Patients were excluded in this study who were not willing consent, patients were not cooperating for study, Claustrophobic patients, pregnant women, post- operative patients (eg. VP shunt in-situ) and patients with mettalic implants, pacemakers, prothesis etc.

Patient preparation:

- Detailed explanation of the procedure to the parents/patient.
- Obtaining informed consent from the parents.

NB: children who are not able to maintain stationary position on the MRI table throughout the whole procedure time will be referred to an attending anesthesiologist who will be responsible for administration of sedative and any preparation and examination required prior to sedation.

MRI PHASE-CONTRAST MRI TECHNIQUE & PROTOCOL

The study was conducted on a 1.5-T MRI scanner (Ingenia, Philips Healthcare 1.5 tesla dStream) using a phase contrast MRI pulse sequence (TR/TE, 25/15 ms) matrix, 256×256 ; slice thickness, 4 mm; flip angle, 15°). The MRI protocol should include brain imaging with T2-weighting in axial and coronal planes, axial fluid attenuation inversion recovery (FLAIR), and sagittal T1-weighted image (T1-WI). High- resolutionheavily T2-weighted volumetric sequence (as three-dimensional driven equilibrium 3D-DRIVE) is acquired in sagittal plane. Axial T2*-WI may be acquired for better detection of intracranial hemorrhage as a cause of hydrocephalus.

Phase contrast MRI (PCMRI) with cardiac synchronous is a dynamic technique used to visualize cerebrospinal fluid (CSF) movement. Cine phase-contrast sequence can demonstrate CSF pulsatile flow throughout the cardiac cycle. It can be acquired in sagittal section to monitor the CSF flow through the aqueduct and basal subarachnoid spaces (qualitative assessment). Also, it can be acquired in axial section for quantification of CSF flow (quantitative assessment). Post-contrastT1-WI may be acquired in three planes in cases with intracranial neoplasms or in suspected inflammatory process.

The PC MRI generates signal contrast between flowing and stationary nuclei by sensitising the phase of the transverse magnetisation to the velocity of motion(8). Two data sets are acquired with opposite sensitisation, yielding opposite phase for moving nuclei and identicalphases for stationary nuclei(9). For stationary nuclei, the net phase is zero, and their signal is eliminated in the final image. However, flowing nuclei move from one position in the field gradient to another between the time of the first sensitisation and that of the second sensitisation. Because phase varies with position in the field, the net phase after subtraction of the two data sets is non-zero, and there is residual signal from flowing CSF(10). When the two data sets are subtracted, the signal contribution from stationary nuclei is eliminated and only flowing nuclei are seen. Before PC MRI data are acquired, the anticipated maximumCSF flow velocity must be entered into the pulse sequence protocol (velocity encoding (VENC)(11). 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(10,11). The mean VENC value is 5–8 cm s⁻¹ for standard CSF flow imaging. We used 6, 12 and 20 cm/s VENC as when required in our study. (6 cm/c VENC used for controls and 12 VENC used for cases. 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 grey scale 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 cranio-caudal direction for flow quantification, and one in the sagittal plane, with in-plane velocity encoding in the cranio-caudal direction for qualitative assessment. Through-plane evaluation is performed in the axial oblique plane perpendicular to the aqueduct and is more accurate for quantitative analysis because the partial volume effects are minimized(9-11). In our study we performed the plane of evaluation in the axial oblique plane perpendicular to the aqueduct in control and communicating cases and in non-communicating cases the plane of evaluation is performed in the axial oblique plane perpendicular to the aqueduct which is proximal to the level of obstruction/stenosis. Quantitative CSF velocity and qualitative flow information can be obtained in 8–10 additional minutes in addition with the routine MRI. CSF flow is pulsatile and synchronous with the cardiac cycle, therefore cardiac gating can be used to provide increased sensitivity(11). Cardiac gating can be provided with two different methods: prospective gating and retrospective gating. In retrospective gating, the computer follows the R wave and the data are acquired throughout the cardiac cycle. While the entire cardiac cycle can be sampled in retrospective gating, the prospectively gated acquisitions must be completed 100–200 ms before the next anticipated R wave. Thus, there appears to be large netflow of CSF in the systolic direction owing to partially sampled cardiac cycle in prospective gating. More accurate results can be obtained with retrospective gating when compared with prospective gating(12).

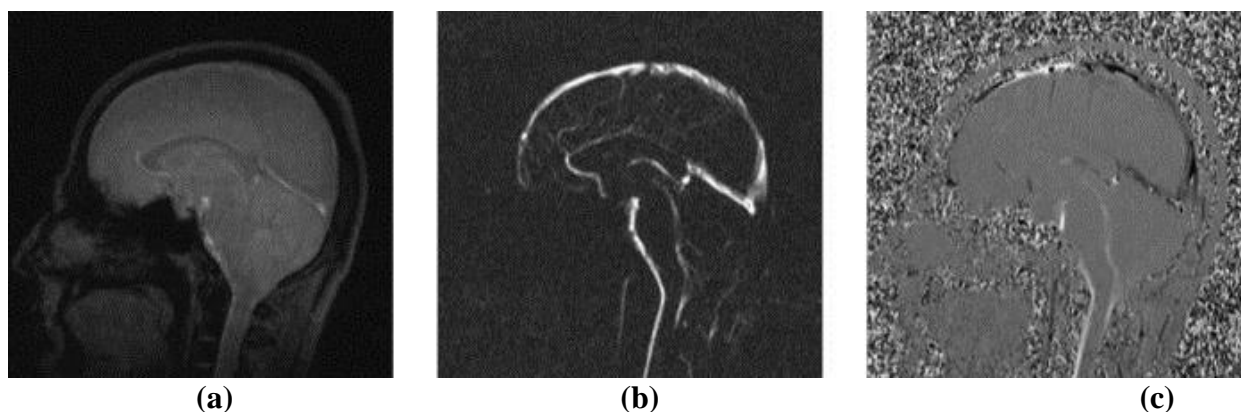


Fig. : Re-phased, magnitude and phase images

(a) Re-phased image is a magnitude of flow compensated signal, in this image the flow is bright and background is visible, (b) magnitude image is a magnitude of difference signal, in this image the flow is bright and the background is suppressed and (c) phase image is a phase of difference signal, in this image forward flow is bright, reverse flow is black and background is mid-grey.

OBSERVATION-

TUKEY HSD – (POST HOC) TEST

Table 1 : Comparison between communicating hydrocephalus and non- communicating hydrocephalus

VARIABLE	GROUP	NO. OF PATIENTS	MEAN DIFFERENCE	Std. Error	P VALE
PV(cm/s)	COMMUNICATING HYDROCEPHALUS	19	-1.21	1.034	0.476
	NON-COMMUNICATING HYDROCEPHALUS	12			
MV (cm/s)	COMMUNICATING HYDROCEPHALUS	19	-1.84	0.442	0.0001*
	NON-COMMUNICATING HYDROCEPHALUS	12			
SV(ml)	COMMUNICATING HYDROCEPHALUS	19	-0.081	0.034	0.058
	NON-COMMUNICATING HYDROCEPHALUS	12			
ASV(ml)	COMMUNICATING HYDROCEPHALUS	19	-0.096*	0.032	0.015*
	NON-COMMUNICATING HYDROCEPHALUS	12			
AGE(YR)	COMMUNICATING HYDROCEPHALUS	19	-9.65	7.14	0.375
	NON-COMMUNICATING HYDROCEPHALUS	12			

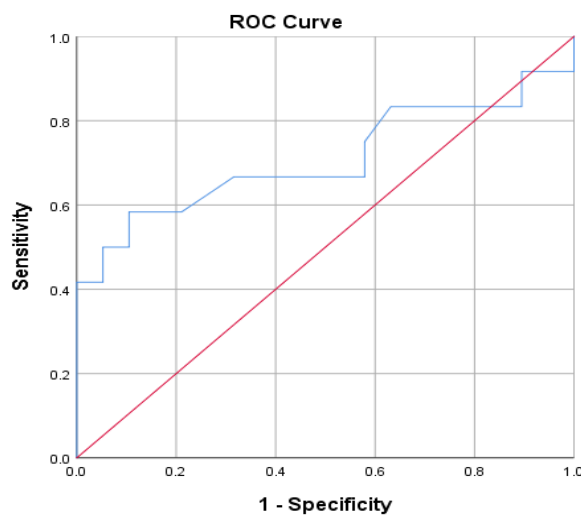
ONE WAY ANOVA TEST:**Table 2 : Peak Velocity (PV), Mean Velocity(MV), Stroke volume (SV) & Absolute stroke volume (ASV) distribution of study subjects**

VARIABLE	GROUP	NO.	MEAN	SD	MINI.	MAX.	F VALUE	P VALUE
PV (cm/s)	Control	16	5.86	0.209	5.10	5.99	3.027	0.059
	Communicating Hydrocephalus	19	7.26	3.56	2.07	11.96		
	Non-Communicating Hydrocephalus	12	8.47	3.26	1.25	11.92		

	Total	47	7.093	2.92	1.25	11.96		
MV (cm/s)	Control	16	0.288	0.186	0.07	0.75	10.99	0.0001
	Communicating Hydrocephalus	19	0.374	0.495	0.01	2.18		
	Non-Communicating Hydrocephalus	12	2.215	2.305	0.00	6.09		
	Total	47	0.815	1.437	0.00	6.09		
SV (ml)	Control	16	0.003	0.004	0.00	0.01	4.129	0.023
	Communicating Hydrocephalus	19	0.018	0.043	0.00	0.18		
	Non-Communicating Hydrocephalus	12	0.100	0.178	0.00	0.64		
	Total	47	0.034	0.099	0.00	0.64		
ASV (ml)	Control	16	0.033	0.010	0.02	0.06	6.95	0.002*
	Communicating Hydrocephalus	19	0.059	0.062	0.00	0.25		
	Non-Communicating Hydrocephalus	12	0.1558	0.159	0.03	0.64		
	Total	47	0.075	0.100	0.00	0.64		

COMMUNICATING VS NON- COMMUNICATING (2 VS 3) GROUP

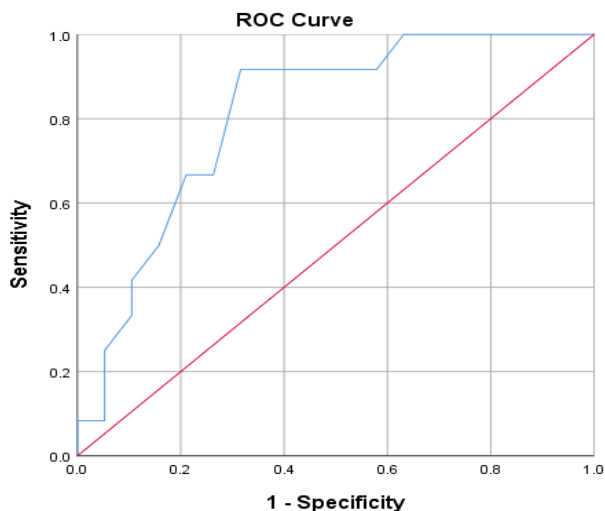
1.) MEAN VELOCITY:



Graph 1 :Communicating vs Non- Communicating (2 vs 3) group (Mean velocity)

Cut-off for MEAN VELOCITY for Non- Communicating group :				
AUC(Area under curve)	Cut-off- Value (cm/s)	Sensitivity	Specificity	Youden's Index
0.708	0.68	0.583	0.895	0.478

2) ABSOLUTE STROKE VOLUME (ASV)



Diagonal segments are produced by ties.

Graph 2 :Communicatingvs Non- Communicating (2 vs 3) group (Absolute StrokeVolume)

Cut-off for ASV for Non- Communicating group :				
AUC(Area under curve)	Cut-off- Value (ml)	Sensitivity	Specificity	Youden's Index
0.811	0.0650	0.917	0.684	0.601

IMAGE GALLERY



Fig. 1 : Re-phased image is a magnitude of flow compensated signal, in this image theflow is bright and background is visible.

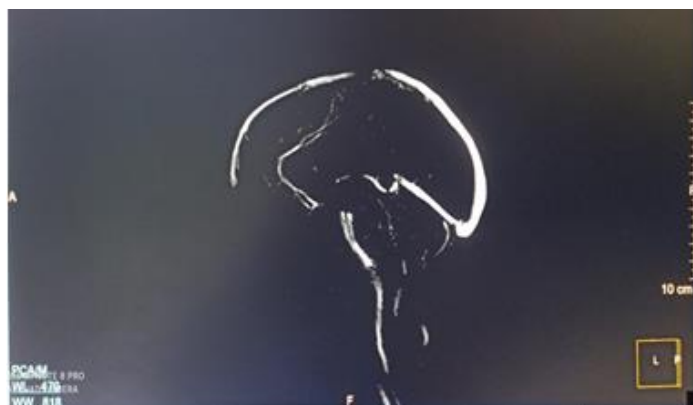


Fig. 2 : Magnitude image is a magnitude of difference signal, in this image the flow is bright and the background is suppressed.



Fig. 3 : Phase image is a phase of difference signal, in this image forward flow is bright, reverse flow is black and background is mid-grey.

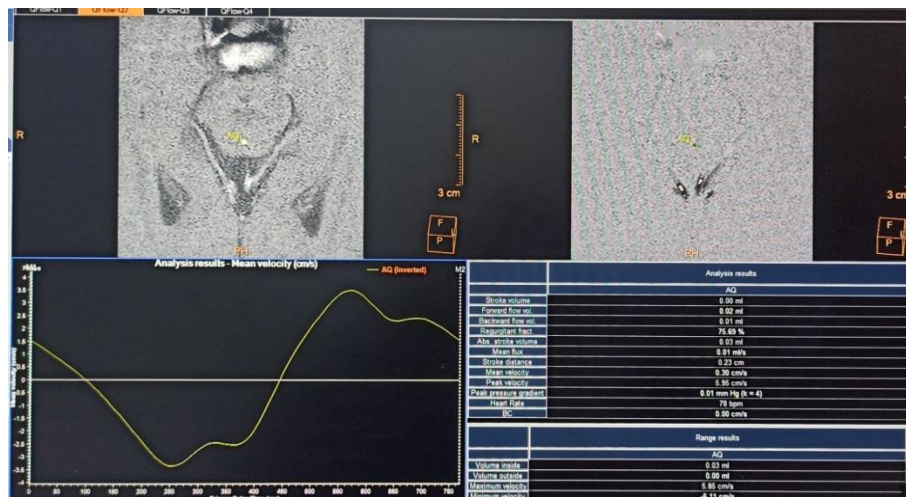


Fig. 4 : Mean velocity curve and parameters of flow derived from phase contrast images.

Region of interest was placed in the perpendicular intersection of the aqueduct. Images were acquired with $VENC = 12$ cm/sec. Peak velocity curve represents the flow plotted against cardiac cycle. The values were obtained and calculated from the ROI. Several parameters can be calculated from the selected ROI. Peak velocity stroke volume, mean velocity and absolute stroke volume are mostly used for quantitative comparison.

COMMUNICATING HYDROCEPHALUS

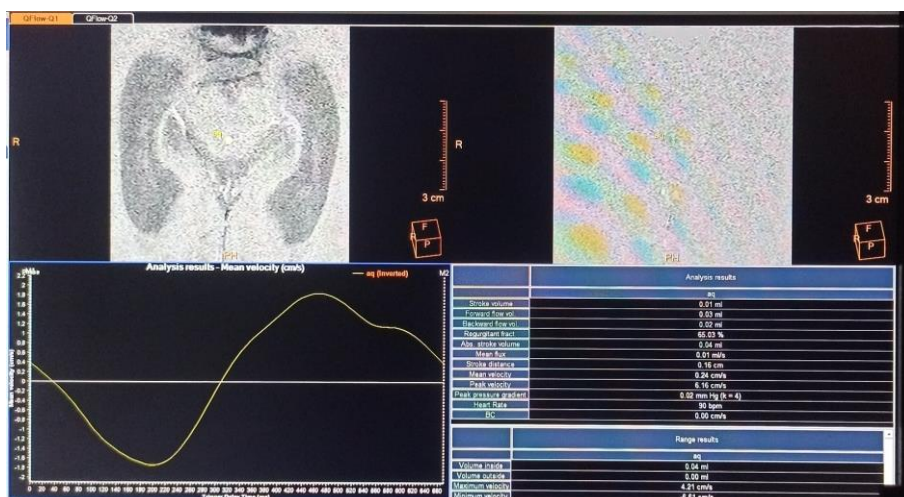


Fig. 5 : Mean velocity curve and parameters of flow derived from phase contrast images in communicating hydrocephalus patient

Region of interest was placed in the perpendicular intersection of the aqueduct. Images were acquired with VENC = 12 cm/sec. Peak velocity curve represents the flow plotted against cardiac cycle. The values were obtained and calculated from the ROI. Several parameters can be calculated from the selected ROI. Peak velocity stroke volume, mean velocity and absolute stroke volume are mostly used for quantitative comparison.

Non-communicating hydrocephalus

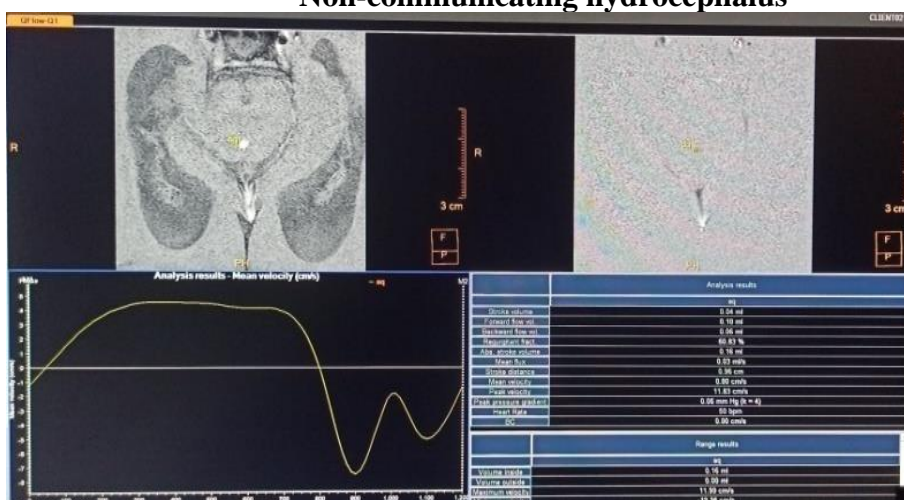


Fig. 6 : Mean velocity curve and parameters of flow derived from phase contrast images in non-communicating hydrocephalus patient

Region of interest was placed in the perpendicular intersection of the aqueduct. Images were acquired with VENC = 12 cm/sec. Peak velocity curve represents the flow plotted against cardiac cycle. The values were obtained and calculated from the ROI. Several parameters can be calculated from the selected ROI. Peak velocity stroke volume, mean velocity and absolute stroke volume are mostly used for quantitative comparison.

DISCUSSION - In our study, 47 patients were included, of which 16 were normal i.e. control (group 1), 19 were patients with communicating hydrocephalus (group 2), and 12

were patients with noncommunicating hydrocephalus (group 3). Mean age of normal control subjects (group 1) was 30.8 years, of communicating hydrocephalus (group 2) was 23.7 years, and of noncommunicating hydrocephalus (group 3) was 33.4 years. There was no statistical significant difference in age distribution of all the three groups (P-value 0.353). Of the total 47 study subjects, 23 were males (49%) and 24 were females (51%). No statistical significant difference was found in gender distribution among the three groups. Among all the study subjects, there was no statistical significant difference found on Tukey-HSD test in age distribution between males and females (P value 0.259). In this study, four CSF flow parameters were studied namely, Peak Velocity (PV), Mean Velocity (MV), Stroke Volume (SV) and Absolute stroke volume (ASV) in all 47 subjects using dedication software, SSPS(version 26) and mean of each of these parameters was used for comparison between these groups. In group 1, mean PV at the level of aqueduct was found to be 5.86 ± 0.209 cm/s (range 5.10-5.99), mean MV was calculated to be 0.288 ± 0.186 cm/s (range 0.07-0.75), mean stroke volume to be 0.0031 ± 0.0047 ml (range 0.001- 0.01) and mean absolute stroke volume (ASV) to be 0.0331 ± 0.010 ml (range 0.02- 0.06). Mean PV in normal controls was earlier reported to be $4.62 (\pm 0.7)$ cm/s by **Elsaftyet. al. (13)** which is close to mean PV found in our study and mean ASV in normal controls was earlier reported to be 35- 40 μ L by **Mohammad SA et al(14)** which is close to mean ASV found in our study. In group 2, mean PV at the level of aqueduct was found to be 7.26 ± 3.56 cm/s (range 2.07- 11.96), mean MV was calculated to be 0.374 ± 0.495 cm/s (range 0.01- 2.18) and mean stroke volume to be 0.0189 ± 0.043 ml (range 0.001- 0.18) and mean absolute stroke volume (ASV) to be 0.0595 ± 0.0628 (range 0.001- 0.25). In group 3, mean PV at the level of aqueduct was found to be 8.47 ± 3.26 cm/s (range 1.25- 11.92), mean MV was calculated to be 2.21 ± 2.3 cm/s (range .001- 6.09) and mean SV to be 0.1 ± 0.178 ml (range 0.001- 0.64). We used Tukey-HSD test to find statistical difference between these parameters between these three groups (P value ≤ 0.05). Between group 1 and 2, none of the parameters were found to be statistically different which indicates that CSF dynamics in patients with communicating hydrocephalus is not significantly different from normal controls. However, in our study, none of the patients in group 2 had normal pressure hydrocephalus (NPH) which is known to have increased absolute stroke volume as was reported by **Elsaftyet. al.(13)** and increased stroke volume as was reported by **Kahlon et.al.(15)** . Between group 1 and 3, there is a significant difference in mean PV (P value 0.011) and mean MV (P value 0.015), stroke volume (P value 0.025) & absolute stroke volume (P value 0.002). ROC curve analysis was done for mean PV and mean MV, mean SV and mean ASV which showed cut-off value for PV of 6.845 with sensitivity 75% and specificity 100 % , cut-off value for MV of 0.76 with sensitivity 58.3% and specificity 100 % and cut-off value for SV of 0.76 with sensitivity 58.3% and specificity 100 % . (Graph 5,6,7,8). We had 2 patients with Chiari malformation, On CSF flow analysis there was increased heterogeneous CSF flow at cerebral aqueduct with bidirectional flow similar to the findings reported by **Mbonaneet. al.(16)**.

Between communicating and non-communicating hydrocephalus patients (group 2 and 3), there is a significant difference in mean MV (P value 0.0001). ROC curve analysis was done for mean MV which showed cut-off value of 0.68 with sensitivity 58.3% and specificity 89 % (Graph 1) and mean ASV (P value 0.015). ROC curve analysis was done for mean ASV which showed cut-off value of 0.65 with sensitivity 91% and specificity 68% (Graph 2)

RESULT

Among CSF flow-metry parameters absolute stroke volume and mean velocity were statistical significant in differentiating patients having communicating and non-communicating hydrocephalus. As there is a significant difference in mean MV (P value 0.0001). ROC curve analysis was done for mean MV which showed cut-off value of 0.68 with sensitivity 58.3% and specificity 89 % (Graph 1) and mean ASV (P value 0.015). ROC curve analysis was done for mean ASV which showed cut-off value of 0.65 with sensitivity 91% and specificity 68% (Graph 2).

ADVANTAGES-

PCMRI can provide valuable additional information to conventional MRI. PCMRI is a complimentary rapid, easy and reproducible sequence, which takes additional 8-10 minutes to evaluate altered CSF dynamics.

LIMITATIONS

- 1) In our study all the measurements were taken at a single point of time with no subsequent interval follow up and evaluation.
- 2) Limitation of the study was that we can't apply PCMRI technique in infants as some of the parents were not giving consent for sedation. Hence we had to exclude 8-10 patients from our study.
- 3) Some patients excluded because they had VP shunt in situ and hence they didn't match our inclusion criteria.
- 4) Upper limits 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 values. (Senger KPS et al.)¹⁷
- 5) On the basis of age group, evaluating causes of hydrocephalus and CSF obstruction at the level of the aqueduct, the fourth ventricle, the outlet foramina of the fourth ventricle and the foramen magnum.

RECOMMENDATION

- We can get better results with more sample size, more analytical parameters and software like arterial and venous flow study software.
- To get better results in patients having obstruction at the level of 4th ventricle and foremen magnum, on the basis of type of symptoms and duration of symptoms (acute or chronic), we need further study with more sample size.
- There is variation in the size of cerebral aqueduct which is used to calculate stroke volume and other CSF flow parameters during the cardiac cycle. The maximum velocity may be inversely proportional to the area of the aqueduct. In order to establish reliable reference values for CSF flow parameters in future studies, a variable ROI, to account for cardiac cycle variation, should be considered and incorporated. (Hongri et al.)⁽¹⁸⁾

CONCLUSION

PC MRI helps in differentiating between communicating and non communicating hydrocephalus and also in evaluation, follow-up, surgical decisions and post operative survey of these disease process. We suggest use of PCMRI sequence to provide the obstruction of CSF circulation at the aqueduct level. Among CSF flow-metry parameters absolute stroke

volume and mean velocity were statistical significant in differentiating patients having communicating and non-communicating hydrocephalus.

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