



Accuracy of MRI CSF Flowmetry in the Diagnosis of Normal Pressure Hydrocephalus

Hussein Zakaria^{1*}, Mohamed A. Hafez², Amr K. Elsamman², Farid G. Amin¹, Ayman Tarek²

¹Cairo University Hospital, Cairo, Egypt; ²Department of Neurosurgery, Cairo University, Cairo, Egypt

Abstract

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***Correspondence:** Hussein Zakaria, Cairo University Hospital, Cairo, Egypt.
E-mail: huseinzakaria1990@gmail.com
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BACKGROUND: Normal pressure hydrocephalus (NPH) is one of the few treatable causes of dementia. NPH is diagnosed using the clinical triad of: Gait disturbance, progressive mental deterioration, urinary urgency, or incontinence in association with radiological findings suggestive of NPH, for example, ventriculomegaly, disproportionately enlarged subarachnoid space hydrocephalus, and narrow callosal angles.

AIM: The purpose of the present study was to assess the accuracy of MRI cine phase flow studies as a non-invasive modality in the diagnosis, and also for the prediction of improvement of symptoms suggestive of NPH without the need for CSF tapping.

METHODS: Twenty-six patients suffering clinically from the triad of NPH, or at least two of them; attending our neurology, psychiatry, and neurosurgery clinics in Cairo University Hospitals, with ages ranging between 50 and 85 years, randomly chosen regarding sex or other comorbidities. All patients underwent a regular MRI in addition to CSF flowmetry studies to correlate the MRI findings that reveal NPH with their known clinical features. Careful clinical assessment was performed to detect severity of symptoms, and patients were classified accordingly, and a disability score was provided. After CSF tapping, patients were reassessed clinically after 6–8 h to detect improvement of symptoms, and the degree of improvement was compared to the result of CSF flow study.

RESULTS: CSF flow studies, particularly stroke volume across the aqueduct of Sylvius, provide the highest significance in diagnosing hyperdynamic circulation evident by many radiological studies in cases of NPH. This was also found to be a good prognostic factor which correlates well with the improvement of symptoms following CSF tapping. However, its use to exclude suspicious cases of NPH seems unreliable, that is, not a good negative predictor. Findings of MRI CSF flow studies also show significance in detecting brain atrophic changes, especially peak systolic velocity, which usually accompany or mimic the clinical picture of NPH.

CONCLUSION: MRI CSF flow studies are an excellent aid as an adjuvant non-invasive technique in selection of suspicious cases as it shows significance in detecting hyperdynamic circulation, especially high stroke volume results in cases of NPH. Both CSF tapping and CSF flowmetry findings "low stroke volume values" were not found to be a good negative predictor for clinical improvement after shunting.

Introduction

Normal pressure hydrocephalus (NPH), also called malresorptive hydrocephalus, is a form of communicating HCP in which excess CSF accumulates within the ventricles, with normal or slightly elevated CSF pressure, and later compressing the brain parenchyma, leading to the classic triad of gait disturbance, dementia, and urinary incontinence [1], [2], [3].

Primary idiopathic NPH (iNPH) is distinguished from secondary NPH (sNPH), whose common causes are subarachnoid hemorrhage (23%), meningitis (4.5%), and traumatic brain injury (12.5%) [4]. A common feature of both iNPH and sNPH is that neither involves any obstruction to the flow of CSF within the ventricular system [5], [6].

The basal ICP must be initially elevated, at least some of the time, for either iNPH or sNPH to

develop [5]. The two entities carry the similar prognosis. The only major clinical difference between iNPH and sNPH is that iNPH affects only the elderly while sNPH affects all age groups [7].

It has continually intrigued clinicians and researchers in establishing diagnostic criteria and prognostic factors that would facilitate a precise selection of candidates for a shunt.

Neuropsychological assessment, Ct cisternography, Magnetic resonance imaging, CSF tapping, magnetic arteriography and venography and recently the cine phase MRI were used for patients selection in our study.

The purpose of the present study was to assess the accuracy of MRI cine phase flow studies as a non-invasive modality in the diagnosis, and also for the prediction of improvement of symptoms suggestive of NPH without the need for CSF tapping.

Patients and Methods

Twenty-six patients attending neurology, psychiatry, and neurosurgery clinics in Cairo University Hospitals were selected and fulfilled the following criteria:

1. Patients clinically suspected as NPH “two symptoms at least from the triad of NPH”
2. Patients with features suggestive of NPH on MRI
3. Patients aging from 50 to 85 years
4. Patients having no secondary cause for hydrocephalus on imaging “obstructive hydrocephalus, communicating”
5. Patients having no manifestations of cortical dementia “agnosia, apraxia, and aphasia”
6. Patients with normal cardiac rhythm as patients with abnormal cardiac rhythm they are not candidates for performing the flow studies.

After fulfillment of the previously mentioned criteria, patients were examined, further investigated and prepared for the next step.

- Patients’ medical history taken in details and its onset is mentioned, for example, diabetes mellitus, hypertension, alcoholism, and previous history of cerebral strokes, tumors, and surgeries
- Onset, course, and duration of symptoms also taken in details with the first to appear and did it follow any other neurological insult, for example, stroke to exclude that it was the direct cause of that symptom
- Patient’s vital signs “pulse, blood pressure,” especially pulse and its regularity as in cases of irregular pulse CSF flowmetry could not be performed and random blood sugar are closely observed then prepared to do MRI CSF flowmetry
- Patient memory and mental status assessed using Mini-Mental State Examination (MMSE) and patients are then categorized after that according to National Institute for Health and Care Excellence to:
 - Normal: Scores of 25–30
 - Mild affection: 21–24
 - Moderate: 10–20 as moderate and
 - Severe: Below <10
- Onset and frequency of urinary manifestations “frequency, urgency, enuresis, and incontinence” and if any of the previously mentioned was found patient considered manifesting, and if any attempt at any time of the day to control urine following CSF tapping, patient was considered improving.
- We examined the gait using timed up and go test (TUGT) to detect risk of falls and observe

the type of gait and accordingly, patients were classified into

- Normal: 11–20 s “elderly and disabled patients”
- Abnormal: 21–30 s means the person needs assistance outside and indicates further examination and intervention
- More prone to fall: >30 s.
- We exclude patients with neurological affection secondary to cortical affection, for example, posterior fossa hematoma causing unsteady gait, frontal strokes causing hemiparesis and alcoholic patients and patients with severe peripheral neuropathy. Secondary to uncontrolled diabetes.
- Patients were classified after that according to the American European Guidelines (AEG) into probable, possible, and unlikely to be diagnosed as iNPH.
- MRI CSF flowmetry was then performed to all our study group using these regimens and criteria:

Routine MRI sequences

- Axial T1, T2, flair, diffusion, ADC map, and SW-weighted images
- Sagittal and coronal T2 Wt Is.

Phase contrast MRI protocol

- Sagittal 2D phase contrast parameters: TR 17–20ms, TE 5–10ms, flip angle 10, matrix 256 × 256 pixels, slice thickness 5mm
- Axial PC TR 12–17ms, TE 7–10ms, flip angle = 15°, matrix 256 × 256 pixels, and slice thickness = 5mm
- Cardiac gating performed with MR compatible peripheral pulse transducer applied to the subject’s finger
- The localizer placed within the aqueduct of Sylvius and PC images obtained in one cardiac cycle. A series of images obtained at different cardiac phases
- CSF flow parameters were automatically extracted
- Data analysis.

Qualitative analysis

Midsagittal phase and magnitude images assessment for CSF flow in both systole and diastole; caudal flow in systole show hyperintense signal, while the diastolic flow (cranial flow) shows hypointense signal, the change of flow in the aqueduct, during systole and diastole, was used to rule out the presence of obstruction; data were tabulated, coded, and then analyzed for statistical significance.

Quantitative calculation data

- Peak systolic velocity (cm/s), highest CSF velocity during systole
- End diastolic velocity (cm/s), highest CSF velocity during diastole
- Mean (average) velocity (cm/s) during both systole and diastole, their sum divided by their number
- Flow rate (ml/min) = ROI (cm²) × mean velocity
- Stroke volume (μl) defined the mean volume of CSF passing the aqueduct during the systole = mean systolic flow × duration of systole.

Results obtained, putting the stroke volume the most important indicator for CSF flow along the aqueduct of Sylvius and making a full picture to exclude brain atrophy and vascular brain affection from the radiologic picture of NPH.

Patients and their families consented written after explaining the result of MRI CSF flowmetry and the role of tap test (TT) “lumbar puncture insertion and withdrawal of about 30–50 cc from the patient CSF” as a diagnostic tool in all cases whom are suspected clinically despite the result of CSF flowmetry.

We reassessed patients clinically 6–8 h following CSF tapping, patients showed that no improvement was prepared for another attempt for CSF tapping 1 day later. “Figure 1” demonstrates the assessment of improvement methodology.

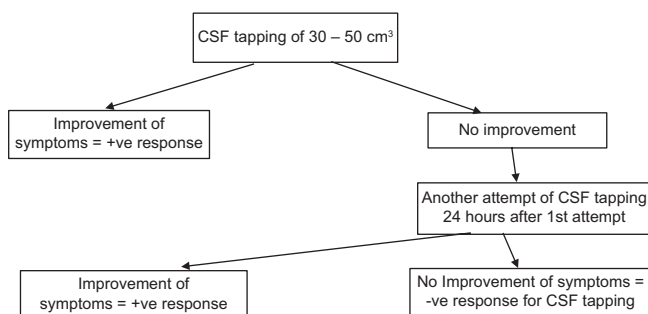


Figure 1: demonstrates the assessment of improvement methodology.

Evaluation of the improvement of the patient condition following TT is compared to the readings and final opinion of the MRI CSF flowmetry studies.

Cases whom improved clinically following TT “single attempt” with MRI CSF flowmetry opinion approving that the patient measurements run with NPH considered good positive radiological assessment.

Cases showed no clinical improvement or minimal non-significant improvement in a single criterion following CSF “after two attempts with 1 day time interval between performing them” with MRI CSF flowmetry opinion approves that the patient measurements run with NPH considered as a false-positive radiological assessment.

Cases showed no clinical improvement following TT “after two attempts with 1 day time interval

between performing them” with MRI CSF flowmetry results irrelevant with NPH considered good negative radiological assessment.

Results

This study included 26 patients with criteria of NPH “at least two of Hakim-Adam’s triad” and radiological evidence of NPH. Patients fulfilled the inclusion criteria.

According to the AEG, there were 16 probable causes and 10 possible causes of NPH, no unlikely cases were found in our study group.

Regarding age distribution in our study cases, it ranged between 50 and 84 years, with mean 62.6 years, median 63.5 years with a standard deviation 8.86 years.

In our study group, 21 cases were male (80.8%) and 5 cases were female (19.2%).

In our study, 11 patients were diabetics, 19 were hypertensives, and four suffered from coronary artery diseases, 11 patients (42.3%) suffered from CNS strokes in the form of ICH in two cases and cerebral infarctions in nine patients.

Incidence of the symptoms in our study group was as follows: 19 patients (73%) showed mental and memory affection, 18 patients (69.2%) showed gait affection, and 21 patients (80.8%) showed urinary symptoms obviously seen in “Figure 2.”

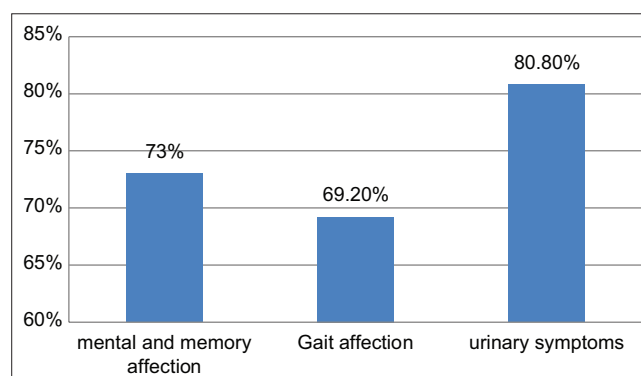


Figure 2: incidence of symptoms in our study group

MMSE at time of assessment before CSF tapping showed minimum score of 18 and maximum score 27, with median of 22 and mean of 22.7 and standard deviation of 2.52.

Seven patients (26.9%) showed normal MMSE score, 14 (53.8%) showed mild affection, and 5 patients (19.2%) showed moderate affection. “Table 1” demonstrates degree of affection in MMSE.

As a conclusion, 19 patients (73%) out of 26 cases showed mental and memory affection

Table 1: MMSE classification of severity prior to CSF tapping

MMSE score		
Normal	7	26.9%
Mild	14	53.8%
Moderate	5	19.2%

MMSE: Mini-Mental State Examination.

TUGT at time of assessment before CSF tapping showed minimum value of 12 s and the maximum was 30 s with median 20 s and mean 20.42 s and standard deviation 4.8 s.

Eight patients (30.8%) showed normal TUGT values, 16 (61.5%) showed abnormal values, and 2 patients (7.7%) showed high risk to fall as shown in "Table 2," and as a conclusion, 18 patients (69.2%) out of 26 showed gait affection.

Table 2: Distribution of our study group regarding TUGT score before CSF tapping

TUGT score		
High risk for fall	2	7.7%
Abnormal	16	61.5%
Normal	8	30.8%

TUGT: Timed up and go test.

Urinary symptoms "incontinence" before CSF tapping was found in 21 patients and only five patients were normal.

Following CSF tapping 10 cases, "52.6% of the affected" showed improvement in MMSE score out of 19 affected cases, 15 cases "83.3 of the affected" showed improvement in TUGT values out of 18 affected cases and 8 cases (38% of the affected) suffering from urinary symptoms showed improvement out of 21 affected cases.

Table 3: significance of CSF tapping on MMSE score

	Mean	Standard deviation	Median	Minimum	Maximum	p-value
MMSE score before CSF tapping	22.77	2.52	22.00	18.00	27.00	<0.001
MMSE score following tap test	24.85	1.93	25.00	21.00	28.00	

MMSE: Mini-Mental State Examination.

As a conclusion, we found statistical significance for improvement following CSF tapping in MMSE and TUGT regarding the mean, median, and the standard deviation, as shown in "Tables 3 and 4," and there was no statistical significance for CSF tapping on the urinary manifestations improvement, however, as patient must have at least two symptoms from the triad so CSF tapping is significant for improvement in our study group.

Table 4: Significance of CSF tapping on TUGT results

	Mean	Standard deviation	Median	Minimum	Maximum	p-value
TUGT score (sec) before CSF tapping	20.42	4.83	20.00	12.00	30.00	< 0.001
TUGT score following tap test (sec)	14.73	3.68	14.00	10.00	27.00	

TUGT: Timed up and go test.

Results of stroke volume and its significance as a qualitative value: As 42 μ l per sec was the cutoff point for diagnosis of hyperdynamic circulation through aqueduct of Sylvius patients were classified into two groups: Positive stroke volume (24 patients, 92.3%)

and negative stroke volume (two patients, only 7.7%) according to the stroke volume value

We then compared positive stroke volume group "radiological evidence of hyperdynamic circulation that mostly will benefit from CSF withdrawal" with the results of improvement following CSF tapping and we noticed that,

Stroke volume as a qualitative value showed statistical significance in the diagnosis of hyperdynamic circulation in cases of NPH with statistical significance ($p < 0.001$) as shown in "Table 5," so it is a good positive predictor in the diagnosis of NPH.

Table 5: Statistical significance of stroke volume as a prognostic method to detect clinical improvement following CSF tapping

CSF tapping results on the stroke volume positive group	Count	%
No	8	33.4
Yes	16	66.6

The two cases with negative stroke volume, that is, <42 μ l, showed improvement in a single symptom in one case and improved in two symptoms in the other, however, the low number of sample with negative CSF flowmetry result (<42 μ l) was not enough to predict the stroke volume result as a good negative predictor to exclude the diagnosis of NPH according to its value.

Discussion

The actual incidence and the nature of NPH is not accurate and many theories were put to describe its etiology, decision-making in those cases is not usually easy and the prediction of outcome when surgical intervention attempted also is difficult [8]. Early detection of the disease "which requires awareness by the disease and its symptoms" may participate in the outcome through preventing irreversible sequelae of the pathogenesis of that disease and that was proved by many studies on the outcome of improvement following surgery [2].

Patient selection is an important factor to predict outcome taking in consideration proper physical, mental affection and precise history taking of accompanied medical morbidities [5].

CSF tapping showed statistical significance in improvement of gait and mental affection that agreed with many other studies [9], [10].

Gait was documented to show the most significant improvement and also the earlier symptom that showed improvement in our study and many other studies [10], [11].

MRI CSF flow studies showed an important role not only in the diagnosis but also in prediction of outcome following CSF withdrawal, selection of patients, and excluding patients with brain atrophy

predominant features “lower systolic peak velocity, systolic mean velocity, and stroke volume values” [12] and stroke volume also showed significance as a good prognostic radiological finding for diagnosing iNPH [13].

In our study group, we found that the age group ranged between 50 and 84 years which was similar to many studies like the retrospective study by Virhammar *et al.* [14] on 108 patients that showed median age of 74 years (range, 54–88 years).

Twenty-one cases were male (80.8%) and 5 cases were female (19.2%); however, this gender distribution was not found in many studies (15 men and 11 women) in Virhammar *et al.* [15] study of TT and its affection on cerebral perfusion and in another retrospective study by Virhammar *et al.* [14] also on 108 patients; 58 (54%) were men and 50 (46%) were women in detecting the pre-operative prognostic value of MRI findings in idiopathic NPH.

In our study group, we have 16 probable cases and 10 possible cases of iNPH, no unlikely cases. Out of our 26 cases, with near numbers found in the study of Virhammar *et al.* [15], 17 probable iNPH, six as possible iNPH, and three as unlikely iNPH.

The incidence of the three main symptoms of Hakim-Adam’s triad in our study was as follow: 19 patients (73%) showed mental and memory affection, 18 patients (69.2%) showed gait affection, and 21 patients (80.8%) showed urinary symptoms, it was near to the incidence of symptoms found in the study of Ashraf Talaat *et al.* [13] on 25 cases that showed gait disturbance in 78.9% as a presenting symptom, dementia in 89.5%, and urine incontinence in 47.4%.

In our study, 10 cases “52.6% of the affected” showed improvement in MMSE score out of 19 affected cases with a statistical significance of CSF tapping as a predictor for mental and memory improvement following CSF tapping. Similar results were seen in the study of Ryan Gallagher *et al.* [9] on 40 patients who used MoCa score for evaluating the mental function. It was also seen in the study of Samanta Fabricio *et al.* [16] on 61 patients with significant improvement after the first puncture in MMSE ($p = 0.031$).

In our study, 15 cases “83.3 of the affected” showed improvement in TUGT values out of 18 affected cases with a statistical significance of CSF tapping as a predictor for gait improvement which was also found in the prospective study by Gallagher *et al.* [17] Using a difference of 3.63 seconds as a cutoff value for gait improvement in his study, the prospective study of Virhammar *et al.* on 40 patients also showed gait improvement using the 10 meters test where 27 cases showed improvement, while in the study of Souza *et al.* on 104 cases detected gait speed improvement following CSF tapping.

In an international study that was performed on 142 patients in nine European countries the best correlation for improvement was seen following CSF

tapping. The best correlation was seen between outcome in iNPH score and the effect of performing the CSF TT was on 10 m of walking “gait assessment” at free speed.

In another study of Sand *et al.* [19] on 29 patients with suspected iNPH, they found improvement in gait mainly and with higher “high normal opening pressure during CSF tapping” and bad results with severe dementia.

We found improvement in 8 cases (38% of the affected) suffering from urinary symptoms out of 21 affected cases with no statistical significance found in our study group. Improvement was also seen in 23 cases out of 55 patients following CSF tapping in the study of Krzastek *et al.* [20] that showed statistical significance according to their criteria and was also seen in other case studies like that of Halil Onder [21].

In our study, eight patients did not show improvement following CSF tapping “about 30% of the cases” most of them had a low CSF stroke volume values ranging between 46 and 78 micro L per sec, in the study of John J. Halperin *et al.* [22], he found that CSF flow rates in the five patients who did not improve clinically after a CSF tapping were higher than in the patients who did improve after LP.

However, many studies suggest that improvement of symptoms following CSF tapping suggests better response for shunting but not excluding that failure of improvement excludes the benefit from CSF diversion as described by John J. Halperin *et al.* [22].

In this study, we used the stroke volume as the main radiological MRI flow study item to diagnose hyperdynamic circulation in cases of iNPH that showed statistical significance with the improvement following CSF tapping, this was also seen in the study of Gallagher *et al.* [17]. On his 53 candidates, values was significant also in another study done by Ashraf Talaat *et al.* [13] on 19 patients that found the significance for improvement following VP shunting in patients with stroke volume higher than 42 μ l. However, in the retrospective study of Virhammar *et al.* [14] on 108 patients, they used a small callosal angle, prevalence of DESH, and wide temporal horns on the pre-operative MR imaging scans as significant predictors for positive shunt outcome, neither stroke volume nor the results of CSF tapping showed any statistical significance in that study.

We also noticed statistical significance in the number of the improved symptoms following CSF tapping and the higher stroke volume result that agrees with results of Ashraf Talaat *et al.* [13].

However, the two cases in our study groups with negative “<42 μ l per second” showed improvement in a single symptom and two symptoms, respectively, which agrees with the study of Ashraf talaat *et al.* [13] who documented improvement of symptoms following CSF diversion in four patients out of 19 with stroke volume

28–42 mL, and also agrees with the study of Bradley *et al.* [23] on 18 patients where 12 patients with positive stroke volume value responded to VP shunting and three out of the six remaining patients with negative stroke volume value also showed improvement following VP shunting.

Hence, stroke volume showed good positive prognostic factor in our study and many others and false-negative result was seen also in our study “only two cases” and others and so considered as a good positive prognostic factor and a poor predictor for negative values.

However, the efficiency of CSF flow studies to diagnose hyperdynamic circulation was documented in many radiological studies like those previously mentioned and the study of Senger *et al.* [24] on 36 patients and the study of Elsafty *et al.* [12] on 20 patients which also revealed similar results with systolic velocities and stroke volume showed higher values among iNPH patients than control groups.

Conclusion

We found that MRI CSF flowmetry “stroke volume” was found to be a good positive diagnostic tool for detecting of hyperdynamic circulation among patients suffering from iNPH.

MRI CSF flowmetry “stroke volume” results match the degree of improvement following CSF tapping and subsequently will match CSF diversion and that was obvious in our study cases whom underwent VP shunting.

Negative stroke volume values are not a good negative predictor for the improvement of symptoms following CSF withdrawal as proved by many studies.

CSF tapping is still the most reliable and is the only procedure to assess the effect of CSF removal “shunting” on the patient, especially with the high costs of surgery, devices, for example, programmable shunt and usual complications that might occur which usually requires performing other surgeries.

However, accurate data collection considering the patient's clinical and radiological assessment was found to be the best predictor for the diagnosis of iNPH, regardless the age of the affected person and, hence, can disregard performing CSF tapping.

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