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Original Research Article

Evaluation of the variability of imaging characteristics in normal pressure hydrocephalus

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Abstract

Background: Normal pressure hydrocephalus (NPH) is a syndrome found in the elderly, which is characterized by the clinical triad of gait disturbance, dementia, and urinary incontinence without overt signs and symptoms of elevated intracranial pressure. NPH has been estimated to account for upto10% of cases of dementia and is significant because it is treatable by ventriculoperitoneal shunting. NPH can be idiopathic or can be secondary. The secondary causes are: traumatic brain injury, meningitis, subarachnoid haemorrhage (SAH) or intracranial surgery. Patients with Idiopathic NPH respond better to treatment than secondary

Materials and Methods: It is a prospective cross-sectional study. Inpatients and outpatients of age group more than 40 years of age, of both gender (males and females) diagnosed with normal pressure hydrocephalus as per consensus criteria were referred to Department of Radiodiagnosis from the department of. The patients underwent Magnetic resonance imaging/computed tomography study of brain.

Results: A total 40 patients were included in this study according to consensus criteria. Computed tomography (CT) and Magnetic resonance imaging (MRI) show ventricular enlargement disproportionate to cerebral atrophy, with associated ballooning of frontal horns, periventricular hyperintensities, thinning and elevation of the corpus callosum and widening of temporal horns without evidence of hippocampal atrophy in NPH.

Conclusion: Although diagnosis can be made based on CT findings alone, MRI is more accurate for disclosing associated pathologies (such as cerebrovascular disease) and for detecting NPH typical signs of prognostic value, besides avoiding exposure to ionizing radiation. MRI is the best modality to image anatomical changes and can further support the diagnosis with CSF flow studies.

Keywords: Normal pressure hydrocephalus, neuroimaging, magnetic resonance imaging, computed tomography, cerebrospinal fluid pressure, shunt surgery

Introduction

Normal pressure hydrocephalus is characterised by a triad of dementia, gait ataxia andurinary incontinence without overt signs and symptoms of elevated intracranial pressure. The triad is famously referred to as Hakim's triad for NPH [1-3]. NPH can be idiopathic or can be secondary. The secondary causes are: traumatic brain injury, meningitis, subarachnoid haemorrhage (SAH) or intracranial surgery. The exact pathology of idiopathic normal pressure hydrocephalus (NPH) is still unclear [4].

The underlying pathophysiological mechanism suggests impaired cerebrospinal fluid (CSF) flow within the ventricles or subarachnoid space or both, defective CSF absorption through

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the arachnoid granulation and impaired intracranial vascular compliance [5].

There are no accepted pathological criteria for postmortem diagnosis of NPH. While potentially causative abnormalities like arachnoid fibrosis, have been reported in brain autopsies of some patients who were diagnosed with NPH but it has not been studied in a systemic manner and therefore it cannot verify a clinical diagnosis of NPH [6].

According to international guidelines, the following are CT or MRI criteria which are decisive for NPH diagnosis: ventricular enlargement disproportionate to cerebral atrophy (Evans index > 0.3), with associated ballooning of frontal horns; periventricular hyperintensities; corpus callosum thinning and elevation. Callosal angle between 40º and 90º and widening of temporal horns not fully explained by hippocampal atrophy and aqueductal or fourth ventricular flow void; enlarged Sylvian fissures and basal cistern and narrowing of sulci and subarachnoid spaces over the high convexity and midline surface of the brain [7].

The newer MRI applications provides indications of abnormal CSF flow by using Proton Density MRI, Phase Contrast MRI, Radionuclide cisternography documenting CSF flow void, ventricular reflux and hyperdynamic flow. Various Advanced MRI measurements can be performed as adjuncts to conventional clinical sequences in patients suspected of having NPH: Volumetric MRI, Diffusion Tensor Imaging, Arterial Spin Label and Phase Contrast Imaging [8].

NPH is an important cause of motor disturbances and cognitive impairment in elderly patients, the social and economic burden attributable to NPH cannot be ignored. Therefore, any kind of research effort aimed at improving the understanding of the epidemiology of NPH is important [9].

NPH is the only form of dementia that can be treated with ventricular shunting. According to some studies, the only evidence pointing to a diagnosis of NPH is good response to ventricular shunting. Normal pressure hydrocephalus is increasingly recognized as a treatable cause [10].

There is no standard gold test to diagnose and monitor response to shunt surgery in normal pressure hydrocephalus. Often, clinical tests like CSF-Tap tests are used in conjunction with radiology for diagnostic and prognostic evaluation. MRI is the best modality to image anatomical changes and can further support the diagnosis with CSF flow studies. In this study, we have assessed the variability of imaging characteristics in normal pressure hydrocephalus.

Materials and Method

Study Design: This study was a prospective cross-sectional study conducted in Department of Radio diagnosis, Bharath Institute of Higher Education and Research, during the period of January 2021 to July 2022.

Subject enrolment: Patients more than 40 years of age diagnosed with normal pressure hydrocephalus as per consensus criteria and referred to Department of Radiodiagnosis from the Department of Neurology. Patients who were sufferings from other types of dementia and other significant neurological illness were not considered for this study.

Study protocol: This study was approved by institutional ethical committee, patients of age group more than 40 years of age, of both gender (males and females) diagnosed with normal pressure hydrocephalus as per consensus criteria and referred to Department of Radiodiagnosis from the department of Neurology were enrolled in the study with a written informed consent. All the selected patients were explained in detail about the procedure. Magnetic resonance imaging/computed tomography study of brain were performed once.
All patients were subjected to Computed Tomography (CT)/ Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging: All MRI brain scans are performed on a 1.5T Siemens 16 channel, using head coil. MRI evaluation of brain was done using T1W, T2W, FLAIR, ADC, DWI, GRE.3D CISS sequences. Findings on these sequences were correlated for the study. Computed Tomography: All CT brain scans were performed on 16 slice Siemens somatomspiri.

Statistical analysis: The data analysis was performed using SPSS Statistics version 25. The test values of continuous variables were expressed as mean ± SD (standard deviation). Means of groups were compared with paired-tests. A p-value < 0.05 was considered statistically significant.

Results

In this present study, the number of valid cases with normal pressure hydrocephalus who fulfilled the inclusion criteria were 40. CT and MRI evaluation of brain was done using T1W, T2W, FLAIR, ADC, DWI, GRE, D CISS sequences. The mean age of patients was 60.82 ± 17.64 (range, 45-77 years). Table 1 shows the general demographic and clinical information of patients. There were 22 (55%) males and 18 (45%) females, respectively.

Table 1: Demographic and clinical information about the Normal Pressure Hydrocephalus

Variables	Patients (n = 40)	
	Male (n = 22)	Female (n = 18)
Age (years)	67.5 ±9.4	53.8 ± 7.6
BMI (Kg/m^2)	26.3 ± 3.8	27.6 ± 2.7
Symptoms reported by patient and/or family		
Duration of symptoms (years)	3.4 ± 1.9	4.1 ± 2.3
Urinary incontinence	16 (72.73%)	13 (72.22%)
Cognitive impairment	19 (86.36%)	15 (83.33%)
Gait disturbance	21 (95.45%)	18 (100%)
Headache	4 (18.18%)	5 (27.78%)
Dizziness	3 (13.64%)	2 (11.11%)
Lethargy	1 (4.55%)	1 (5.56%)

Data expressed as mean ± SD

Agreement over time and modalities for one investigator Intra-rater agreement (test-retest reliability) was equally distributed for both modalities, with higher values for continuous data Table 2. The comparable CT and MRI scans in the same patient in whom the assessment remained the same, independent of the modality. When the results were compared for different modalities for the same reader, the intra-rater agreement was lower for white matter changes and for focally enlarged sulci. Callosal angle assessment showed almost perfect intra-rater agreement for both CT and MRI and intra-rater agreement was only slightly lower when the two modalities were compared for the same reader Table 2.

Table 2: Analysis of agreement between consecutive assessments by CT and MRI

Variables	CT	MRI	CT vs. MRI (95% CI)
Evans' index	0.86 ± 0.08	0.88± 0.07	0.87± 0.04
Temporal horns	0.90± 0.07	0.78± 0.03	0.84± 0.02
Callosal angle	0.79± 0.04	0.83± 0.05	0.82± 0.03
White Matter Changes (WMC)	0.67± 0.09	0.53± 0.03	0.59± 0.04
Narrow sulci	0.69± 0.03	0.77± 0.06	0.74± 0.03
Sylvian fissures	0.73± 0.06	0.81± 0.08	0.77± 0.07
Enlarged sulci	0.82± 0.08	0.51± 0.04	0.68± 0.02

Data expressed as mean ± SD

The MRI biomarkers of CSF space anatomy, Evans' index, callosal angle and DESH, differed significantly between NPH and logistic regression analysis adjusting for age showed that the anatomical biomarkers differentiated the patient cohorts Table 2.

Table 3: Evaluation of CSF space anatomy in NPH subjects

Variables	Patients (n = 40)	
	Male (n = 22)	Female (n = 18)
Evans' index	0.41 ± 0.06	0.29 ± 0.04
Callosal angle	72.4 ± 26.3	93.7 ± 14.8
DESH Present Absent	 16 (72.73%) 6 (27.27%)	 13 (72.22%) 5 (27.78%)
Visual rating scale for ESF 0, narrowed/1, normal/2, mildly dilated/3, severely dilated	6/15/11/1	0/14/5/14
Visual rating scale for TMC 0, dilated/1, normal/2, mildly tight/3, severely tight	2/31/0/0	0/5/9/19

DESH-disproportional enlarged subarachnoid space hydrocephalus; TMC tightness of the medial subarachnoid spaces and with/without tight high convexity sulci, ESF enlarged sylvian fissures. Data expressed as mean ± SD.

Sensitivity and specificity for different cut-offs of the imaging markers are presented in Table 4. The specificity was higher for all markers in the combined group of differential diagnoses. Specificity for discriminating NPH from differential diagnoses (with HC excluded) was 88% for the presence of DESH, and 94% for callosal angle<63^0. Vascular Dementia was the differential diagnosis with most overlap with NPH, Table 4.

Table 4: Sensitivity and specificity for presence of imaging features and some predefined cut-offs to discriminate shunt-responsive in patients

Variables	Vascular Dementia (n = 18)	Atrophy Parkinsonian (n = 14)	Supranuclear Palsy (n = 8)
Callosal angle<90°	8 (44.44%)	9 (64.29%)	2 (25%)
Callosal angle <63°	6 (33.33%)	5 (35.71%)	6 (75%)
Temporal horns≥4 mm	7 (38.89%)	10 (71.43%)	5 (62.5%)
Temporal horns≥6 mm	9 (50%)	4 (28.57%)	3 (37.5%)
Evans' index>0.3	10 (55.56%)	7 (50%)	6 (75%)
Crowded sulci	16 (88.89%)	11 (78.57%)	5 (62.5%)
Ventricular bulgings	14 (77.78%)	10 (71.43%)	5 (62.5%)
Focally enlarged sulci	9 (50%)	6 (42.86%)	4 (50%)
Sylvian fissure	7 (38.89%)	8 (57.14%)	3 (37.5%)

Data expressed as mean ± SD

Cut-off values that resulted in a specificity >95% for discriminating NPH from all other control groups combined were: callosal angle≤90° (sensitivity 56%); temporal horns≥6 mm (sensitivity 61%); Evans' index≥0.3 (sensitivity 57%); bilateral ventricular bulgings (sensitivity 38%); focally enlarged sulci (sensitivity 48%).

Discussion

Normal pressure hydrocephalus (NPH) is as a syndrome of gait ataxia, dementia, and incontinence associated with normal CSF pressures and dilated ventricles. This condition predominantly affects the elderly population [11].Imaging techniques are increasingly being used for diagnostic and prognostic evaluation of NPH due to lack of a single standard test.Computed tomography (CT) and magnetic resonance imaging (MRI) shows ventricular enlargement disproportionate to cerebral atrophy, with associated ballooning of frontal horns, periventricular hyperintensities, thinning and elevation of the corpus callosum, and widening of temporal horns without evidence of hippocampal atrophy. Although CT findings alone can suggest a diagnosis of NPH, MRI may be more useful for disclosing associated pathologies (such as cerebrovascular disease), prognostic signs, avoiding exposure to ionizing radiations [12].

The present cross section observational study evaluated imaging characteristics (CT & MRI) in patients with normal pressure hydrocephalus at a tertiary care center. The outcome variables evaluated were the Evans index, Callosal angle, sulci, sylvian fissure dilation, diameters of third ventricle and temporal horns of lateral ventricle, Flow voids through aqueduct of sylvius, deep white matter hyper intensities, periventricular hyperintensity, disproportionately enlarged subarachnoid hydrocephalus (DESH) and focal bulging of lateral ventricles. The impact of independent variables like age and gender on these indices were also evaluated.

Evan's Index (the ratio which compares the maximum width of the frontal horns of the lateral ventricle to the maximum transverse diameter of the inner table of the skull) is an important parameter for diagnosis of NPH and ventriculoperitoneal shunt surgery follow-up [13].

Bradley WG Jr. [14] conducted a case control study to define the value of quantitative MRI biomarkers (Evans' Index (EI), Aqueduct Flow Rate, and Apparent Diffusion Coefficient) in idiopathic NPH. Nine patients (age, 57-79 years; mean, 70.2 years) with a clinical diagnosis of idiopathic NPH were studied and compared with nine age and gender-matched controls. The authors found a significant difference in EI between cases and controls.For patients presenting with signs and symptoms of NPH, readings on MRI greater than 0.3, 10 mL/min, and 10.65 104 mm^2/s for EI, peak diastolic flow rate, and ADC, respectively, further reinforces the diagnosis.

Benedetto N*et al*. evaluated EI in patients using computed tomography. One hundred subjects (5 to 90 years) with normal CT brain were analyzed retrospectively. There were 54 males and 46 females. The authors found that the mean EI was 0.27 ± 0.04 in males, 0.26 ± 0.03 in females, respectively. No significant statistical difference was observed in the EI between males and females [15].

However, with advancing age, mild increase in Evan's index was seen. In our study, no significant difference (P=0.342) was observed in EI between males and females.

The wide range of EI measurement in elderly suggest that a cut-off value of 0.3 cannot differentiate between normal and enlarged ventricles [16]. Callosal angle (the angle between the lateral ventricles) is considered as a prognostic indicator in NPH.In NPH, it is usually between 40º and 90º.

Aqueduct flow void is a loss (increased hypo-intensity) of signal seen within the aqueduct and neighbouring third and fourth ventricles, particularly on T2 weighted MRI images may or may not predict outcome after shunt surgery. In NPH, there is greater outflow of CSF through

the aqueduct with subsequent increase in signal loss (void sign). Krauss *et al*. investigated the predictive value of CSF flow void on outcome after shunting in a prospective series of patients with idiopathic NPH [17-19].

Hashimoto *et al*.[20] conducted a multicenter prospective study (Study of Idiopathic Normal Pressure Hydrocephalus on Neurological Improvement: SINPHONI) to evaluate the utility of the MRI-based diagnosis in NPH. Hundred patients (60 and 85 years) with one or more of symptoms (gait, cognitive, and urinary problems) and MRI evidence of ventriculomegaly and tight high-convexity and medial subarachnoid spaces received VP shunt using the height/weight-based valve pressure-setting scheme. The authors suggested that tight high-convexity and medial subarachnoid spaces and enlarged Sylvian fissures with ventriculomegaly, defined as disproportionately enlarged subarachnoid-space hydrocephalus (DESH), are worthwhile for the diagnosis of NPH [20].

Periventricular signal changes may be associated with subcortical vascular encephalopathy (also with lacunar infarctions) in NPH. Periventricular and deep white matter hyperintensities were observed in 90% NPH patients in our study [21].

Gait ability need for sleep, urinary incontinence, living conditions, and psychometric test performance were also assessed pre- and postoperatively. The authors suggested that presence of DWMH or subcortical lacunar infarctions in NPH did not predict a poor outcome from shunt surgery and should not be used as exclusion criteria for shunting. No MR imaging findings could predict outcome of shunt surgery in patients with NPH. Clinical improvement after surgery was associated with reduction in the irregular type of PVH located around the frontal horns [22].

In a study by Virhammar*et al*., forty patients (21 men and 19 women) under evaluation for NPH underwent a tap test. Standardized gait analyses were performed before and 2, 4, 6, 8 and 24 h after the TT and repeated twice on every occasion. The test was responsive in 67.5% patients. These results agreed with our study [23].

Correlations often exist between radiological markers in idiopathic NPH. Decrease in ventricle size is usually not detectable postoperatively either by visual assessment or by measuring the Evans index in NPH patients. Virhammar*et al*. investigated the correlation between the callosal angle and ventricular volume after shunt surgery. Magnetic resonance imaging of the brain was performed before and 3 months after shunt surgery in 18 patients with NPH [23].

Conclusion

Computed tomography (CT) and Magnetic resonance imaging (MRI) show ventricular enlargement disproportionate to cerebral atrophy, with associated ballooning of frontal horns, periventricular hyperintensities, thinning and elevation of the corpus callosum, and widening of temporal horns without evidence of hippocampal atrophy in NPH. Although diagnosis can be made based on CT findings alone, MRI is more accurate for disclosing associated pathologies such as grading of PVH and DWMH, transport sulciand presence and location of flow voidsand presence of aqueductal stenosis and for detecting NPH typical signs of prognostic value, besides avoiding exposure to ionizing radiation. Evan's index did not differ significantly between males and females. A significant correlation was observed between ventricular width and Evans index, temporal horn, and size of third ventricle, callosal angle and focalbulge of left ventricle. DESH correlated with callosal angle and focal LV bulge.

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