RESEARCH ARTICLE

The role of magnetic resonance imaging cerebrospinal fluid flowmetry in differentiation between normal flow hydrocephalus and involutional brain atrophy

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Abstract

Objective: To assess the value of phase contrast magnetic resonance imaging cerebrospinal fluid flowmetry in differentiating between normal pressure hydrocephalus and involutional atrophy.

Methods: The descriptive case-control study was conducted at the Al-Yarmouk Teaching Hospital, Baghdad, Iraq, from April to December 2017, and comprised patients with normal pressure hydrocephalus and involutional brain changes. Healthy volunteers were included as controls. Demographic data was recorded and the patients were divided according to age. Conventional magnetic resonance imaging of the brain was performed followed by the assessment of cerebrospinal fluid flow dynamics, was done at the level of the aqueduct of Sylvius. Data was analysed using SPSS 25.

Results: Of the 23 subjects with a mean age of 52.3±16.8 years (range: 25-75 years), There were 13(56.5%) males and 10(43.5%) were females. Also, there were 17(74%) patients and 6(26%) controls. Among the patients, 8(47%) had brain atrophic changes based on magnetic resonance imaging, and 9(53%) had normal pressure hydrocephalus signs clinically and scanning criteria. Flowmetry showed mean systolic velocity 1.5±0.3 cm\sec, peak systolic velocity 1.5±0.3 cm\sec and systolic stroke volume 28.5±4.7µLin the control group which was significantly different from the patients ($p<0.001$).

Conclusion: Phase-contrast magnetic resonance imaging was found to be a useful tool to differentiate between normal pressure hydrocephalus and age-related brain atrophy.

Keywords: Hydrocephalus, MRI-CSF flowmetry. (JPMA 69: S-78 (Suppl. 3); 2019)

Introduction

The cerebrospinal fluid (CSF) compromises all spaces including ventricles, spinal and subarachnoid spaces, such as sulci and cistern as well as the central canal of the spinal cord. The rate of CSF formation in humans is about 0.3-0.4 ml min^{-1}.[1] The portion of the fluid formed in the lateral ventricles escapes by the foramen of Monro into the third ventricle and then via the aqueduct into the fourth ventricle.[2] Two components can be distinguished in CSF circulation; bulk flow which is circulation, and pulsatile flow which is back-and-forth motion. In bulk flow, 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, the CSF movement is pulsatile and results from pulsations related to the cardiac cycle of the choroid plexus and the subarachnoid portion of the cerebral arteries.[3] Because very little CSF truly circulates through the subarachnoid space, pulsatile flow, rather than bulk flow, can be measured and demonstrated by phase contrast (PC) magnetic resonance imaging (MRI).[3]

MRI of CSF flow began with the qualitative observation of the degree of flow void in the aqueduct of Sylvius and the adjacent third and fourth ventricles, but it was not used commonly because it is influenced by many acquisition parameters and often may be difficult to quantify.[3] Phased contrast MRI generates signal contrast between flowing and stationary nuclei by sensitising the phase of the transverse magnetisations of the velocity of motion.[4] Two data-sets are acquired with opposite sensitisations, yielding opposite phases for the moving nuclei, and identical phases for the stationary nuclei.[5] Because the 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 the flowing CSF.[6] When the two data-sets are subtracted, the signal contribution from the stationary nuclei is eliminated and only the flowing nuclei are seen. Pre-PC-MRI data is acquired and, the anticipated maximum CSF flow velocity must be entered into the pulse sequence protocol called velocity encoding (VENC).[7] To obtain the optimal signal, the CSF flow velocity should be the same as, or slightly less than, the selected VENC. CSF flow velocities >VENC can produce

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aliasing artefacts, whereas velocities singnificantly smaller than VENC result in a weak signal.[6,7] In normal pressure hydrocephalus (NPH), significantly higher VENC values 20-25 cms^{-1} are detected owing to hyperdynamic CSF flow within the cerebral aqueduct.

The signal initially contains phase and magnitude information. Magnitude and phase image scan are generated for both anatomy and velocity information. 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 represented 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 VENC in the craniocaudal direction for flow quantification, and the other in the sagittal plane, with VENC in the craniocaudal direction for qualitative assessment. 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 minimised.[6,8] Cardiac gating can be provided with prospective and retrospective gating. In retrospective gating, the computer follows the R-wave and the data is acquired throughout the cardiac cycle. The entire cardiac cycle can be sampled in retrospective gating, while in prospective gating, acquisitions must be completed 100-200ms before the next anticipated R-wave. More accurate results can be obtained with retrospective gating when compared with prospective gating.[9]

NPH is a state of chronic hydrocephalus in which the CSF pressure is in the physiological range, but a slight pressure gradient persists between the ventricles and the brain parenchyma. The diagnosis of NPH is supported by 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.[10,11] This pathology is described in elderly patients and has a classic symptom triad of gait disturbance, urinary incontinence and dementia.[12] PC-MRI is useful in the 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 <18 $mlmin^{-1}$ with a sinusoidal flow pattern is normal, while a flow >18 ml min^{-1} suggests idiopathic NPH at the cerebral aqueduct.[13] Gait disturbance is typically the initial and most prominent symptom of the triad and may be progressive.[14,15] NPH is caused by an increase in intracranial pressure (ICP) due to an abnormal accumulation of CSF in the ventricles of the brain, leading to ventriculomegaly. The ICP gradually falls but still remains slightly elevated, and the CSF pressure reaches a high normal level of 150-200mmH2O. ICP values, therefore, are not usually elevated, and because of that the patients do not exhibit the classic signs that accompany increased ICP such as headache, nausea, vomiting, or altered consciousness. Although some studies have shown pressure elevations to occur intermittently, enlarged ventricles put increased pressure on the adjacent cortical tissue and cause myriad effects in such patients.[16] The diagnosis of NPH is usually first led by brain imaging, either computed tomography (CT) or MRI, to rule out any mass lesions in the brain. This is then followed by lumbarpuncture and the evaluation of clinical response to CSF removal. This can be followed by continuous external lumbar CSF drainage over 3-4 days.[16] MRI may show some degree of trans-ependymal migration of CSF surrounding the ventricles on T2/fluid attenuated inversion recovery (FLAIR) sequence. Imaging, however, it cannot differentiate between pathologies with similar clinical picture, like Alzheimer's dementia, vascular dementia or Parkinson's disease.[17] Involutional brain atrophy is the morphological presentation of brain parenchymal volume loss that is frequently seen on cross-sectional imaging in elderly population.[18]

It is a common finding in the elderly, and so there is some controversy as to when imaging changes are labelled as cerebral atrophy, rather than simply involutional or age-related when the patient has normal cognition.[19,20] Cerebral atrophy is simply the compensatory enlargement of the CSF spaces from reducing brain parenchymal volume, representing idiopathic generalised changes seen with age. As it is not a distinct disease on its own, there is no uniform mode of presentation and the finding of atrophy is often incidental when imaging is taken for some other indication. Features that favour hydrocephalus include dilatation of the temporal horns; lack of dilatation of para-hippocampal fissures[21]; increased frontal hornradius; acute ventricular angles; peri-ventricular interstitial oedema from trans-ependymal flow; intra-ventricular flow void from CSF movement on MRI; widening of the third ventricular recesses (midsagittalplane); upward displacement of the corpus callosum (midsagittalplane); depression of the posterior fornix (midsagittalplane); decreased mamillo-pontine distance (midsagittalplane); narrow callosal angle; and cingulate sulcussign.[21]

The current study was planned to assess the value of PC-MRI CSF flowmetry in differentiating between NPH and involutional atrophy.

Patients and Methods

The descriptive case-control study was conducted at Al-Yarmouk Teaching Hospital, Baghdad, Iraq, from April to December 2017, and comprised patients with NPH and involutional atrophy patients as well as healthy controls. The protocol study was approved by the Ethical Committee of Scientific Researches of Diagnostic Radiology at Al-Yarmouk Teaching Hospital.

Patients of either gender, aged 25-75 years, were included on the basis of presenting clinical features of NPH symptoms who were referred to have an MRI scans during which involutional brain changes were discovered. Those who were unable to tolerate complete MRI scan were excluded. Healthy volunteers without neurological symptoms and with normal MRI findings were included as the control group.

Demographic data was recorded and additional data was collected from the patients' case sheet and clinical evaluation reports. Normal pressure hydrocephalus diagnosis was made on the basis of clinical symptoms and MRI criteria which included Ventriculomegaly; frontal and temporal horns of the lateral ventricles; upward bowing of the corpus callosum; peri-ventricular high signal on T2-weighted sequences; narrow callosal angle; changes in sulcalsize; a line parallel to the floor of the 4th ventricle; and Sylvian fissures out of proportion to the sulcal enlargement, which was minimal, and hippocampal and mesial temporal lobe volumes, which were near-normal.

Imaging features of cerebral atrophic changes in old patients included prominent cerebral sulci (cortical atrophy); and Ventriculomegaly (central atrophy) without bulging of the third ventricular recesses.

CSF flowmetry protocol[23] depends on the analysis of the CSF flow properties at the level of the aqueduct of Sylvius in all patients. All MRI scans were done using a single unit (Philips Achieva 1.5 Tesla SE), and a circular polarized neurovascular coil was chosen.

Conventional MRI of the brain was performed, standard axial T1-weight image (T1W1), axial and sagittal T2WI and axial FLAIR images were obtained before CSF flow measurements were made.

In PC-MRI, CSF flow dynamics study and electrocardiogram (ECG) gated protocol[23] was used with a high-resolution axial PC protocol[23] and an imaging plane perpendicular to the cerebral aqueduct. PC images were displayed on a gray scale, where low signal intensity indicated caudal flow and bright signal intensity represented cranial flow, while CSF flow quantification was performed on the images using the region of interest (ROI) measurements[23] and a CSF flow wave form was generated. A circular ROI was drawn to include the pixels that reflected the CSF flow signals of the cerebral aqueduct on the phase images. The ROI was placed in the aqueduct shown on a magnified image with the aid of a mouse driven cursor and was substituted for the diameter of the aqueduct.

Because the phase images only showed the CSF flow and not the real anatomical lumen of the aqueduct, the area of the circular ROI was controlled at 1-5mm^2 which contains no stationary brain tissue and is slightly smaller than the diameter of the aqueduct. Following the acquisition of the CSF flow velocity curves, CSF hydrodynamics were analysed in terms of the peak systolic velocity and mean systolic velocity. The mean flow was calculated from the equation: mean flow (cm^3/sec) = mean systolic velocity (cm/sec) x area of ROI (cm^2), where the mean systolic velocity was automatically determined from the mean value of the measured velocities of each cardiac phase, and the selection of ROI was measured with the aid of a mouse-driven cursor.[23]

Finally, systolic stroke volume was calculated using the equation: systolic stroke volume = mean systolic flow x duration of CSF systole.[23]

Data was analysed using SPSS25, and was presented as mean, standard deviation (SD) and range. Independent t-test and two-tailed analysis of variance (ANOVA) were used to compare the continuous variables between the groups and the least square difference (LSD) post-hoc test was used to sort out significant values. Pearson's Chi-square test was used to assess statistical association between the patients' gender and diagnosis. P<0.05 was considered significant.

Results

Of the 23 subjects with a mean age of 52.3±16.8 years (range: 25-75 years), There were 13(56.5%) males and 10(43.5%) females. Also, there were 17(74%) patients and 6(26%) controls. Among the patients, 8(47%) had brain

Table-1: Relation between gender and diagnosis.

Diagnosis	Gender No.(%)		Total	Overall P-value
	Male	Female		
Normal	4 (30.8%)	2 (20%)	6 (26.1%)	0.637 Not significant
Atrophy	5 (38.5%)	3 (30%)	8 (34.8%)	
Normal pressure hydrocephalus	4 (30.8%)	5 (50%)	9 (39.1%)	
Total	13 (100%)	10 (100%)	23 (100%)	

atrophic changes based on magnetic resonance imaging, and 9(53%) had normal pressure hydrocephalus signs clinically and scanning criteria (Table-1).

There was no significant difference between patients' age and MRI findings (p>0.05).

Table-2: comparison of magnetic resonance imaging (MRI) parameters, according to diagnosis (n=23).

Parameters	Normal Mean±SD	Atrophy Mean±SD	NPH Mean±SD	P-value
Meansystolic velocity(cm/Sec.)	1.5 ± 0.3	0.7 ± 0.3	3.1 ± 0.9	<0.001*
Peak systolic velocity(cm/Sec.)	1.5 ± 0.3	0.9 ± 0.3	5.8 ± 1	<0.001*
Systolicstroke volume (Microliter)	28.5 ± 4.7	9.1 ± 2.8	85.3 ± 13.9	<0.0001*

*Significant at 0.05 level by ANOVA test.
SD: Standard Deviation.

Table-3: Least square difference(LSD) post-hoc test of magnetic resonance imaging (MRI) parameters, according to diagnosis (n=23).

	Parameters	Mean difference	P-value
Mean systolic velocity (cm/Sec.)			
Normal	Atrophy	0.8	0.023*
	Normal pressure hydrocephalus	-1.7	<0.001*
Atrophy	Normal pressure hydrocephalus	-2.5	<0.001*
Peak systolic velocity (cm/Sec.)			
Normal	Atrophy	1.3	0.006*
	Normal pressure hydrocephalus	-3.6	<0.001*
Atrophy	Normal pressure hydrocephalus	-4.9	<0.001*
Systolic stroke volume (Microliter)			
Normal	Atrophy	19.5	0.001*
	Normal pressure hydrocephalus	-56.8	<0.001*
Atrophy	Normal pressure hydrocephalus	-76.2	<0.001*

Peak systolic velocity, mean systolic velocity and systolic stroke volume values were significantly higher in NPH patients, and markedly lower in cerebral atrophy compared to healthy controls (Tables-2, 3).

Discussion

The study found consistent MRI flow patterns in healthy controls compared to involutional brain atrophy and NPH patients. There were no statistically significant differences in mean velocity, cranial and caudal volume, net volume, gender, and mean flow parameters among different age groups. This is in accordance with an earlier study.[22]

In pathological CSF flow dynamics in NPH patients, the systolic peak velocity and the systolic stroke volume were significantly higher than the controls, which means NPH patients had hyper-dynamic aqueduct CSF flow.

In cerebral atrophy, blood flow to the brain is decreased, and there was markedly lower systolic peak velocity, systolic mean velocity and stroke volume values compared to the controls which reflect a hypodynamic CSF circulation in the former.

In the current study there was a significant difference between specific MRI flowmetry parameters and patients diagnosis, which was in agreement with a study.[23]

A relatively wide range of normal aqueduct CSF velocity values measured by the cine-phase contrast MRI technique has been reported In literature and this may be attributed to the different gradient strengths and parameters used by different groups according.[24]

Stroke volume of >42 microL has been shown to predict good response from shunting.[25] Upper limit of stroke volume is variable from institution to institution, and is related to intrinsic scanner differences with the suggested upper limit being two times the normal value.[25]

Conclusion

PC-MRI was found to be a useful tool in the diagnosis of NPH noninvasively, especially in the elderly, to differentiate it from age-related brain atrophy where differentiation based on clinical and conventional radiological basis may be difficult. PC-MRI provides the potential for non-invasive CSF flow quantification and this should allow for the exclusion of patients with similar symptomatology resulting in dementia caused by vascular, toxic or other causes.

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Conflicts of Interest: None.

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References

1. Segal MB, Pollay M. The secretion of cerebrospinal fluid. Exp Eye Res 1977;25(Suppl 1):127-48.
2. Gray H, Lewis WH. Anatomy of the Human Body,20th ed. Philadelphia: Lea &Febiger, 1918.
3. Barkhof F, Kouwenhoven M, Scheltens P, Sprenger M, Algra P, Valk J. Phase-contrast cine MR imaging of normal aqueductal CSF flow. Effect of aging and relation to CSF void on modulus MR. Acta Radiol1994;35:123-30.
4. Al-Kayat RHA. The role of diffusion-weighted MRI in the evaluation of nonpalpable undescended testis. Mustansiriya Med J 2018;12:1-6.
5. Dumoulin CL, Yucel EK, Vock P, Souza SP, Terrier F, Steinberg FL, et al. Two- and three-dimensional phase contrast MR angiography of the abdomen. J Comput Assist Tomogr1990;14:779-84.
6. Battal B, Kocaoglu M, Bulakbasi N, Husmen G, Tuba Sanal H, Tayfun C. Cerebrospinal fluid flow imaging by using phase-contrast MR technique. Br J Radiol2011;84:758-65.
7. Saloner D. The AAPM/RSNA physics tutorial for residents. An introduction to MR angiography. Radiographics1995;15:453-65.

8. Connor SE, O'Gorman R, Summers P, Simmons A, Moore EM, Chandler C, et al. SPAMM, cine phase contrast imaging and fast spin-echo T2-weighted imaging in the study of intracranial cerebrospinal fluid (CSF) flow. Clin Radiol2001;56:763-72.
9. Nitz WR, Bradley WG Jr, Watanabe AS, Lee RR, Burgoyne B, O'Sullivan RM, et al. Flow dynamics of cerebrospinal fluid: assessment with phase-contrast velocity MR imaging performed with retrospective cardiac gating. Radiology 1992;183:395-405.
10. Bradley WG Jr, Whittemore AR, Kortman KE, Watanabe AS, Homyak M, Teresi LM, et al. Marked cerebrospinal fluid void: indicator of successful shunt in patients with suspected normal-pressure hydrocephalus. Radiology 1991;178:459-66.
11. Ng SE, Low AM, Tang KK, Lim WE, Kwok RK. Idiopathic normal pressure hydrocephalus: correlating magnetic resonance imaging biomarkers with clinical response. Ann Acad Med Singapore 2009;38:803-8.
12. Al-Tamimi MA. Criteria of ventriculoperitoneal Shunt-related Infections in Iraqi Children patients: A Retrospective study over a 2-Year Period. Mustansiriya Med J 2018;15:5.
13. Brean A, Eide PK. Prevalence of probable idiopathic normal pressure hydrocephalus in a Norwegian population. Acta Neurol Scand2008;118:48-53.
14. Krauss JK, Faist M, Schubert M, Borremans JJ, Lücking CH, Berger W. Evaluation of gait in normal pressure hydrocephalus before and after shunting. Adv Neurol 2001;87:301-10.
15. Ropper AH, Samuels MA. Adams and Victor's Principles of Neurology, 9th ed. New York, NY: McGraw-Hill, 2009; pp 1572.
16. Adams RD, Fisher CM, Hakim S, Ojemann RG, Sweet WH. Symptomatic occult hydrocephalus with "normal" cerebrospinal-fluid pressure.a treatable syndrome. N Engl J Med 1965;273:117-26.
17. Tarnaris A, Toma AK, Kitchen ND, Watkins LD. Ongoing search for diagnostic biomarkers in idiopathic normal pressure hydrocephalus. Biomark Med 2009;3:787-805.
18. Brant WE, Helms CA. Fundamentals of Diagnostic Radiology 4th ed. Philadelphia, USA: Lippincott Williams & Wilkins, 2007; pp 1559.
19. Davies SG. Chapman &Nakielny's Aids to Radiological Differential Diagnosis 6th ed. Philadelphia, USA: Saunders Elsevier, 2014; pp 550.
20. Holodny AI, Waxman R, George AE, Rusinek H, Kalnin AJ, de Leon M. MR differential diagnosis of normal-pressure hydrocephalus and Alzheimer disease: significance of perihippocampal fissures. AJNR Am J Neuroradiol1998;19:813-9.
21. Gammal TE, Allen MB Jr, Brooks BS, Mark EK. MR evaluation of hydrocephalus. AJR Am J Roentgenol1987;149:807-13.
22. Unal O, Kartum A, Avcu S, Etlik O, Arslan H, Bora A. Cine phase-contrast MRI evaluation of normal aqueductal cerebrospinal fluid flow according to sex and age. Diagn IntervRadiol2009;15:227-31.
23. Abdallah AEA, Shabaan MH, Hassan MA, Yassin AN. The role of MRI-CSF flowmetry in differentiation between NPH and involutional brain changes. European Congress of Radiology. [Online] 2015 [Cited 2017 December 15]. Available from URL: https://posterng.netkey.at/esr/viewing/index.php?module=viewing_poster&task=viewsection&pi=127855&ti=427887&si=1476&searchkey=
24. Yousef MI, El Mageed AEA, Yassin AEN, Shaaband MH. Use of cerebrospinal fluid flow rates measured by phase-contrast MR to differentiate normal pressure hydrocephalus from involutional brain changes. Egypt J Radiol Nucl Med 2016;47:999-1008.
25. Senger KPS, Singh KR, Singh AK, Singh A, Dashottar S, Sharma V, et al. CSF flowmetry: an innovative technique in diagnosing normal pressure hydrocephalus. Int J Adv Med 2017;4:682-7.