Indications for Shunting in Patients with Idiopathic Normal Pressure Hydrocephalus Presenting with Dementia and Brain Atrophy (Atypical Idiopathic Normal Pressure Hydrocephalus)

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Abstract

The indications for shunt operation in patients with idiopathic normal pressure hydrocephalus accompanied by brain atrophy (atypical idiopathic normal pressure hydrocephalus; AINPH) were investigated in 25 patients who satisfied the diagnostic criteria and underwent ventriculoperitoneal (VP) shunting. All patients had no apparent history of intra- or extracranial disease; dementia and gait disturbance as the main complaints; moderate to severe cerebral atrophy and ventricular dilatation and at least periventricular low density around the anterior horn on computed tomography; normal cerebrospinal fluid (CSF) pressure and filling of ventricles or cortical surface space with contrast medium at 24 hours on cisternography. The 15 male and 10 female patients were aged 47–83 years (mean 60.4 years). VP shunting was effective in 12 improved patients and not effective in 13 unimproved patients according to NPH grading.

Pathological pressure wave on epidural pressure monitoring was observed in eight of 12 improved patients, but none of 13 unimproved patients. CSF outflow resistance was $35.33 \pm 11.16$ mmHg/ml/min in improved patients and $8.12 \pm 5.31$ mmHg/ml/min in unimproved patients. Preoperative serum alpha-1-antichymotrypsin value (alpha-1-ACT) was $42.02 \pm 8.64$ mg/dl in improved patients and $61.72 \pm 11.03$ mg/dl in unimproved patients. Alpha-1-ACT over 55 mg/dl occurred only in unimproved patients. Cerebral arteriovenous difference of oxygen content value (c-AVDO₂) before and after surgery was $6.34 \pm 0.9$ ml% and $5.91 \pm 0.78$ ml% in improved patients and $4.75 \pm 1.85$ ml% and $4.81 \pm 1.73$ ml% in unimproved patients, respectively. The two cases with preoperative c-AVDO₂ value over 8.5 ml% were both unimproved. Mean cerebral blood flow value before and after surgery was $23.51 \pm 4.20$ ml/100 g/min and $45.22 \pm 8.11$ ml/100 g/min in improved patients and $21.77 \pm 5.12$ ml/100 g/min and $24.82 \pm 4.97$ ml/100 g/min in unimproved patients, respectively.

Cerebral atrophy in improved patients is caused by a cerebral circulation disturbance defined as a cerebral blood flow of penumbra or more due to cerebral arteriosclerosis, etc. A flow-chart of indications of shunt surgery for AINPH was prepared based on the results of the present study.

Key words: normal pressure hydrocephalus, brain atrophy, shunt surgery, serum alpha-antichymotrypsin, cerebral arteriovenous difference of oxygen content, cerebrospinal fluid outflow resistance

Introduction

Idiopathic normal pressure hydrocephalus (INPH) is well known but the pathology and indications for shunt surgery or preoperative prediction of surgical outcome remain unclear.

This study investigated the effectiveness of shunt surgery in patients with INPH presenting with cerebral atrophy as the basic pathologic condition, defined as atypical INPH (AINPH).\textsuperscript{29,40}

Materials and Methods

The subjects were 25 patients, 15 males and 10
females aged 47–83 years (mean 60.4 years), with AINPH treated between July 1995 and December 1997. Criteria for inclusion were as follows: no history of apparent intra- or extracranial diseases; main complaint of dementia, sometimes with gait disturbance; intermediate or severe cerebral atrophy (cerebral atrophy was defined as the sum of cerebral grooves at four sites on the computed tomography [CT] slice in descending order from the maximum of 7 mm or more), bilateral symmetrical ventricular dilatation (ventricular index [ratio of length of posterior horn to anterior horn on one CT slice] 1.0 or less), and at least periventricular low density at the anterior horn on CT; and cerebrospinal fluid (CSF) pressure within the normal range with inflows of contrast medium into the cerebral ventricle or cortical surface 24 hours later on cisternography (Fig. 1).

Evaluation of the severity of AINPH and improvement of the symptoms after shunt surgery was based on the standards for NPH grading established by the Research Committee on Intractable Hydrocephalus sponsored by the Ministry of Health and Welfare of Japan in 1996 (chairman Koreuki Mori). The accumulative score in the triad of NPH (gait disturbance: G, dementia: D, urinary incontinence: U) is used for the overall estimation of the severity of NPH, ranging from normal (0) to most severe state (12). The symptoms are expressed as, for example: NPH grade = 8 (G2, D3, U3) (Table 1). Shunt surgery was considered effective when the grade improved by one or more.

Ventriculoperitoneal (VP) shunt surgery using Medos type shunt system (set pressure = epidural basic pressure × 13.6 – 20 mmH_{2}O, omission of lower number of one figure) was performed on all subjects. VP shunting was effective in 12 patients (Group E: mean age 62.7 years; preoperative NPH grade is 1–3 scores in one patient, 4–6 in seven, 7–9 in two, and 10–12 in two), and non-effective in 13 patients (Group NE: mean age 58.7 years; preoperative NPH grade is 1–3 in one, 4–6 in eight, 7–9 in three, and 10–12 in one).

The following characteristics were compared between the Groups E and NE.

I. Appearance of pressure wave (PW) on epidural pressure monitoring (EDPM)\(^{30}\)
II. Preoperative CSF outflow resistance (Ro)\(^{30}\)
III. Preoperative serum alpha-1-antichymotrypsin level (alpha-1-ACT)\(^{30}\)
IV. Cerebral arteriovenous difference of oxygen content (c-AVDO\(_2\))\(^{30}\) before and after surgery
V. Pre- and postoperative mean cerebral blood flow (mCBF)\(^{30}\)

Table 1 Grading scale for normal pressure hydrocephalus by Research Committee on Intractable Hydrocephalus, the Ministry of Health and Welfare of Japan, 1996

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>normal</td>
</tr>
<tr>
<td>1</td>
<td>unstable, but independent gait</td>
</tr>
<tr>
<td>2</td>
<td>walking with one cane</td>
</tr>
<tr>
<td>3</td>
<td>walking with two canes or a walker frame</td>
</tr>
<tr>
<td>4</td>
<td>walking not possible, wheelchair-bound</td>
</tr>
<tr>
<td>0</td>
<td>within normal range</td>
</tr>
<tr>
<td>1</td>
<td>no apparent dementia but apathetic</td>
</tr>
<tr>
<td>2</td>
<td>socially dependent but independent at home</td>
</tr>
<tr>
<td>3</td>
<td>partially dependent at home</td>
</tr>
<tr>
<td>4</td>
<td>totally dependent</td>
</tr>
<tr>
<td>0</td>
<td>absent</td>
</tr>
<tr>
<td>1</td>
<td>absent but with pollakiuria or urinary urgency</td>
</tr>
<tr>
<td>2</td>
<td>sometimes only at night</td>
</tr>
<tr>
<td>3</td>
<td>sometimes even during the day</td>
</tr>
<tr>
<td>4</td>
<td>frequent</td>
</tr>
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Total grade = G + D + U.

Fig. 1 Plain computed tomography (CT) scans (left column) and CT cisternograms at 6 (center column) and 24 hours (right column) showing atypical idiopathic normal pressure hydrocephalus.

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VI. Outcome and postoperative complications

Results

I. EDPM
Preoperatively, a transducer was inserted for microsensor EDP (Higashimatsuyama Municipal Hospital improved type; Codman Co., Raynham, Mass., U.S.A) into the epidural cavity in all patients. The appearance of pathological PW and basic EDP were investigated by EDPM (measurement time 5–9 hours, mean 7.5 hours). EDP was 8–13 mmHg (mean 8.8 ± 1.3 mmHg), with no significant difference between Groups E and NE. PW was seen in 8/12 patients (66.7%) in Group E but 0/13 (0%) in Group NE. The eight patients with PW were all in Group E and the four of 17 patients without PW (23.5%) were also in Group E.

II. Preoperative Ro
Lumbar puncture was performed in all patients during EDPM and the Ro was calculated from the expression for the infusion test using a physiological saline 10–15 ml single bolus injected into the lumbar subarachnoid cavity (infusion speed 1 ml/sec).26 The mean Ro level was significantly higher (p < 0.01) in Group E (35.33 ± 11.16 mmHg/ml/min) compared to Group NE (9.12 ± 3.51 mmHg/ml/min). All patients with Ro of 20 mmHg/ml/min or higher were in Group E (Fig. 2).

III. Preoperative alpha-1-ACT
A catheter was inserted into the internal jugular vein before surgery to collect a venous blood sample (5 ml) from near the bulb site of the internal jugular vein to measure the alpha-1-ACT level by the nephelometry method. Blood samples were collected once to three times for each patient, and the mean level was calculated. The alpha-1-ACT level was significantly lower (p < 0.05) in Group E (42.02 ± 8.64 mg/dl) compared to Group NE (61.72 ± 11.03 mg/dl). The border between Groups E and NE was about 55 mg/dl, and all patients with alpha-1-ACT level of 55 mg/dl or more were in Group NE (Fig. 3).

IV. c-AVDO₂
Venous and arterial blood samples (1 ml each) were collected from near the bulb site of the internal jugular vein and the femoral artery, respectively, before and 1–3 months after surgery (mean 1.1 ± 0.4 months). The c-AVDO₂ was calculated from the Voldby’s expression.27
\[
c\text{-AVDO}_2 = \left[ \frac{1.34 \times Hb \times O_2 \text{ saturation (A-V)/100}}{\text{PaO}_2 \times 0.03} \right]
\]

Fig. 2 Preoperative cerebrospinal fluid outflow resistance (Ro) measured by the single bolus injection infusion test.26 Each circle indicates individual values, and the circle with bar shows the mean ± SD.

Fig. 3 Preoperative serum alpha-1-antichymotrypsin (alpha-1-ACT) values. Each circle indicates individual values, and the circle with bar shows the mean ± SD. *Cerebral arterial venous difference of oxygen content (c-AVDO₂) 8.62 ml%, **c-AVDO₂ 9.01 ml%.

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where Hb is hemoglobin level (g/dl), PaO₂ is arterial oxygen tension, A is arterial blood, and V is venous blood.

The c-AVDO₂ before and after surgery was 6.34 ± 0.9 mll% and 5.91 ± 0.78 ml% in Group E, and 4.75 ± 1.65 mll% and 4.61 ± 1.73 ml% in Group NE, respectively. The c-AVDO₂ was significantly higher (p < 0.05) in Group E before surgery. Two Group NE patients showed 8.5 ml% or higher (8.82 ml% and 9.01 ml%), with 42 mg/dl and 39 mg/dl of alpha-1-ACT. All Group E patients had c-AVDO₂ level within the range of 5–8.5 ml% (Fig. 4). Postoperative c-AVDO₂ levels tended to be lower than preoperative levels in Group E, whereas no significant change was found in Group NE.

V. mCBF

mCBF was determined by technetium-99m-hexamethylpropylene amine oxime single photon emission computed tomography before and 1–6 months after surgery (mean 2.1 ± 0.6 months). mCBF was 23.51 ± 4.20 ml/100 g/min before surgery and 45.22 ± 8.11 ml/100 g/min after surgery in Group E, showing a significant increase in comparison with the former (p < 0.001). mCBF was 21.77 ± 5.12 ml/100 g/min before surgery and 24.82 ± 4.97 ml/100 g/min after surgery in Group NE with no significant difference (Fig. 5).

VI. Outcome and postoperative complications in Group E

Outcome: The NPH grade in Group E (12 cases) was 1–3 scores in one case (8.3%), 4–6 in seven (58.3%), 7–9 in two (16.7%), and 10–12 in two

Fig. 4 Preoperative cerebral arteriovenous difference of oxygen content (c-AVDO₂) values. Each circle indicates individual values, and the circle with bar shows the mean ± SD. *Serum alpha-1-antichymotrypsin (alpha-1-ACT) 39 mg/dl, **alpha-1-ACT 42 mg/dl.

Fig. 5 Pre- (preope.) and postoperative (postope.) mean cerebral blood flow (mCBF) on technetium-99m-hexamethylpropylene amine oxime single photon emission computed tomography. Each circle with bar shows mean ± SD. ●: shunt effective, ○: shunt non-effective.

Fig. 6 Operative improvement of shunt effective group on grading scale for normal pressure hydrocephalus by Research Committee on Intractable Hydrocephalus, the Ministry of Health and Welfare of Japan, 1996. □: 0–3 scores, △: 4–6 scores, ■: 7–9 scores, □□: 10–12 scores. preope.: preoperative, postope.: postoperative.
Discussion

NPH is characterized by the presence of two or more of the triad of symptoms (gait disturbance, dementia, and incontinence) associated with CSF pressure within the normal range, and the symptoms resulting from bilateral symmetrical ventricular dilatation are improved by shunt surgery. However, cerebral atrophy is absent or mild, and radioactive iodine-tagged human serum albumin (RHISA) or metrizamide infused into the cerebrospinal cavity accumulates only in the cerebral ventricle, and hardly on the cortical surface characteristically. INPH has no apparent underlying intracranial disease in the medical history except for disturbance of CSF circulation. INPH accounts for about 10–17% of all NPH cases. Shunt surgery can be applied to all INPH but the effectiveness in aged patients is very low at 40–46.8%. But there is an interesting report in which the shunt is not effective among aged patients with INPH. A group of eight aged patients with progressive dementia as the chief complaint was identified who had cerebral atrophy and bilateral symmetrical ventricular dilatation. In this group, RHISA accumulated both on the cerebral ventricles and the cortical surface. The pathologic conditions were assumed to be degenerative changes due to underlying cerebral arteriosclerotic circulatory disturbance and CSF circulation disturbance. These patients were considered to suffer from a pathologic condition similar to NPH that is now described as INPH. However, since we believe that the presence of underlying cerebral atrophy is essentially different from INPH, we defined cases satisfying our four criteria described previously as AINPH.

As for the application of shunt surgery in NPH, the appearance of PW and high wave relative frequency (9 mmHg or higher in the sum of amplitudes of three high waves) has been reported. Some investigators reported that shunting was effective in patients with a central motor conduction time within the normal range, measured by motor-evoked potentials. However, as in this study, this finding indicates that surgery will be effective, but also surgery is effective in some cases not satisfying this condition. Recently, the effects of elimination of CSF by lumbar continuous drainage have been evaluated. However, surgery is not effective even when favorable effects were seen with this method. This method poses problems because of load on patients and the risk of infection. Thus, at present, the surgical effects in NPH are generally difficult to clearly predict.

Disturbance of the flow of CSF, especially disturbance in absorption, is the most important factor in evaluation of the effectiveness of shunting in AINPH. Our measurement of Ro showed significantly higher levels and all cases of 20 mmHg/ml/min or more were in Group E. Various reports have shown that responsive cases have a significantly high Ro values. The borderline Ro value between improved and unimproved patients varies according to the volume, rate, and site of saline infusion, and the site of intracranial pressure measurement, but is thought to be about 10–20 mmHg/ml/min. Leptomeningeal fibrosis, detected by intraoperative biopsy, does not affect the Ro values.

The effectiveness of shunt surgery depends on reversibility of any abnormality of the cerebral parenchyma in NPH. Cerebral atrophy in AINPH can be divided into cases caused by degeneration of the neurocytes (Alzheimer’s disease, Pick disease, etc.) and cases caused by disturbance of cerebral circulation (cerebral arteriosclerosis, Binswanger disease, etc.). In the former, the energy demand decreases due to reduction of the neurocytic function which causes secondary reduction of CBF. However, the supply of oxygen to the neurocytes is maintained to some extent (aerobic metabolism), so functional recovery of neurocytes is difficult even when the CBF improves. In the latter, oxygen supply to neurocytes decreases due to primary reduction of the CBF and the function of the neurocytes consequently decreases (anaerobic metabolism). Thus, when its pathologic condition is penumbra or more, improvement of CBF may lead to improvement of the function of neurocytes.

Generally, under NPH pathologic conditions, edema among interstitial cells occurs due to lesser pathways from the cerebral ventricles, resulting from a disturbance of CBF circulation, and oxygen
supply to the cells decreases due to diffusion disturbance. Consequently, the function of neurocytes is reduced due to secondary reduction of CBF.\textsuperscript{43} Thus, when edema among interstitial cells is alleviated by shunt surgery, oxygen supply to the cells increases and secondary CBF increases, which leads to improvement of symptoms.\textsuperscript{35,11,22,20} Therefore, when cerebral atrophy in AINPH is caused by disturbance of cerebral circulation due to cerebral arteriosclerosis, etc. and the pathologic condition is penumbra or more, the symptoms may improve after shunt surgery. Autoregulation of the periventricular white matter was impaired in responsive NPH cases when the CBF was measured with xenon-enhanced CT.\textsuperscript{41} The Group E patients in this study had mCBF of $23.51 \pm 4.20$ ml/100 g/min before surgery, a penumbra condition, and increased markedly to $45.22 \pm 8.11$ ml/100 g/min after surgery.

The causes of cerebral atrophy can be investigated using alpha-1-ACT as a marker differentiating from neuroytic degenerative diseases such as Alzheimer’s disease, etc. Alpha-1-ACT is a type of acute reaction protein belonging to the serine protease inhibitor, which is present in adult neurogliocytes, neurocytes, and choroidae. Our previous study demonstrated that increase of alpha-1-ACT is correlated with the degree of neuroytic damage areas.\textsuperscript{39} Alpha-1-ACT is a structural component of amyloid, a basic body in senile spots.\textsuperscript{1,15,16} Alpha-1-ACT is an inhibitor of serine protease which decomposes beta-amyloid precursor protein. When alpha-1-ACT increases due to neuroytic degeneration, the amyloid deposits formed by production of beta-amyloid protein increases,\textsuperscript{1,15,31} Beta-amyloid protein and alpha-1-ACT may be correlated\textsuperscript{31,35} as an indicator of amyloid formation.\textsuperscript{13} Measurement of alpha-1-ACT levels in 77 healthy persons and 110 dementia patients showed the mean alpha-1-ACT was $42.0 \pm 5.80$ mg/dl in healthy subjects, $65.50 \pm 15.60$ mg/dl in patients with Alzheimer’s type dementia, $49.90 \pm 5.00$ mg/dl in patients with cerebrovascular dementia, and $52.80 \pm 11.80$ mg/dl in patients with mixed dementia.\textsuperscript{29,39} In particular, the level in patients with Alzheimer’s type dementia was significantly higher.

In this study, the alpha-1-ACT in Group NE was $61.72 \pm 11.03$ mg/dl, a significantly high level, and all cases of 55 mg/dl or higher were in Group NE. However, some cases of 55 mg/dl or less, a relatively low level, were also in Group NE. This fact indicates irreversible conditions because the metabolism or CBF markedly decreased (to less than penumbra), although the pathologic conditions of cerebral atrophy are based on disturbance of cerebral circulation. To evaluate this hypothesis, we calculated c-AVDO\textsubscript{2}. c-AVDO\textsubscript{2} increases in inverse proportion to reduction of CBF and decreases when cerebral metabolism is reduced markedly. We previously measured c-AVDO\textsubscript{2} in patients with severe head trauma and found that c-AVDO\textsubscript{2} in patients having poor prognosis was 5 ml% or less.\textsuperscript{30} In this study, the c-AVDO\textsubscript{2} in Group E was significantly higher. However, two cases of 8.5 ml% or more (8.82 ml% and 9.01 ml%) were in Group NE, and the alpha-1-ACT levels in those cases were 42 mg/dl and 39 mg/dl, respectively, c-AVDO\textsubscript{2} in Group E ranged from 5.0 to 8.5 ml%, indicating the pathologic conditions under which cerebral metabolism decreases markedly when c-AVDO\textsubscript{2} is 5.0 ml% or less, and CBF decreases to less than penumbra when c-AVDO\textsubscript{2} is 8.5 ml% or more.

These results show that when the alpha-1-ACT was low at 55 ml/dl or less, and c-AVDO\textsubscript{2} ranged from 5 to 8.5 ml%, there was a significant increase in postoperative CBF, and the pathologic condition of cerebral atrophy was caused by disturbance of cerebral circulation with mCBF of penumbra or more in Group E. In contrast, when alpha-1-ACT level was high at 55 mg/dl or more, and c-AVDO\textsubscript{2} levels were 5 ml% or less or 8.5 ml% or more, there was no variation in postoperative CBF, and the pathologic condition of cerebral atrophy was caused by disturbance of cerebral circulation with mCBF of less than penumbra due to cerebral arteriosclerosis or neuroytic degenerative disease in Group NE. Shunt surgery should be effective for aged INPH patients with a periventricular deep white matter lesion indicated as vascular encephalopathy on magnetic resonance imaging, and disturbance of cerebral circulation is important as a cerebral pathologic base in responsive cases.\textsuperscript{10} Based on these results, we propose a flow-chart for the indication of shunt surgery in patients with AINPH based on Ro, presence or absence of PW, and alpha-1-ACT and c-AVDO\textsubscript{2} measurements (Fig. 7).

Postoperative complications after treatment with the Medos type shunt system were found in three of 25 patients (12%), markedly fewer than those in other series.\textsuperscript{29} Moreover, the two patients with shunt dysfunction were underdrainage, in contrast to previous results which indicated many overdrainage cases.\textsuperscript{25,64} The reason was presumably that the set pressure was EDP, which was 0.5–1 mmHg higher than CSF pressure.

As a conclusion, comparison of patients with AINPH who were improved after VP shunt surgery with those who were not improved indicated the following: 1) Patients with pathological PW on EDPM responded to shunting, but some cases with
no PW also responded. 2) Ro was significantly higher in Group E, and all cases with Ro of 20 mmHg/ml/min or more were in Group E. 3) Alpha-1-ACT level was significantly lower in Group E, and all cases with alpha-1-ACT of 55 mg/dl or more were in Group NE. 4) c-AVDO₂ was significantly higher (range 5 to 8.5 ml%) in Group E, but two cases with c-AVDO₂ of 8.5 ml% or more were in Group NE. 5) Postoperative CBF increased significantly in Group E. 6) The pathologic condition of cerebral atrophy was caused by disturbance of cerebral circulation with CBF of penumbra or more due to cerebral arteriosclerosis, etc. in Group E. 7) Based on the results, we made a flow-chart of shunt surgery in AINPH.

Acknowledgments

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Commentary

The authors analyzed the effectiveness of VP shunting in 25 patients with gait disturbance, dementia and urinary incontinence. Epidural pressure measurement, preoperative CSF outflow resistance, preoperative serum alpha-1-antichymotrypsin level, cerebral arteriovenous difference of oxygen content and cerebral blood flow were also monitored. VP shunting was effective in 12 patients and ineffective in the other 13 patients. I wonder why these various monitoring methods, some of which are truly invasive, were necessary. I am also concerned that all monitored items but one (CSF outflow resistance) cannot represent the evidence of CSF flow disturbance. I cannot understand why VP shunting was effective only in 48% of the series, even though they had so many monitoring parameters. Even though I am very much impressed by the beautiful data presented, I do not want to obey the flow chart they have proposed. I expect that more non-invasive methods that provide a definite indicator will be developed for patients with atypical idiopathic normal pressure hydrocephalus.

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The present study is a very meticulous and careful approach to the difficult problem of atypical idiopathic normal pressure hydrocephalus (AINPH) in patients who underwent ventriculo-peritoneal shunt for its tentative treatment. The authors have established a very rational flow-chart for indication of shunt surgery for these patients with dementia and brain atrophy based on their important findings, giving a special emphasis on the values of preoperative CSF outflow resistance, presence or absence of the pressure wave or epidural pressure monitoring and measurement of alpha-1-antichymotrypsin levels and cerebral arterio-venous difference of oxygen content before and after surgery. They have encountered good response in those with pathological pressure waves, and some response also in those who did not have them. We still have the feeling that in spite of all the sophisticated testing to clarify the precise indication of shunting for NPH and its variants, its indication and prognosis still remain unclear and more or less empirical due to conflicting results.

In our opinion, the magnetic percutaneous controllable valves introduced by Dr. Hakim, the father of NPH, will help to improve the problem of underdrainage and overdrainage found in some of the more difficult cases.

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The indications for shunt surgery in patients with idiopathic normal pressure hydrocephalus are still controversial, especially in those with accompanying brain atrophy (AINPH), due to the lack of reliable and objective diagnostic criteria for preoperative prediction of shunt effectiveness. The authors have proposed a flow chart for this purpose based on the results of a comparative study of epidural pressure (pressure wave), CSF outflow resistance, serum alpha-1-antichymotrypsin level and cerebral arteriovenous difference in oxygen content between patients in whom shunts were effective and non-effective. Introduction of these new criteria based on multimodal parameters for the diagnosis of AINPH will aid more accurate prediction of shunt effectiveness. However, I have some concern about the difficulty in performing all these tests without sedation, since every test or measurement necessitates invasive maneuvers. It is expected that newly developed non-invasive neuroimaging techniques will eventually replace the invasive ones used in this chart.

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There have been many investigations and reports over the years aiming to establish dependable criteria for the shunt operation for normal pressure hydrocephalus. This paper is another such study but the flow chart proposed here seems very reasonable. I
AINPH

Shunt surgery is the major treatment for idiopathic normal pressure hydrocephalus (INPH) but for INPH presenting with cerebral atrophy (atypical INPH: AINPH), the outcome of shunt operation is unclear. The authors report 25 cases of AINPH and have performed many investigation tests for all cases before and after shunt operation. The ventriculoperitoneal shunt will be effective if the pressure wave appears on epidural pressure monitoring, if the preoperative CSF outflow resistance is higher than 20 mmHg/ml/min, if preoperative alpha-1-antichymotrypsin is lower than 55 mg/dl, if the postoperative cerebral arteriovenous difference of oxygen content level tends to be lower than preoperative, and if the postoperative mean cerebral blood flow increases compared to before shunt surgery. These data give us the basic method to assess the outcome of shunt surgery for AINPH. This may be the indication for AINPH patients who need a shunt. I do appreciate this paper very much.

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hope this solves the problems we have had before with somewhat exceptional cases.

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The authors report 25 patients, who were operated on because of normal pressure hydrocephalus. Very intensive examinations were done before and after shunting. The outcome is scored according to the grading scale for normal pressure hydrocephalus by the Research Committee on Intractable Hydrocephalus. Treatment was scored successful when this score improved at least one point. It remains unclear when the postoperative scoring was done. It is reported that the cerebral blood flow was determined 1-6 months after operation (mean 2.1 ± 0.6 months). This interval seems rather short. A follow-up interval of 12 months would have been better. The preoperative resistance outflow test predicts the result of operation in 24 of 25 patients. But the improved patients differ also in the preoperative serum levels of alpha-1-ACT and in the preoperative cerebral arteriovenous difference of oxygen content value (c-AVDO₂). The authors propose a flow-chart for indications of shunt surgery depending on these three tests. They did not show that the improvement of success rate by considering the c-AVDO₂ and the serum level of alpha-1-ACT is statistically significant and that this improvement justifies the high effort of these additional tests.

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