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MRI ASSESSMENT OF CSF FLOW AND DIAGNOSIS OF NORMAL PRESSURE HYDROCEPHALUS

By

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ABSTRACT

Background: Normal-pressure Hydrocephalus is a clinical triad of gait disturbance, subcortical dementia, and urinary incontinence in a patient who has communicating hydrocephalus.

Objective: To reveal the role of phase-contrast MR imaging in the detection of normal pressure hydrocephalus among patients with ventriculomegaly.

Patient and Methods: The study group included 40 patients with ventriculomegaly. Patients were referred to the multiple MRI centers (including Nile Scan Radiology Center and Watani Scan Radiology Center), Radiology Department of AL Mokatam Hospital. The consensus about final diagnosis in the ventriculomegaly group was reached on the light of the typical clinical findings and typical conventional MRI findings. The study was done between January 2018 and June 2020. The study was performed on 1.5 Tesla imager, using pulse -gated, cine-phase-contrast MRI technique and CSF quantification software.

Results: This study revealed that the surest phase contrast MRI parameters in predicting normal pressure hydrocephalus was a CSF aqueductal stroke volume greater than 42 μL having a positive predictive value100%.

Conclusion: The study yielded considerable information on the physiology of the normal CSF circulation, and in the evaluation of pathological CSF flow dynamics in normal pressure hydrocephalus that provided a better method of selecting those patients with hydrocephalus who gain benefit most from shunt operation.

Keywords: Normal pressure hydrocephalus; cine phase contrast; ventriculomegally; atrophy.

INTRODUCTION

The production and flow of human cerebrospinal fluid has been studied since the 1940s, however, early investigations were hampered by a lack of non-invasive studies *(Leinonen et al., 2018)*. Magnetic resonance investigation in CSF flow began with the qualitative observation of the degree of flow void in the aqueduct of Sylvius and adjacent third and fourth ventricles *(Korbecki et al., 2019)*. Although this early MR method was useful in the evaluation of patients with suspected NPH, the clinical success was limited and this observational method was not significantly used because the presence of flow void phenomenon in the aqueduct is a qualitative measure, which is influenced by many acquisition parameters and often may be difficult to quantify *(Yamada et al., 2015)*.

Phase contrast cine MR flow imaging provides a simple way to better characterize CSF flow. The application of cine phase-contrast MRI technique in patients with NPH holds great promise for improvement of the diagnosis, especially in those cases where the differentiation from atrophy on clinical and conventional radiological basis is difficult. In the normal patient, consistent flow patterns are observed and are quite different from those patterns that are seen in CSF flow disorders *(Yamada et al., 2015)*. The phase contrast technique is extremely sensitive even to slow flow and provides the potential for noninvasive flow quantification. The results of these measurements have yielded considerable information on the physiology of the normal CSF circulation. In addition, pathological CSF flow dynamics in normal pressure hydrocephalus has been analyzed *(Algin et al., 2012)*.

This study aimed to analyze the characteristics of CSF flow through the aqueduct of Sylvius at normal pressure hydrocephalus and atrophy patients.

MATERIALS AND METHODS

Forty patients were recruited in the study and written consents were obtained from all patients. Quantitative analysis of CSF flow through the aqueduct of Sylvius in 40 patients with dilated ventricles in whom diagnosis of normal pressure hydrocephalus needs to be confirmed.

The study was performed on 1.5 Tesla imager, using pulse -gated, cine-phase-contrast MRI technique and CSF quantification software. The aqueduct was visualized, using a midsagittal T1- or T2-weighted fast-spin-echo technique. A pulse -gated flow-compensated gradient-echo sequence with velocity encoding in the slice-selective direction was used to produce a series of phase-contrast images at different cardiac phases. Velocity maps were acquired in an oblique axial plane perpendicular to the aqueduct. Phase-contrast images was displayed on a gray scale, where low signal intensity indicated caudal flow and high signal intensity indicates rostral flow. Mean velocity measurements were obtained at each cardiac phase, by using an oval region-of-interest (ROI) placed over the aqueduct.

Parameters of CSF flow dynamics to be evaluated were systolic temporal parameters (systolic duration), velocity parameters (peak systolic velocity, PSV, peak diastolic velocity (PDV), volumetric flow parameters (mean flow rate and systolic stroke volume, SSV.

Statistical analysis was done using the SPSS software package version 18.0. Statistical analysis was done to obtain the mean and standard deviation of each mean and for comparison between the different groups involved in this study by independent sample t test for numeric variables and Chi square test was used for comparison between categorical variables.The following were used in statistical analysis: standard deviation (SD) , Chi-square (X2) , independent t test; analysis of variance and probability "p" value was considered significant when $p< 0.05$.

RESULTS

The hydrocephalus group comprised 20 patients; their age averaged 47.85 years (SD, 21.9575; range, 8-77 years. The atrophy group of an average age of 61 years (SD, 8.544; range, 46-82 years). Age differences were found among the hyrdrocephalus, and atrophy patients, with younger age preferential to the hydrocephalus patient while older preferential to atrophy patient's.

Mean values of peak velocities and volumetric flow parameters in hydrocephalus patients were found to be significantly higher. In eleven patients, the values were markedly elevated (hyperpulsatile pattern). In the remaining nine patients, the velocity and volumetric flow parameters were mildly elevated. There was significant increase of peak systolic velocities and stroke volume in normal hydrocephalus patients **(Table 1)**.

Table (1): Aqueductal CSF Dynamics In The Normal Pressure Hydrocephalic Patients

Parameters / Patients	Temporal parameters	Velocity parameters		Volumetric flow rates			Stoke volume
	Systolic Duration	PSV	PDV	PSF	PDF	mean flow	SSV
No (20)	20	20	20	20	20	20	20
mean	0.49	5.29	4.06	31.84	24.13	16.80	122.60
SD	0.07	1.75	1.87	15.62	13.12	8.55	63.73
minimum	0.38	2.32	2.15	9.60	12.00	6.28	45.73
maximum	0.64	8.85	9.12	61.20	54.00	33.19	227.10

There was significant decrease of peak systolic velocities and stroke volume in atrophy patients **(Table 2)**.

Table (2): Aqueductal CSF Flow Parameters In Atrophy Patients

Parameters / Patients	Temporal parameters	Velocity parameters		Volumetric flow rates			Stoke volume
	Systolic Duration	PSV	PDV	PSF	PDF	mean flow	SSV
No (20)	3	3	3	3	3	3	3
mean	0.44	2.81	1.80	6.00	3.80	2.74	22.56
SD	0.035	0.34	0.71	2.75	1.73	1.19	10.90
minimum	0.40	2.44	1.21	3.60	1.80	1.50	10.79
maximum	0.47	3.11	2.59	9.00	4.80	3.88	32.30

Mean values of peak velocities and volumetric flow parameters in hydrocephalus patients were found to be significantly higher, compared to atrophy group **(Table 3)**.

Table (3): Descriptive Statistics Of Aqueductal CSF Flow Parameters In NPH and Atrophy Patients

Patients / Parameters	First group	Second Group	Mean +\- Standard deviation	Significance
Age	**NPH**	**Atrophy**	**-13.1429 +\-10.9394 10.9394**	**0.238**
PSV	**NPH**	**Atrophy**	**2.4790 +\- 0.8116 0.8116**	**0.004**
PDV	**NPH**	**Atrophy**	**2.2640 +\- 0.8787 0.8787**	**0.014**
PSF	**NPH**	**Atrophy**	**25.8429 +\- 6.1932 6.1932**	**0.00**
PDF	**NPH**	**Atrophy**	**20.3286 +\- 5.2621 5.2621**	**0.00**
Mean flow	**NPH**	**Atrophy**	**14.0586 +\- 3.3822 3.3822**	**0.00**

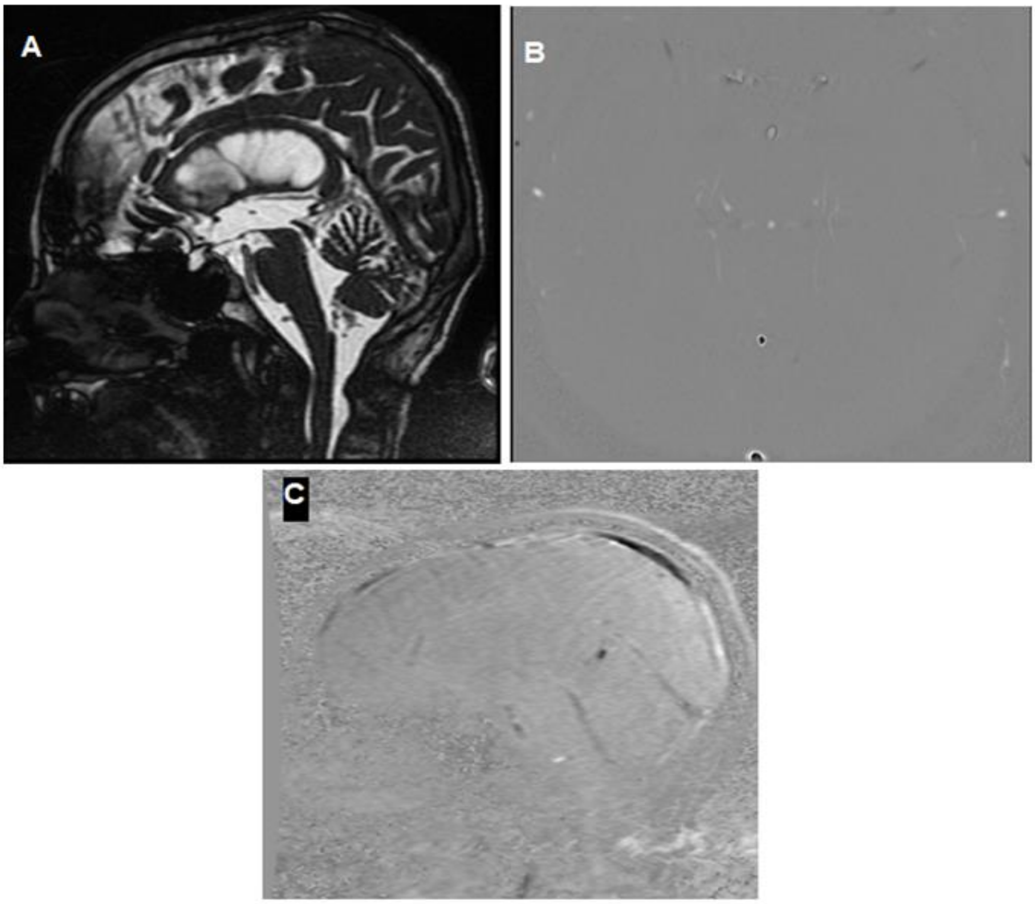

Figure (1) : Example of NPH patient ,a. sagittal localize , b. axial phase contrast image through the aqueduct of Sylvius , C. Sagittal phase contrast image

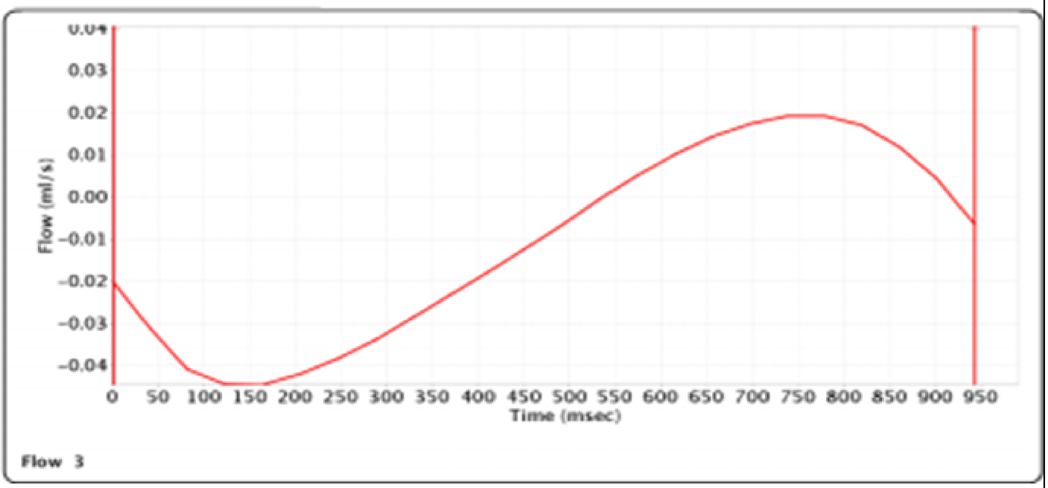

Figure 2 : CSF flowmetry Curve

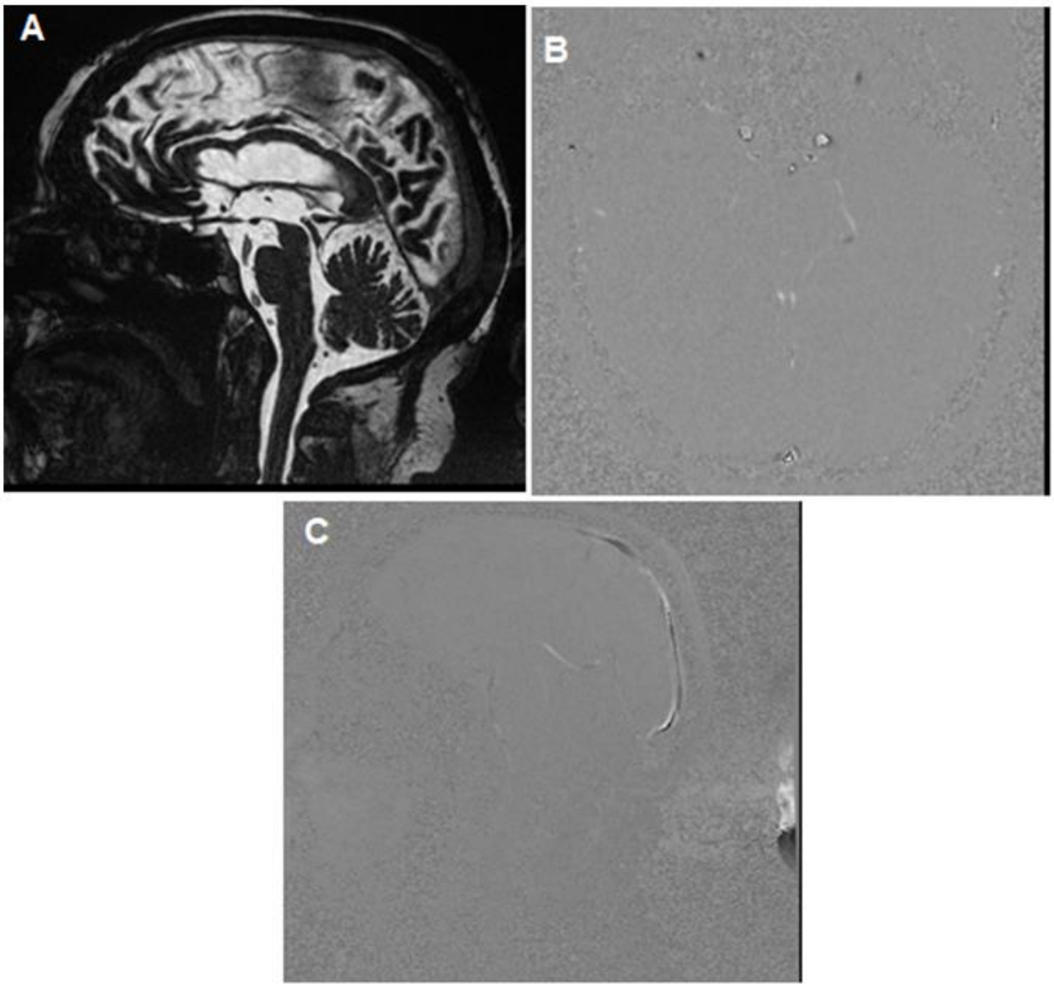

Figure (3): Example of atrophy patient a sagittal localizer, b. axial phase contrast image through aqueduct of Sylvius, c. sagittal phase contrast image of aqueduct of Sylvius

DISCUSSION

During the last two decades, cardiac-gated phase-contrast MRI has emerged as a fascinating technique for dynamic imaging of the CSF flow and evaluating different parameters of CSF dynamics, both qualitatively and quantitatively.

The technique has been successfully used in evaluating patency of endoscopic 3rd ventriculocisternostomy *(Bueno and Garcia, 2016)*. It is being increasingly used as an alternative to traditional CSF shunting in non-communicating hydrocephalus, measuring aqueductal CSF flow in patients with IAHS and predicting successful response to CSF shunting, and characterizing the flow of CSF in the foramen magnum in patients with Chiari 1 malformations *(El Ouadih et al., 2020)*.

In this study, we attempted to characterize patterns of CSF flow in the aqueduct of Sylvius in selected disorders of CSF dynamics; i.e. NPH and atrophy. The technique allowed both quantitative and qualitative assessment of CSF flow. Qualitative assessment included cardiac-cycle-related direction of CSF flow as well as homogeneity of flow. Several quantitative parameters of CSF flow were reported, these were conventionally grouped into velocity and volumetric flow parameters.

The results of our study were consistent with the current theory on the physiology of CSF circulation. Normal CSF flow in the control group was pulsatile with to-and-fro movement. The resultant CSF velocity/flow curves were triphasic with sinusoidal pattern. With ECG-gating, we found both aqueductal and cervical subarachnoid CSF flow to be caudocranial-craniocaudal-caudocranial (diastolic-systolic-diastolic), as the R wave, which marks the start of the ECG-gated acquisition, coincides with the iso-volumetric ventricular contraction phase at which the aortic valves are closed and the aortic pressure is decreasing. With peripheral gating using a finger pulsimeter CSF flow was craniocaudal-caudocranial-craniocaudal (systolic-diastolic-systolic) as the pulse peak coincides with maximum ventricular ejection of blood into the aorta *(Elsafty et al., 2018)*.

The pulsatility of CSF flow within the cranial vault and the spinal canal originates from the cardiac cycle-related variations in the cerebral blood volume *(Elsafty et al., 2018)*. During systole, arterial blood flows into the fixed cranial vault and the brain at a faster rate than venous blood exits these structures, yielding a net gain in parenchymal and intracranial blood volume. CSF flows caudally from the ventricles and the subarachnoid space into the spinal canal, with the distal spinal canal acting as a capacitor that accommodates the excess CSF. During CSF diastole, venous blood exits the cranial vault at a faster rate than arterial blood enters it, with a resultant net loss in intracranial blood volume and a reversal of CSF flow *(Hashimoto, 2020)*.

We investigated aqueductal CSF flow dynamics at the level of intercollicular sulcus, being the narrowest part of the aqueduct. In their study, *Bradley (2017)* found no significant differences in the mean flow rates at different levels the aqueduct.

We investigated aqueductal CSF flow characters in two groups, i.e normal volunteers, communicating hydrocephalus patients, and cerebral atrophy patients. Sex differences were found among the two groups. Mean ages, however, were differed mildly. The influence of this difference in age among the three groups on our results might be insignificant, considering the insignificant age-related variations in the velocity and flow parameters in the adult populations *Gruszecki et al. (2018)*.

In this study, we measured peak velocities, mean volumetric flow and stroke volumes for the three groups of patients. Most reports, however, investigated mean flow rates and stroke volumes for diagnosing communicating hydrocephalus and predicting successful response to ventriculoperitoneal shunts. *Gruszecki et al. (2018)* reported that flow volume data may be more helpful as velocity measurements depend on the diameter of the cerebral aqueduct at the level of measurement. Flow volume measurements are less dependent on aqueduct diameter or true perpendicular slice placement. As slice obliquity is introduced, measured velocity decreases but measured cross sectional area increases proportionally which essentially self-corrects flow measurements at shallow degrees of obliquity.

We found velocities and volumetric flow parameters in hydrocephalus patients to be significantly higher, compared to the normal control group and the atrophy group. Both hyperpulsatile and normopulsatile pattens of aqueductal CSF flow were reported in the hydrocephalus group. In their study, *Guerra et al. (2015)* categorized CSF flow in patients with communicating hydrocephalus into two patterns: hyperpulsatile or normopulsatile. The authors reported an aqueductal stroke volume of 288 + 124 microliter/cycle in the hyperpulsatile pattern group, and aqueductal stroke volume of 72 + 22 microliter/cycle in the normopulsatile group, which were within the normal range of their control group.

Lacking of a “gold standard” to confirm the clinical diagnosis of IAHS and to predict successful response to ventriculoperitoneal shunts poses a clinical dilemma. Some studies reported a flow rate higher than of 18 mL/min in elderly patients to be suggestive of idiopathic AHS. Other studies reported flow rate more than 24.5 mL/min to be specific to IAHS. Many MRI studies using cine-phase-contrast techniques have indicated that the aqueductal flow of CSF may be increased in patients with IAHS with marked aqueductal flow voids and elevated aqueductal volumetric flow have been shown to respond better to CSF diversionary procedures than those without significant CSF flow *Guerra et al. (2015)*.

In our study, mean systolic duration was significantly shorter in the hydrocephalus group (0.49 + 0.07), compared to the normal control group (0.55 + 0.04), *(Elsafty et al., 2018)*. In agreement with the results of Haughton et al. (2011) who reported mean aqueductal CSF systole of 0.47 + 0.04 of the cardiac cycle for communicating hydrocephalus patients versus 0.53 + 0.02 of the cardiac cycle for their control group.

CONCLUSION

The results of these measurements have yielded considerable information on the physiology of the normal CSF circulation and in the evaluation of pathological CSF flow dynamics in normal pressure hydrocephalus. This provided a better method of selecting those patients with hydrocephalus who would benefit most from shunt operation.

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تقييم سريان السائل المخى الشوكى عن طريق الرنين المغناطيسى فى حالات استسقاء المخ ذو الضغط الطبيعى

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خلفية البحث: إستسقاء الرأس ذو الضغط الطبيعي هو مثلث سريري يشمل إضطراب المشي، والخرف تحت القشري، وسلس البول لدى مريض يعاني من إستسقاء الرأس.

الهدف من البحث: تقييم ديناميكية تدفق السائل المخى الشوكى في مرضى الاستسقاء المخى وذلك باستخدام الرنين المغناطيسي ذي التباين الوضعي.

المرضى وطرق البحث: ضمت مجموعة الدراسة 40 مريضا يعانون من تضخم البطين المخي؛ وتمت إحالة المرضى إلى مراكز التصوير بالرنين المغناطيسي المتعددة والعيادات الخارجية الحكومية والخاصة والتي تشمل مركز نايل سكان للأشعة ومركز وطني سكان للأشعة إضافة إلى قسم الأشعة التابع لمستشفى المقطم، وتم التوصل إلى التوافق حول التشخيص النهائي في مجموعة تضخم البطين في ضوء الفحوصات السريرية وطرق التصوير بالرنين المغناطيسي التقليدية النموذجية. وقد أجريت هذه الدراسة بين يناير 2018 ويونيو 2020على جهاز بقوة 1.5 تسلا، باستخدام تقنية التصوير بالرنين ذي التباين الوضعي.

نتائج البحث: كشفت هذه الدراسة أن أدقمعيار في تقنية التصوير بالرنين المغناطيسي ذو التباين الوضعي لتشخيص استسقاء الضغط الطبيعي في المخ هو بلوغ حجم تدفق السائل النخاعي أكثر من 42 ميكرولتر مع قيمة تنبؤية إيجابية نحو100٪.

الأستنتاج: أسفرت الدراسة عن معلومات معتبرة بخصوص فسيولوجيا الدورة الدموية الطبيعية للسائل النخاعي وتقييم ديناميكيات تدفق السائل الدماغي النخاعي المرضي في استسقاء الرأس ذي الضغط الطبيعي الذي وفر بدوره طريقة أفضل

لاختيـــار المرضــــى الـــذين يعـــانون مـــن استســـقاء الـــرأس والـــذين سيســـتفيدون أكثـــر مـــن عملية تحويل مسار السائل النخاعي.

الكلمات الدالة: إستسقاء الرأس، السائل المخي الشوكي، الرنين المغناطيسي.