

# The Utility of Neuroimaging Parameters in Discriminating Patients of Normal-Pressure Hydrocephalus with Positive Cerebrospinal Fluid Tap Test Response from Healthy Controls

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## Abstract

**Objective:** To investigate the frequency of previously defined neuroimaging signs of normal pressure hydrocephalus in our NPH patient group with positive cerebrospinal fluid (CSF) tap test response. **Methods:** Twenty-two patients with probable NPH and 33 healthy control individuals were enrolled in this study. Previously defined 9 parameters including Evan's index, narrow high convexity sulci, dilation of the Sylvian fissures, focally enlarged sulci, enlargement of the temporal horns, callosal angle, periventricular hyperintensities, bulging of the lateral ventricular roof, and disproportionately enlarged subarachnoid space hydrocephalus were evaluated on conventional magnetic resonance imaging. A total radiological score was formed in both groups. The total radiological score, scores, and frequency of each radiological parameters were compared between patient and healthy control groups. **Results:** The mean age of the patient group was  $67.31 \pm 7.27$  (F/M ratio was 7/15), whereas it was  $69.09 \pm 4.89$  (F/M ratio was 11/22) in healthy control group. The result of these analyses revealed that scores of all the radiological parameters, except callosal angle score, were found to be higher in NPH patient group. The parameters with the highest positive predictive values were narrow high convexity sulci, narrowing of callosal angle, and DESH (100%, 100%, and 100%, respectively). On the other hand, enlargement of temporal horns had the highest negative predictive value among all parameters (96%). **Conclusion:** The results of our study support the use of neuroimaging parameters as an alternative method for CSF tap test. We suggest that in the presence of narrow high convexity sulci and/or narrowing of callosal angle, the decision of shunt surgery may be made in patients with suspicion of NPH, without performing CSF tap test. Confirmation of these results, in the future, large-scale studies may certainly provide critical perspectives to be used in the clinical practice.

**Keywords:** CSF tap test, diagnosis, neuroimaging, normal pressure hydrocephalus

## INTRODUCTION

Normal pressure hydrocephalus (NPH) is an increasingly recognized diagnosis, made in patients with ventriculomegaly by excluding secondary hydrocephalic disorders, and supported by the amelioration of gait, urinary, and cognitive difficulties in response to cerebrospinal fluid (CSF) drainage. The clinical triad of gait disturbance, cognitive impairment, and urinary incontinence is critical for suspicion of NPH as well as diagnosis. However, it has been acknowledged that full triad present in under 60% of the patients<sup>[1]</sup> and their individual occurrences are nonspecific as they may be encountered in many other etiologies and also in elderly individuals without any neurological disease. On the other hand, the gold standard diagnosis of this disease is the short-term response to CSF drainage.<sup>[2]</sup> However, it is an invasive method constituting an increased workload, occasionally technical difficulties as well as ethical problems. Besides, lumbar puncture has some complications, including infections, hematomas in puncture site, subarachnoid hemorrhage, and radiculopathy. Up to the present, to increase diagnostic accuracy and thus select appropriate patients for shunt surgery, several radiologic markers have emerged including the Evan's index, narrowing of the callosal angle, enlargement of the width of temporal horns, disproportionately enlarged subarachnoid

space hydrocephalus (DESH), and focally dilated sulci.<sup>[3-8]</sup> However, the results of these studies are controversial as the prognostic value of these neuroimaging signs and their utility in the selection of shunt candidates still remain to be elucidated. Shunt surgery is the optimal treatment method of NPH and it is indicated for patients who respond to CSF drainage or who have CSF hydrodynamic variables consistent with NPH.<sup>[9-11]</sup> However, there are many reports emphasizing the high rates of perioperative and long-term morbidity and mortality related to CSF shunting procedures. Such that, the pooled mean response rate to shunting for iNPH was found to be 59% in a crucial meta-analysis,<sup>[12]</sup> and in another study, sustained improvement after surgery was found to be at a rate

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of 39% documented 5 years after surgery.<sup>[13]</sup> Remarkably, the basic cause of shunt unresponsiveness is surgery-related complications including death, infection, seizures, shunt malfunction, subdural hemorrhage, or effusion which were reported to occur at mean rate of 38%.<sup>[12]</sup> Combining that short-term response to CSF tap test is the gold standard of NPH and it is the critical criteria in determination of the decision of shunt surgery, we have aimed to investigate the presence of previously identified neuroimaging parameters of NPH in our NPH patient groups who had given positive response to CSF tap test, thus eliminating the confounding effect of surgery-related complications. Via this method, we have planned to investigate the neuroimaging profile of NPH pathophysiology more precisely, which might not be the case in the previous related neuroimaging studies focusing on the prognosis after shunt surgery as the primary outcome.<sup>[10,14-16]</sup> We have aimed to interrogate the clinical significance of these neuroimaging parameters and their potential utility for indirect determination of the decision of shunt surgery. Ergo, we hope to provide substantial contributions to NPH pathophysiology from a distinct perspective.

## MATERIALS AND METHODS

The sample consisted of 22 patients with probable NPH who were diagnosed in Yozgat City Hospital Neurology Clinic between January 2017 and August 2019. Patients were diagnosed based on the guidelines approved by the Japanese Society of Normal Pressure Hydrocephalus<sup>[7]</sup> and included age >60 years, 1–3 symptoms related to normal pressure hydrocephalus, and ventricular enlargement. All patients also fulfilled the criteria for probable idiopathic NPH in the INPH guidelines.<sup>[9]</sup> In all patients with clinical and radiological suspicion of NPH, a CSF tap test was suggested. Patients who were not evaluated with CSF tap test were excluded from the study. Besides, patients with negative CSF tap test results were also excluded. All NPH patients with positive CSF tap test responses were included in the study. In all patients, a high-volume (>30 mL) CSF tap test was performed while patients were lying on their sides, with legs pulled up and chin tucked in. The assessment of improvement after CSF tap test was made 4–5 h after LP. Improvement in gait was evaluated using the 10-m walk-in time test. No standardized tests have been performed to evaluate improvement in cognitive status and symptoms of urinary incontinence. However, cognitive improvement and recovery in urinary symptoms have been evaluated according to individual interviews and examinations. The short-term improvement after CSF tap test has also been discussed with the patient and the patients' relatives. Patients with slight improvement (or unclear) were not included in the study. The healthy control group consisted of 33 individuals who had admitted to neurology polyclinic with symptoms like peripheral vertigo or non-specific headache and were investigated with conventional magnetic resonance imaging (MRI) including coronal and axial FLAIR, axial and sagittal T1-weighted, axial T2-weighted,

DWI ( $b = 1000 \text{ sn/mm}^2$ ), and ADC images. Patients with a diagnosis of any other neurological disease affecting central nervous system were also excluded from control group. Two of the individuals in the control group were diagnosed with benign paroxysmal positional vertigo, whereas ten of them were diagnosed with tension-type headache.

The presence of eight radiological signs which had been investigated by cranial computed tomography in a population-based study of iNPH by Kockum *et al.* were evaluated in all study group.<sup>[17]</sup> Besides, DESH, which has been as a neuroimaging hallmark of NPH, was also investigated.<sup>[15,16]</sup> Radiological signs except periventricular hyperintensity were evaluated on T2-weighted images. Periventricular hyperintensities were evaluated using FLAIR images.

The following radiological parameters were evaluated in both patient and healthy control groups by a radiologist who is particularly interested in neuroimaging (GG).

- Evan's index, the ratio between the maximum width of the frontal horns of the lateral ventricles and the maximum inner diameter of the cranium in the same transverse slice.<sup>[3]</sup>
- Narrow parietal high-convexity and medial parafalcine sulci, assessed in the transverse plane in the most superior slices and in the coronal plane.<sup>[4]</sup>
- Dilation of the Sylvian fissures, in the coronal plane, compared with surrounding sulci, in a simplified two-grade variant of the method of Kitagaki *et al.*<sup>[5]</sup> used by Virhammar *et al.*<sup>[8]</sup>
- Focally enlarged sulci, usually found in coronal or transverse planes, were defined by comparing them with surrounding sulci.<sup>[6]</sup>
- Temporal horns, measured in the transverse plane<sup>[8]</sup> and reported as mean width of the right and left side.
- Callosal angle, measured between the lateral ventricles in the coronal plane, through the posterior commissure perpendicular to the anterior–posterior commissure plane.<sup>[18]</sup>
- Periventricular hyperintensities along the lateral ventricles were graded as not present, present around frontal horns (as a cap), or diffusely extending around the lateral ventricles.<sup>[19]</sup>
- Bulging of the lateral ventricular roof, assessed in the sagittal plane at the posterior half of the ventricular roof.<sup>[8]</sup>
- DESH, the combination of high-convexity tightness, Sylvian fissure dilation, and ventriculomegaly which has been increasingly recognized as a neuroimaging hallmark of iNPH.<sup>[15]</sup>

These parameters were scored according to the iNPH Radscale, previously defined by Kockum *et al.*<sup>[17]</sup> However, we have also evaluated the presence of “bulging of the lateral ventricular roof” in analyses and compromised the total score including this parameter. The presence of DESH was evaluated; however, based on that it is a finding of the combination of all three parameters evaluated in the iNPH Radscale, no additional score has been given for this finding. Taken together, the total

of the first eight parameters above was used to compromise the total radiological score.

### Statistical analysis

Radiological and clinical findings were presented with descriptive statistics (SPSS Statistics for Windows-version 20, IBM Corp., Armonk, NY, USA). Groups were compared using Mann–Whitney U-test and Student's *t*-test.  $P < 0.05$  was regarded as significant. For all nine radiological parameters, values of sensitivity, specificity, positive predictive values, and negative predictive values were evaluated.

## RESULTS

Overall, 22 patients of NPH with positive CSF tap test responses and 33 healthy control individuals were included in this study. The mean age of the patient group was  $67.31 \pm 7.27$  years (F/M ratio was 7/15), whereas it was  $69.09 \pm 4.89$  years (F/M ratio was 11/22) in healthy control group [Table 1]. Mean values  $\pm$  SD of MR findings in the patient group were the following: Evan's index,  $0.34 \pm 0.079$  and callosal angle,  $112.95 \pm 23.04$ , whereas they were  $0.24 \pm 0.03$  and  $132.33 \pm 7.92$  in control group, respectively ( $P = 0.000$ ,  $P = 0.001$ ). The presence of all of the radiological signs was scored as mentioned in the method section and comparisons between patient group and healthy control groups were made for all the radiological parameters. The result of these analyses revealed that scores of all the radiological parameters, except callosal angle score, were found to be higher in NPH

patient group. The total radiological score was  $7.63 \pm 1.89$  in the patient group, whereas it was  $1.93 \pm 1.41$  in control group ( $P = 0,000$ ) [Table 2]. All patients had got at least 4 points from this structured radiological scale and at least three of these nine parameters were present in all of the patients. However, three of these nine parameters were also present in 7 individuals of the healthy control group.

The parameter with the highest sensitivity was enlargement of temporal horn (95%), whereas the highest specific findings were narrowing of the callosal angle (less than  $90^\circ$ , 100%), narrow high convexity sulci (100%), and DESH (100%). Remarkably, narrow high convexity sulci, narrowing of callosal angle, and DESH were the parameters with the highest positive predictive values (100%, 100%, and 100%, respectively). On the other hand, the parameter with the highest negative predictive value was enlargement of temporal horns (96%) [Table 3]. Samples of the neuroimaging parameters in the patient group and healthy control group are demonstrated in Figure 1 and Figure 2.

## DISCUSSION

Owing to its unique feature of reversibility by shunt surgery, NPH has attracted interest from many researchers up to date since it was first described by Adams *et al.* in 1965.<sup>[20]</sup> However, despite efforts in this field, etiology and pathomechanisms remain to be elucidated as well as there are many pitfalls associated with a diagnosis of NPH whose

**Table 1: Frequency of the presence of radiological signs in the patient group and healthy controls**

Parameters	Presence	Total individuals (n=55)	
		Patients n=22	Healthy Controls n=33
Periventricular hyperintensities	Not present	2 (9%)	13 (39%)
	Frontal horn caps	5 (23%)	15 (45%)
	Confluent areas	15 (68%)	5 (15%)
Evan's index	$\leq 0.25$	1 (5%)	16 (48%)
	0.25-0.3	3 (14%)	15 (45%)
	$>0.3$	18 (82%)	2 (6%)
Callosal angle	$>90$	19 (86%)	33 (100%)
	90-60	2 (9%)	0
	$\leq 60$	1 (5%)	0
Bulging of the lateral ventricular roof	Not present	11 (50%)	30 (91%)
	Present	11 (50%)	3 (9%)
Dilatated sylvian fissures	Normal	8 (36%)	28 (85%)
	Enlarged	14 (64%)	5 (15%)
Focally dilatated sulci	Not present	13 (59%)	32 (97%)
	Present	9 (41%)	1 (3%)
Temporal horns	$<4$ mm	1 (5%)	26 (79%)
	4-6 mm	6 (27%)	3 (9%)
	$\geq 6$ mm	15 (68%)	4 (12%)
Narrow high-convexity sulci	Normal	8 (15%)	33 (100%)
	Parafalcine	8 (15%)	0
	Vertex	6 (27%)	0
Disproportionately enlarged subarachnoid space hydrocephalus	Not present	13 (59%)	0 (0%)
	Present	9 (41%)	33 (100%)

**Table 2: Comparison of age and radiological signs between patients and healthy control groups (T test, Mann-Whitney U test, Cross tabs)**

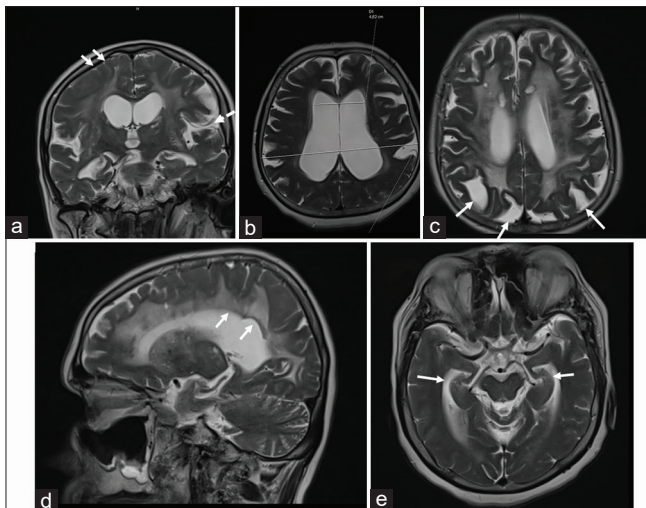
Parameters	Groups	Mean	Std. error mean	P
Age	Patients (n=22)	67.31±7.27	1.55057	0.324
	Healthy controls (n=33)	69.09±4.89	0.85210	
Evan's index	Patients (n=22)	0.34±0.079	0.01696	0.000
	Healthy controls (n=33)	0.24±0.03	0.00668	
Evan's index classification	Patients (n=22)	1.77±0.52	0.11266	0.000
	Healthy controls (n=33)	0.57±0.61	0.10687	
Narrow sulci	Patients (n=22)	0.90±0.81	0.17294	0.000
	Healthy controls (n=33)	0.00±0.00	0.00000	
Dilatated Sylvian fissures	Patients (n=22)	0.63±0.49	0.10497	0.000
	Healthy controls (n=33)	0.15±0.36	0.06338	
Focal dilatated sulci	Patients (n=22)	0.40±0.50	0.10729	0.002
	Healthy controls (n=33)	0.03±0.17	0.03030	
Enlargement of temporal horn	Patients (n=22)	1.63±0.58	0.12389	0.000
	Healthy controls (n=33)	0.33±0.69	0.12050	
Callosal angle classification scale point	Patients (n=22)	0.18±0.50	0.10683	0.104
	Healthy controls (n=33)	0.00±0.00	0.00000	
Callosal angle	Patients (n=22)	112.95±23.04	4.91243	0.001
	Healthy controls (n=33)	132.33±7.92	1.37941	
Periventricular hyperintensities	Patients (n=22)	1.59±0.66	0.14202	0.000
	Healthy controls (n=33)	0.75±0.70	0.12332	
Bulging of the lateral ventricular roof	Patients (n=22)	0.50±0.51	0.10911	0.002
	Healthy controls (n=33)	0.09±0.29	0.05082	
Total radiological score	Patients (n=22)	7.63±1.89	0.40316	0.000
	Healthy controls (n=33)	1.93±1.41	0.24595	

**Table 3: Sensitivity, specificity, positive, and negative predictive values of the radiological signs one by one**

Parameters	Presence	Total individuals (n=55)					
		Patients n=22	Healthy Controls n=33	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Periventricular hyperintensities	Present	20/22	20/33	91%	39%	50%	87%
Evan's index greater than 0.3	Present	18/22	2/33	82%	94%	90%	89%
Callosal angle less than 90°	Present	3/22	0/33	14%	100%	100%	63%
Bulging of the lateral ventricular roof	Present	11/22	3/33	50%	91%	79%	73%
Dilatated Sylvian fissures	Present	14/22	5/33	63%	85%	74%	78%
Focally dilatated sulci	Present	9/22	1/33	41%	97%	90%	63%
Temporal horns diameter more than 4 mm	Present	21/22	7/33	95%	79%	75%	96%
Disproportionately enlarged subarachnoid space hydrocephalus	Present	9/22	0/33	41%	100%	100%	72%
High-convexity narrow sulci	Present	14/22	0	42%	100%	100%	80%

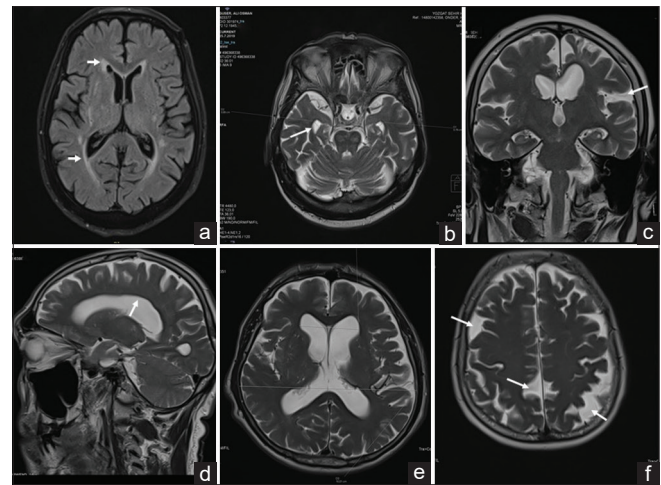
gold standard is the short-term response to CSF drainage.<sup>[2,7]</sup> On the other hand, there are many handicaps of performing a CSF tap test owing to its invasive nature and sometimes it cannot be performed by the reason of that some patients may not tolerate or accept the procedure. For all these reasons, radiologic data have been investigated to avoid the need to perform invasive CSF tap testing. The results of our study are important due to that studies investigating the radiological features of NPH patients with particularly positive CSF tap test responses are very rare in the literature.<sup>[18,21]</sup> In one of these studies, Ishii *et al.* also compared the neuroimaging

findings of patients with probable NPH (all responsive to CSF tap test) with healthy control group.<sup>[18]</sup> In conclusion, they found that Evan's index was significantly larger, whereas callosal angle was significantly smaller in NPH patients group according to healthy control group ( $0.338 \pm 0.025$ ,  $0.259 \pm 0.025$ ;  $66 \pm 14$ ,  $112 \pm 11$ , respectively). Besides, mean visual rating score of periventricular hyperintensity was higher in NPH patients group according to healthy control group ( $P < 0.005$ ). However, many other crucial neuroimaging signs of NPH such as high-convexity narrow sulci, focally dilatated sulci, DESH, and bulging of the lateral ventricular



**Figure 1:** MRI images showing samples of neuroimaging parameters in NPH patient group. (a) Narrow high-convexity sulci (arrows), dilated Sylvian fissures (jagged arrows). (b) Evan's index greater than 0.3. (c) Focally dilated sulci. (d) Bulging of the lateral ventricular roof. (e) Enlargement of temporal horns

roof were not investigated in this study,<sup>[18]</sup> constituting a crucial limitation. In the other study by Otero-Rodriguez *et al.*,<sup>[21]</sup> 107 patients with possible NPH were divided into two groups as group 1, comprising patients with resistance to CSF outflow <12 mm Hg/mL/min, and group 2, comprising patients with resistance to CSF outflow >12 mm Hg/mL/min. The authors concluded that the measurements of callosal angle and width of temporal horns were significantly discriminative between groups (0.001 and <0.001, respectively) and DESH was significantly more frequent in group 2 (<0.001). Remarkably, after matching the radiologic variables, the authors found that positive predictive values were >80% for all pairwise combinations (DESH ± callosal angle, DESH ± width of temporal horns, width of temporal horns ± callosal angle, etc.). Furthermore, based on their high positive predictive values of matched radiological variables, they suggested that the lumbar infusion test could be avoided in the diagnosis of idiopathic normal pressure hydrocephalus.<sup>[21]</sup> These study results showing high sensitivities and positive predictive values of the neuroimaging parameters were all compatible with our findings. In our study, we have found extremely high rates of existence of these previously defined neuroimaging parameters in our NPH patient group with positive CSF tap test response. Remarkably, narrow high convexity sulci and narrowing of callosal angle were the findings with highest positive predictive values (both 100%). These two findings were not present in any of the individuals in healthy control group. The positive predictive values of other neuroimaging parameters were also considerably high (Evan's index greater than 0.3: 90%, focally dilated sulci: 90%, bulging of the lateral ventricular roof: 90%, all are demonstrated in Table 3). On the other hand, enlargement of temporal horn (≥4 mm) was the parameter with highest sensitivity, which was found in 95% of patients. This (enlargement of temporal horn)



**Figure 2:** MRI images showing samples of neuroimaging parameters in healthy control group. (a) Periventricular hyperintensities. (b) Enlargement of temporal horns. (c) Dilated Sylvian fissures. (d) Bulging of the lateral ventricular roof. (e) Evan's index greater than 0.3. (f) Focally dilated sulci (arrows)

had also the highest negative predictive value among all parameters (96%). Negative predictive values of the other parameters were also high [Table 3] in comparison to the results of the previous study by Otero-Rodriguez *et al.*<sup>[21]</sup> However, this may be due to that we have compromised control group from healthy individuals rather than patients. Considering that CSF tap test (or other short-term diversion methods) has a considerable high predictability of shunt effectiveness (>90% according to American guidelines<sup>[10]</sup>) and it is the gold standard for diagnosis; the results of our study may be adaptable while making interpretations regarding the radiological features of treatable NPH patients as well as the potential utility of conventional MRI in clinical practice. Besides, considering that many other surgery-related complications (at high rates<sup>[12]</sup>) and other medical conditions might interact with the clinical status of the patients in the follow-up after shunt surgery, we think that via a method of including patients with positive short-term response to CSF diversion (instead of shunt responsive patients), the confounding effect of surgery-related complications and other medical comorbidities have been eliminated allowing a more clear investigation of the neuroimaging profile of NPH pathophysiology.

Taken together, our findings suggest that the existence of narrow high convexity sulci and narrowing of callosal angle may be a critical supportive paraclinical markers to be kept in mind while making decision of shunt surgery. On the other hand, lack of enlargement of the temporal horns may give rise to the thought that the diagnosis of NPH and its possibility of improvement by shunt surgery need to be reinterrogated. On the other hand, although its specificity and positive predictive values were extremely high, the sensitivity of the parameter of "callosal angle less than less than 90°" was found to be strictly low (14%) in comparison to the previous reports.<sup>[21]</sup>

In the literature, data regarding the utility of neuroimaging signs in the clinical practice of NPH mainly derive from studies focusing on their predictive values for shunt responsiveness.<sup>[8,14-16]</sup> In the crucial study by Hashimoto *et al.*, narrow high-convexity sulci and dilatated Sylvian fissures were found to be worthwhile findings in the diagnosis of NPH and prediction of shunt responsiveness.<sup>[15]</sup> Based on the results of high positive predictive values of neuroimaging findings in their study, they suggested that MRI-based diagnosis is useful for the diagnosis of iNPH.<sup>[15]</sup> These results have also been confirmed by the reports of Sasaki *et al.*, Narita *et al.*, and Shinoda *et al.* in which they found high-convexity tightness and Sylvian fissures dilatation as useful markers for the prediction of shunt responsiveness and prognosis for NPH.<sup>[4,14,16]</sup> We have also found high positive predictive values for these two signs (high-convexity narrow sulci: 100%, dilatated Sylvian fissures: 74%). In another previous report by Virhammar *et al.*,<sup>[8]</sup> a small callosal angle, wide temporal horns, and occurrence of DESH (the combination of high-convexity tightness, Sylvian fissure dilation, and ventriculomegaly) were found to be common in patients with idiopathic normal pressure hydrocephalus and were significant predictors of a positive shunt outcome. In the crucial report by Kockum *et al.* which was a prospective, population-based study, the authors found a significant correlation ( $r = 0.55$ ,  $P < 0.001$ ) between the total iNPH Radscale score (also used in our study) and clinical symptoms drawing attention to the importance of radiological evaluation in patients with NPH.<sup>[17]</sup> Besides, they also found that the inter-rater agreement for the included radiological parameters was high supporting the practical utility of these parameters in the clinical backgrounds. Based on this data, a crucial point may be that, although there was no prominent clinic in any of the individuals in healthy control patients with positive neuroimaging signs, we cannot exclude an underlying NPH pathophysiology which might be asymptomatic and unrecognized as well in the polyclinic evaluations. On the other hand, there is also a condition without a clinic, but including neuroimaging signs of NPH which was proposed by Iseki *et al.* in conclusion of their general population-based unique study.<sup>[22]</sup> However, during a follow-up period of 4–8 years, two of their 8 asymptomatic subjects had developed NPH clinic. Based on their results, they hypothesized that asymptomatic ventriculomegaly with the NPH features on MRI may represent a preclinical stage of iNPH. Future prospective studies including long-term follow-up of these asymptomatic patients with neuroimaging clues of NPH may provide substantial perspectives in this regard. However, the results of this study in light of the previous study results should be evaluated very meticulously. We know that radiological evaluation is a critical stage for diagnosis of patients with NPH. Such that, the clinical triad of NPH may be encountered in many other neurological diseases (mainly neurodegenerative subgroup) as well as elderly individuals which may be easily excluded based on nonexistence of hydrocephalus on MRI. On the other hand, in some circumstances, ventriculomegaly on CT or MRI is sometimes misinterpreted as brain atrophy, and

NPH may be misdiagnosed as AD or other neurodegenerative diseases.<sup>[7]</sup> Therefore, we cannot support consideration of that neuroimaging may replace the value of clinical evaluation overall. Rather, these results may support the predictor value of these neuroimaging parameters in the determination of tap test response, thus avoiding the need for this invasive test. On the other hand, our control group consisted of healthy individuals, instead of negative CSF tap test response patients, which avoids to suggest certain conclusions regarding the neuroimaging profile of solely positive CSF tap test response.

We have also confirmed the importance of the neuroimaging signs in diagnosis of NPH which were also investigated by Kockum *et al.*<sup>[17]</sup> However, our study groups consisted of probable NPH patients (proven with LP investigation) and all individuals were investigated with conventional MRI which were the basic differences as well as superiorities of our study. On the other hand, there was a high rate of patients with false-positive screening for the two signs of periventricular hyperintensities and enlargement of temporal horns (20/33, 7/33, respectively; Table 3) making these parameters nonspecific for the diagnostic purposes. Besides, narrowing of callosal angle and focally dilatated sulci were the two findings which were present in considerable low rates in patient group (3/22 and 9/22, respectively) making these signs nonsensitive markers for diagnosis. However, their diagnostic specificities were extremely high [Table 3].

The main limitation of our study may be that we have not included NPH patients without CSF tap test response which avoids further deliberations regarding the neuroimaging features of responsiveness of CSF diversion. Future reports of larger number of cases including also NPH patients with negative responses to CSF tap test may give substantial contributions in this regard. Besides, another limitation may be that we have not conducted a method for discriminating patients as primary or secondary NPH, which may lead a heterogeneity in the study group. Furthermore, no effort to identify a possible accompanying neurodegenerative pathology such as Lewy body dementia, PSP, or AD (which have been frequently reported to be comorbid to NPH) has been given. Nonetheless, we think that constituting a unique patient group with positive short-term responses to CSF tap test may provide certainly substantial contributions to our understanding the NPH pathophysiology from a distinct perspective.

## CONCLUSION

In conclusion, our study results support the use of neuroimaging parameters as an alternative method for CSF tap test. We suggest that in the presence of narrow high convexity sulci and/or narrowing of callosal angle, the decision of shunt surgery may be made in patients with suspicion of NPH, without performing CSF tap test. However, in the absence of enlargement of temporal horn, the diagnosis should be extra careful during the differential diagnostic procedures and reinterrogate the diagnosis of NPH. Confirmation of these

results, in the future, large-scale studies may certainly provide critical perspectives to be used in the clinical practice.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

### REFERENCES

- Marmarou A, Young HF, Aygok GA, Sawauchi S, Tsuji O, Yamamoto T, *et al.* Diagnosis and management of idiopathic normal-pressure hydrocephalus: A prospective study in 151 patients. *J Neurosurg* 2005;102:987-97.
- Espay AJ, Da Prat GA, Dwivedi AK, Rodriguez-Porcel F, Vaughan JE, Rosso M, *et al.* Deconstructing normal pressure hydrocephalus: Ventriculomegaly as early sign of neurodegeneration. *Ann Neurol* 2017;82:503-13.
- WAJ. E. An encephalographic ratio for estimating ventricular enlargement and cerebral atrophy. *Arch Neurol Psychiatry* 1942;47:931-7.
- Sasaki M, Honda S, Yuasa T, Iwamura A, Shibata E, Ohba H. Narrow CSF space at high convexity and high midline areas in idiopathic normal pressure hydrocephalus detected by axial and coronal MRI. *Neuroradiology* 2008;50:117-22.
- Kitagaki H, Mori E, Ishii K, Yamaji S, Hirono N, Imamura T. CSF spaces in idiopathic normal pressure hydrocephalus: Morphology and volumetry. *AJNR Am J Neuroradiol* 1998;19:1277-84.
- Holodny AI, George AE, de Leon MJ, Golomb J, Kalnin AJ, Cooper PR. Focal dilation and paradoxical collapse of cortical fissures and sulci in patients with normal-pressure hydrocephalus. *J Neurosurg* 1998;89:742-7.
- Mori E, Ishikawa M, Kato T, Kazui H, Miyake H, Miyajima M, *et al.* Guidelines for management of idiopathic normal pressure hydrocephalus: Second edition. *Neurol Med Chir (Tokyo)* 2012;52:775-809.
- Virhammar J, Laurell K, Cesarini KG, Larsson EM. Preoperative prognostic value of MRI findings in 108 patients with idiopathic normal pressure hydrocephalus. *AJNR Am J Neuroradiol* 2014;35:2311-8.
- Relkin N, Marmarou A, Klinge P, Bergsneider M, Black PM. Diagnosing idiopathic normal-pressure hydrocephalus. *Neurosurgery* 2005;57 (3 Suppl):S4-16.
- Marmarou A, Bergsneider M, Klinge P, Relkin N, Black PM. The value of supplemental prognostic tests for the preoperative assessment of idiopathic normal-pressure hydrocephalus. *Neurosurgery* 2005;57 (3 Suppl):S17-28.
- Williams MA, Relkin NR. Diagnosis and management of idiopathic normal-pressure hydrocephalus. *Neurol Clin Pract* 2013;3:375-85.
- Hebb AO, Cusimano MD. Idiopathic normal pressure hydrocephalus: A systematic review of diagnosis and outcome. *Neurosurgery* 2001;49:1166-84.
- Kahlon B, Sjunnesson J, Rehncrona S. Long-term outcome in patients with suspected normal pressure hydrocephalus. *Neurosurgery* 2007;60:327-32.
- Narita W, Nishio Y, Baba T, Iizuka O, Ishihara T, Matsuda M, *et al.* High-Convexity Tightness Predicts the Shunt Response in Idiopathic Normal Pressure Hydrocephalus. *AJNR Am J Neuroradiol* 2016;37:1831-7.
- Hashimoto M, Ishikawa M, Mori E, Kuwana N; Study of Ioni. Diagnosis of idiopathic normal pressure hydrocephalus is supported by MRI-based scheme: A prospective cohort study. *Cerebrospinal Fluid Res* 2010;7:18.
- Shinoda N, Hirai O, Hori S, Mikami K, Bando T, Shimo D, *et al.* Utility of MRI-based disproportionately enlarged subarachnoid space hydrocephalus scoring for predicting prognosis after surgery for idiopathic normal pressure hydrocephalus: Clinical research. *J Neurosurg* 2017;127:1436-42.
- Kockum K, Lilja-Lund O, Larsson EM, Rosell M, Soderstrom L, Virhammar J, *et al.* The idiopathic normal-pressure hydrocephalus Radscale: A radiological scale for structured evaluation. *Eur J Neurol* 2018;25:569-76.
- Ishii K, Kanda T, Harada A, Miyamoto N, Kawaguchi T, Shimada K, *et al.* Clinical impact of the callosal angle in the diagnosis of idiopathic normal pressure hydrocephalus. *Eur Radiol* 2008;18:2678-83.
- Fazekas F, Chawluk JB, Alavi A, Hurtig HI, Zimmerman RA. MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. *AJR Am J Roentgenol* 1987;149:351-6.
- 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.
- Otero-Rodriguez A, Sousa-Casasnovas P, Cruz-Terron H, Arandia-Guzman DA, Garcia-Martin A, Pascual-Argente D, *et al.* Utility of radiologic variables to predict the result of lumbar infusion test in the diagnosis of idiopathic normal pressure hydrocephalus. *World Neurosurg* 2019;127:e957-64.
- Iseki C, Kawanami T, Nagasawa H, Wada M, Koyama S, Kikuchi K, *et al.* Asymptomatic ventriculomegaly with features of idiopathic normal pressure hydrocephalus on MRI (AVIM) in the elderly: A prospective study in a Japanese population. *J Neurol Sci* 2009;277:54-7.