Utility of MRI-based disproportionately enlarged subarachnoid space hydrocephalus scoring for predicting prognosis after surgery for idiopathic normal pressure hydrocephalus: clinical research

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OBJECTIVE The presence of disproportionately enlarged subarachnoid space hydrocephalus (DESH) on brain imaging is a recognized finding of idiopathic normal pressure hydrocephalus (iNPH), but the features of DESH can vary across patients. The aim of this study was to evaluate the utility of MRI-based DESH scoring for predicting prognosis after surgery.

METHODS In this single-center, retrospective cohort study, the DESH score was determined by consensus between a group of neurosurgeons, neurologists, and a neuroradiologist based on the preoperative MRI findings of the patients with suspected INPH. The DESH score was composed of the following 5 items, each scored from 0 to 2 (maximum score 10 points): ventriculomegaly, dilated sylvian fissures, tight high convexity, acute callosal angle, and focal sulcal dilation. The association between the DESH score and improvement of the scores on the modified Rankin Scale (mRS), iNPH Grading Scale (iNPHGS), Mini–Mental State Examination (MMSE), Trail Making Test-A (TMT-A), and Timed 3-Meter Up and Go Test (TUG-t) was examined. The primary end point was improvement in the mRS score at 1 year after surgery, and the secondary outcome measures were the iNPHGS, MMSE, TMT-A, and TUG-t scores at 1 year after surgery. Improvement was determined as improvement of 1 or more levels on mRS, ≥ 1 point on iNPHGS, ≥ 3 points on MMSE, a decrease of > 30% on TMT-A, and a decrease of > 10% on TUG-t.

RESULTS The mean DESH score for the 50 patients (mean age 77.6 ± 5.9 years) reviewed in this study was 5.58 ± 2.01. The mean rate of change in the mRS score was −0.50 ± 0.93, indicating an inverse correlation between the DESH score and rate of change in the mRS score (r = −0.749). Patients who showed no improvement in mRS score tended to have a low DESH score as well as low preoperative MMSE and TMT-A scores. There were no differences in the areas of deep white matter hyperintensity and periventricular hyperintensity on the images between patients with and without an improved mRS score (15.6% vs 16.7%, respectively; p = 1.000). The DESH score did differ significantly between patients with and without improved scores on the iNPHGS (6.39 ± 1.76 vs 4.26 ± 1.69, respectively; p = 0.001), MMSE (6.32 ± 1.97 seconds vs 5.13 ± 1.93 seconds; p = 0.042), and TUG-t (6.48 ± 1.81 seconds vs 4.33 ± 1.59 seconds; p < 0.001).

CONCLUSIONS MRI-based DESH scoring is useful for the prediction of neurological improvement and prognosis after surgery for iNPH.

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KEY WORDS idiopathic normal pressure hydrocephalus, disproportionately enlarged subarachnoid space hydrocephalus, SINPHONI trial, ventriculoperitoneal shunt, DESH score
Utility of the MRI-based DESH score for postoperative iNPH prognosis

In the Study of Idiopathic Normal Pressure Hydrocephalus on Neurological Improvement (SINPHONI) trial, the diagnosis of idiopathic normal pressure hydrocephalus is supported by an MRI-based scheme, and DESH was shown on MRI to have a high positive predictive value in identifying shunt-responsive iNPH patients. Most cases of iNPH have characteristic imaging findings of DESH, but a subgroup of patients has much less typical DESH findings, and therefore the prognostic difference according to the nature of the imaging findings is unclear.

Hashimoto et al. demonstrated that the MRI features of DESH—namely, ventriculomegaly, high-convexity and medial subarachnoid spaces, and enlarged sylvian fissures—are useful for the diagnosis of iNPH, but they did not describe other features, particularly the callosal angle and focal sulcal dilation. Furthermore, they did not explain the prognostic difference separated by the degree of the MRI features of DESH (e.g., more typical DESH findings, better outcome). In this study, we quantitatively evaluated the appearance of DESH on MRI prior to surgery in elderly patients with iNPH and investigated if the resulting DESH score was useful for predicting neurological improvement and prognosis. The principal utility of this study is the potential to develop a noninvasive and easy method for predicting response to CSF diversion in patients with iNPH.

Methods

Study Design

Patients with suspected iNPH—defined as the presence of 1 or more symptoms of the classic triad of gait disturbance, cognitive impairment, and urinary disturbance—underwent MRI. The resulting images were reviewed by a group of neurosurgeons, neurologists, and a neuroradiologist, who assigned a DESH score that was reached by consensus. When their opinions were divided, they discussed it again and adopted the opinion of the majority. By separating the raters and the operating surgeon, there were no factors that influenced the data.

DESH Score

The DESH score was composed of the following 5 items, each scored from 0 to 2 (maximum score 10): ventriculomegaly, dilated sylvian fissures, tight high convexity, acute callosal angle, and focal sulcal dilation (Table 1).

**Ventriculomegaly**

The Evans’ index was measured on transverse images as the ratio between the maximum diameter of the frontal horns of the lateral ventricles and the maximum inner diameter of the skull in the same section. Ventriculomegaly was graded as follows: 0, normal (Evans’ index < 0.3); 1, slight dilation (Evans’ index 0.3–0.35); or 2, dilation (Evans’ index > 0.35).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal (Evans’ index &lt;0.3)</td>
</tr>
<tr>
<td>1</td>
<td>Slight dilation (Evans’ index ≥0.3 &amp; ≤0.35)</td>
</tr>
<tr>
<td>2</td>
<td>Dilation (Evans’ index &gt;0.35)</td>
</tr>
</tbody>
</table>

**Dilated sylvian fissures**

0 Not present
1 Slight dilation or unilateral
2 Bilateral dilatation

**Tight high convexity**

0 Normal or wider than normal
1 Slight compression
2 Definitive compression

**Acute callosal angle**

0 Obtuse angle (>100°)
1 Not acute, but not obtuse angle (≥90° & ≤100°)
2 Acute angle (<90°)

**Focal sulcal dilation**

0 Not present
1 Some present
2 Many present

**Table 1. Summarized DESH scales**

Dilated Sylvian Fissures

The coronal images used for the sylvian fissure ordinal were reconstructed at the level of the central part of the brainstem and angulated along the brainstem. Dilation was graded as follows: 0, normal or narrow; 1, slight dilation or unilateral; or 2, bilateral dilation.

**Dilated sylvian fissures**

0 Not present
1 Slight dilation or unilateral
2 Bilateral dilatation

**Tight High Convexity**

Tight high convexity was evaluated on coronal and transverse images and graded as follows: 0, normal or wider than normal; 1, slight dilation or unilateral; or 2, bilateral dilation.

**Acute Callosal Angle**

The callosal angle measured on a coronal MR image is the angle between the lateral ventricles through the posterior commissure and perpendicular to the anterior-posterior commissure plane. The angle was graded as 0, obtuse (>100°); 1, not acute or obtuse (90°–100°); or 2, acute (<90°).

**Focal Sulcal Dilation**

The accumulation of CSF in focally enlarged sulci, which has previously been referred to as “transport sulci,” was graded as follows: 0, no sulci; 1, some sulci present; or 2, many sulci present.

Regardless of a high or low DESH score, patients were
included in the study if they satisfied the inclusion criteria stated below.

Participants and Protocol

The study was approved by the institutional review board and adhered to the principles set forth in the Declaration of Helsinki. It was performed as a retrospective, single-center cohort study to examine the 1-year outcome in iNPH patients who received a ventriculoperitoneal shunt with the Codman-Hakim programmable valve (CSF shunt valve, Codman, a Johnson & Johnson Co.) at our institution between April 2007 and March 2016. The initial pressure for the shunt system was set according to the patient’s height and body mass index based on the estimated hydrostatic pressure and intraabdominal pressure.13,14

The criteria for patient selection were determined in reference to the SINPHONI trial.6 The inclusion criteria were as follows: 1) age 60 years or older; 2) presence of 1 or more symptoms of the triad (gait disturbance, cognitive impairment, and urinary symptoms), which were measurable on iNPHGS13; 3) MRI features of iNPH, with ventriculomegaly indicated by an Evans’ index score of ≥ 3.0 on MRI;12 4) the absence of known disorders causing ventriculomegaly; 5) normal CSF content (protein ≤ 50 mg/dl and cell count ≤ 3 cells/μl) and pressure (≤ 20 cm H2O); and 6) positive response on the CSF tap test.24 The exclusion criteria were: 1) the presence of a musculoskeletal, cardiopulmonary, renal, hepatic, or mental disorder that would make it difficult to evaluate changes in symptoms; 2) obstacles to 1-year follow-up; and 3) bleeding diathesis or taking anticoagulant medication. In addition, we performed SPECT in patients with a Mini–Mental State Examination (MMSE) score of less than 20 and excluded other differential diseases, including Alzheimer’s disease.

Outcome Measures

According to both the iNPH guidelines9 and “Guideline for management of idiopathic normal pressure hydrocephalus: second edition,”16 improvement was determined as improvement of 1 or more levels on mRS, ≥ 1 points on the iNPH grading scale, ≥ 3 points on MMSE, a decrease of greater than 30% on TMT-A, and a decrease of greater than 10% on TUG-t.

The primary end point was improvement in the mRS score23 at 1 year after surgery, and the secondary outcome measures were the iNPHGS,27 MMSE,4 TMT-A,5 and TUG-t18 scores at 1 year after surgery. We examined the association between the DESH score and an improved score for these 5 measures at 1 year after surgery. In addition, we investigated leukoaraoisosis on MR images, deep white matter hyperintensity, and periventricular hyperintensity, which are reported to be associated with the risk factors for vascular diseases such as hypertension and smoking.3,12

Statistical Analysis

The analysis was performed using R statistical software (Foundation for Statistical Computing). Statistical significance was examined using the Student t-test, and the correlation coefficients were tested using Microsoft Excel (version 2016; Microsoft Corp.).

Results

Patient Population

The flow chart for this study is shown in Fig. 1. Of the 110 preregistered patients, 10 patients had a diagnosis of Alzheimer’s disease or other disease as determined by SPECT and assessment of cognitive function, and 45 patients did not fulfill the CSF inclusion criteria or had positive findings on a tap test. Of the 55 patients who proceeded to registration, 5 withdrew (1 patient each due to traumatic intracranial hemorrhage, acute ischemic stroke, or aggravation of cirrhosis, and 2 patients were lost to follow-up), leaving 50 patients for analysis.

Baseline Data

The baseline data for the 50 patients are summarized in Table 2. Almost all patients were older than 70 years of age (mean age 77.6 ± 5.9 years [± SD]). The objective symptoms on iNPHGS were gait disturbance in 94% patients, cognitive impairment in 82% of patients, urinary symptoms in 64% of patients, and the classic triad in 48% of patients.

On MRI review, the Evans’ index typically demonstrated a slight dilation (Evans’ index 0.3–0.35), and, in most cases, the callosal angle was ≤ 100°. The mean DESH score was 5.58 ± 2.01 (range 2–10) and showed a normal distribution (Fig. 2).

Clinical Outcomes

The mean initial valve pressure of the ventriculoperitoneal shunt was 14.5 ± 3.5 cm H2O, and 8 patients needed

### TABLE 2. Background characteristics and preoperative status of 50 patients with suspected iNPH

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
</tr>
<tr>
<td>Mean age, yrs</td>
<td>77.6 ± 5.9 (61–87)</td>
</tr>
<tr>
<td>Male sex</td>
<td>33 (66)</td>
</tr>
<tr>
<td>Symptoms present</td>
<td></td>
</tr>
<tr>
<td>Triad of symptoms</td>
<td>24 (48)</td>
</tr>
<tr>
<td>Gait + cognitive impairment</td>
<td>13 (26)</td>
</tr>
<tr>
<td>Gait + urinary symptom</td>
<td>6 (12)</td>
</tr>
<tr>
<td>Cognitive impairment + urinary symptom</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Gait impairment only</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Cognitive impairment only</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Urinary symptom only</td>
<td>0</td>
</tr>
<tr>
<td>Lumbar puncture finding</td>
<td></td>
</tr>
<tr>
<td>Mean CSF pressure, cm H2O</td>
<td>13.3 ± 1.92 (10.0–17.5)</td>
</tr>
<tr>
<td>MRI findings</td>
<td></td>
</tr>
<tr>
<td>Mean Evans’ index, %</td>
<td>33.2 ± 2.8</td>
</tr>
<tr>
<td>Mean callosal angle, °</td>
<td>91.7 ± 13.1</td>
</tr>
<tr>
<td>Mean DESH score</td>
<td>5.58 ± 2.01</td>
</tr>
</tbody>
</table>

Data are presented as the mean ± SD (range) or number (%) of patients.
to have the pressure readjusted throughout the follow-up period.

At 1 year after surgery, the mean mRS score improved from 2.54 ± 0.76 to 2.02 ± 1.17 (p = 0.010). The improvement rate—defined as a 1 or more levels of improvement on mRS—was 64.0%, and the mean rate of change in the mRS score was −0.50 ± 0.93 (range −2 to 2) (Fig. 3A and B), indicating an inverse correlation between the DESH score and the rate of change in the mRS score (r = −0.749; Fig. 4).

**FIG. 1.** Flow chart for this study from the initial screening to the final analysis.

**FIG. 2.** Distribution map of the DESH scores.
Table 3 compares the preoperative scores between the patients with an improved mRS score (n = 32; 64.0%) and those without an improved mRS score (n = 18; no change in 10 patients and aggravation in 8 patients). There were marked significant differences between patients with and without improvement in relation to the DESH score (6.50 ± 2.0 vs 3.94 ± 1.5, respectively; p < 0.001) and preoperative MMSE score (23.7 ± 3.5 vs 17.7 ± 3.0; p < 0.001), as well as a difference in the preoperative TMT-A score (159.5 ± 49.2 vs 212.0 ± 51.8; p = 0.020). On the other hand, no differences were found in relation to leukoaraisis on the MR images between patients with and without improved mRS scores (15.6% vs 16.7%; p = 1.000). Thus, patients with an improved mRS score tended to have low preoperative DESH, MMSE, and TMT-A scores.

All the secondary outcomes showed significant improvement at 1 year after surgery (Table 4). The mean iNPHGS score improved from 6.00 ± 1.93 to 5.00 ± 2.85 (p = 0.043), MMSE improved from 21.54 ± 4.02 to 23.38 ± 4.53 (p = 0.047), TMT-A improved from 178.4 ± 69.4 seconds to 134.3 ± 59.8 seconds (p = 0.049), and TUG-t improved from 27.5 ± 11.3 seconds to 21.1 ± 10.1 seconds (p = 0.046). As for the overall improvements after surgery, 62.0% of patients had an improved iNPHGS score of 1 or higher, 32.0% had an improved MMSE score of 3 or higher, 30% had a decreased TMT-A time, and 58.0% had a greater than 10% decrease on TUG-t. Furthermore, there was a significant difference in the DESH score between patients with and without an improved iNPHGS score (DESH score 6.39 ± 1.76 vs 4.26 ± 1.69; p < 0.001), MMSE (DESH score 6.63 ± 1.82 vs 5.09 ± 1.93; p = 0.010), TMT-A (DESH score 6.32 ± 1.97 vs 5.13 ± 1.93; p = 0.042), and TUG-t (DESH score 6.48 ± 1.81 vs 4.33 ± 1.59; p < 0.001) (Table 5).

Based on these findings, the DESH score appears to have a strong association with the mRS, iNPHGS, MMSE, TMT-A, and TUG-t scores.

**Discussion**

The improvement rate of 1 or more levels on mRS was 64.0% in our cohort, which is similar to the rate of 69.0% reported by the SINPHONI trial. Our findings suggest that a high DESH score has an important positive predictive value in relation to neurological improvement after surgery for iNPH, in turn suggesting that MRI-based DESH scoring has diagnostic utility. A previous multicenter, prospective cohort study found an MRI-based diagnostic scheme highly useful and concluded that the DESH sign—tight high convexity, medial

**TABLE 3. Comparison of preoperative scores between patients with and without an improved mRS score after surgery**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Improvement in mRS Score (n = 32)</th>
<th>No Improvement in mRS Score (n = 18)*</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESH score</td>
<td>6.50 ± 2.0</td>
<td>3.94 ± 1.5</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>iNPHGS score</td>
<td>5.68 ± 2.13</td>
<td>6.56 ± 2.35</td>
<td>0.066†</td>
</tr>
<tr>
<td>MMSE score</td>
<td>23.7 ± 3.5</td>
<td>17.7 ± 3.0</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>TMT-A, sec</td>
<td>159.5 ± 49.2</td>
<td>212.0 ± 51.8</td>
<td>0.020†</td>
</tr>
<tr>
<td>TUG-t, sec</td>
<td>27.0 ± 8.3</td>
<td>28.4 ± 7.1</td>
<td>0.649†</td>
</tr>
<tr>
<td>DWMH or PVH on MRI</td>
<td>5 (15.6)</td>
<td>3 (16.7)</td>
<td>1.000‡</td>
</tr>
</tbody>
</table>

DWMH = deep white matter hyperintensity; PVH = periventricular hyperintensity.
Data are presented as the mean ± SD or number (%). of patients.

* No change was observed in 10 patients, and aggravation was observed in 8 patients.
† Determined using the Student t-test.
‡ Determined using the Fisher exact test.
subarachnoid spaces, and enlarged sylvian fissures with ventriculomegaly—is valuable for the diagnosis of iNPH.6

We assigned the DESH score on the basis of 5 parameters, each of which was scored simply from 0 to 2 for a maximum of 10 points: ventriculomegaly, dilated sylvian fissures, tight high convexity, acute callosal angle, and focal sulcal dilation. These 5 features mentioned above are very important in diagnosing iNPH, but we must be aware of their correlations. Ishii et al.9 reported that the Evans’ index correlated well with the relative volume of the enlarged ventricle systems and sylvian fissures, and it correlated inversely with the relative volume of the sulci at the high convexity and midline. The callosal angle also showed a good negative correlation with the relative volume of the ventricle systems and sylvian fissures, and it correlated positively with the relative volume of the sulci at the high convexity and midline. In addition, Virhammar et al.22 reported that the callosal angle correlated with focal sulcal dilation (r = −0.28), and they concluded that a small callosal angle, wide temporal horns, and the occurrence of disproportionately enlarged subarachnoid space hydrocephalus were significant predictors of a positive shunt outcome.

In our study, leukoaraiosis was not related to improvement after surgery. A previous study showed that this parameter was a negative factor associated with the clinical improvement of iNPH;21 however, a recent study reported that patients must not be excluded from shunt surgery on the basis of leukoaraiosis findings because patients with severe leukoaraiosis had a positive outcome rate similar to that of the entire sample.22 There may be room for debate about this result, but the presence of leukoaraiosis on MRI does not predict a poor outcome of surgery and therefore should be used as an exclusion criterion for shunting.

Our study examined both the usefulness of the DESH score that followed an MRI-based diagnostic scheme and the beneficial effect of shunt surgery on iNPH after 1 year. The diagnosis of iNPH is established in terms of response to surgery, and the efficacy of surgery depends on the diagnostic accuracy.6 Therefore, the more accurate the diagnosis is, the more efficacious the treatment will be. Our study suggests a strong association between the DESH score and prognosis after surgery. MRI-based DESH scoring appears to be a useful objective method as it allows an easy and quantitative evaluation for predicting prognosis.

Conclusions

A typical, high DESH score had a positive predictive value for neurological improvement after surgery for iNPH. The DESH score does appear to be useful for the prediction of neurological improvement and prognosis after surgery.

References


Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Shinoda. Acquisition of data: Shinoda. Analysis and interpretation of data: Shinoda, Hirai. Drafting the article: Shinoda. Critically revising the article: Shinoda. Reviewed submitted version of manuscript: Shinoda. Approved the final version of the manuscript on behalf of all authors: Shinoda. Statistical analysis: Shinoda. Administrative/technical/material support: all authors. Study supervision: Hirai, Ueno.

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