Prediction of Effectiveness of Shunting in Patients with Normal Pressure Hydrocephalus by Cerebral Blood Flow Measurement and Computed Tomography Cisternography

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Abstract

Measurement of cerebral blood flow (CBF) and computed tomography (CT) cisternography were performed in 37 patients with a tentative diagnosis of normal pressure hydrocephalus (NPH) to predict their surgical outcome. The mean CBF of the whole brain was measured quantitatively by single photon emission computed tomography with technetium-99m-hexamethylpropylene amine oxime before surgery. The results of CT cisternography were classified into four patterns: type I, no ventricular stasis at 24 hours; type II, no ventricular stasis with delayed clearance of cerebral blush; type III, persistent ventricular stasis with prominent cerebral blush; type IV, persistent ventricular stasis with diminished cerebral blush and/or asymmetrical filling of the sylvian fissures. The mean CBF was significantly lower than that of age-matched controls (p < 0.005). Patients with a favorable outcome had a significantly higher mean CBF than patients with an unfavorable outcome (p < 0.005). Patients with the type I pattern did not respond to shunting. Some patients with type II and III patterns responded to shunting but improvement was unsatisfactory. Patients with type IV pattern responded well to shunting, and those with a mean CBF of 35 ml/100 g/min or over achieved a favorable outcome. The combination of CBF measurement and CT cisternography can improve the prediction of surgical outcome in patients with suspected NPH.

Key words: cerebral blood flow, computed tomography cisternography, normal pressure hydrocephalus, surgical outcome

Introduction

Normal pressure hydrocephalus (NPH) is characterized by progressive dementia, gait disturbances, and urinary incontinence in patients with ventricular enlargement but normal intracranial pressure. Occasionally, treatment by cerebrospinal fluid (CSF) shunting will result in a hopelessly bedridden and demented patient being able to return to a normal life. However, the diagnosis of NPH as a major contributing cause of dementia may be obscure in patients with dementia of mixed etiology, for example, NPH associated with multi-infarct dementia or senile dementia of the Alzheimer type. Surgical treatment can only be expected to alleviate the symptoms caused by the NPH syndrome without improving the underlying pathology. Therefore, it is difficult not only to select patients who are likely to respond to shunting but also to predict their surgical outcome.

The present study evaluated cerebral blood flow (CBF) measurement using technetium-99m-hexamethylpropylene amine oxime single photon emission computed tomography (99mTc-HMPAO SPECT) and computed tomography (CT) cisternography as predictors of clinical outcome in patients with NPH who underwent shunting procedures.

Materials and Methods

Thirty-seven patients who underwent shunting procedures and CBF measurements were included...
in the present study. All patients, 18 males and 19 females aged 42–82 years (mean 66.6 years), were admitted to our hospital under a tentative diagnosis of NPH between June 1993 and July 1998. Their symptoms consisted of at least one of the triad of progressive dementia, gait disturbance, and urinary incontinence. The etiology of NPH was subarachnoid hemorrhage in 14 patients, trauma in 10, intraparenchymal hemorrhage in three, postsurgical removal of brain tumor in one, and idiopathic in nine. CT showed an enlarged ventricular system in all patients with or without cortical atrophy. Patients were selected for shunting based on their clinical history and/or the findings of ventricular reflux with diminished convexity flow or delayed clearance of cerebral blush on CT cisternograms.

Shunting was performed using ventriculoperitoneal or lumboperitoneal shunt systems with differential or programmable pressure valves. A high or medium pressure system is selected if the patient is expected to be able to walk. If the patient is expected to remain bedridden, a low or medium pressure system is used. If symptoms did not improve and shunt dysfunction was suspected, the shunt patency was checked by shuntography. Underdrainage or overdrainage of CSF sometimes occurred and the shunt was revised to another type with a different pressure. Recently, the lumboperitoneal shunt system with the Codman-Medos programmable valve (Codman, a Johnson & Johnson Co., Raynham, Mass., U.S.A.) has been used. The initial opening pressures were chosen principally according to the CSF pressure measured by lumbar puncture, with the patient in the lateral recumbent position. If symptoms or complications due to overdrainage of CSF appeared, such as headache and vomiting, or subdural effusion, the pressure of the valve was increased. If underdrainage of CSF was suspected, the pressure of the valve was lowered slowly. Three patients developed a slight asymptomatic subdural effusion, which resolved after increasing the valve pressure.

The mean CBF of the whole brain was measured 1–2 weeks before shunting. Informed consent was obtained from the patients or their families before the study. Mean CBF was measured by the Patlak plot method using $^{99m}$Tc-HMPAO SPECT.2,12) Following bolus injection of 740 MBq of $^{99m}$Tc-HMPAO (Ceretec; Nycomed Amersham plc, Amersham, U.K.) into the right brachial vein, the passage through the heart to the brain was monitored using a rotating scanner (Starcam 400 AC/T; General Electrics, Milwaukee, Wis., U.S.A.) with a sequence of 70 frames taken at 1 second intervals in a 128 × 128 format. The mean hemispheric CBF was calculated from the hemispheric brain perfusion index (BPI) using the linear regression equation, $y = 2.75x + 17.7$, between the BPI and $^{133}$Xe-CBF measurements obtained from the early image method. The mean CBF of the whole brain was determined from the mean CBF of both hemispheres.

CT cisternography was performed with the patient in the lateral recumbent position. A lumbar puncture was made using a 21 gauge spinal needle, and 6–8 cm$^3$ of iohexol (180 mgI/ml) was introduced intrathecally. The spinal needle was then removed, and the patient turned into the supine position. After one hour rest, the patient's physical activities were unrestricted. CT scans were obtained after 3, 6, 24, and 48 hours. The results of CT cisternography were classified into four patterns4) with some modifications (Table 1).

The clinical outcome was evaluated according to a modified Stein and Langfitt grading classification14) as follows: Excellent, resumed pre-illness activity, able to work or function independently at home; good, improved but some supervision required at home; fair, improved but no practical capacity for independent function; poor, no change or worse. Patients with excellent and good outcome were

<table>
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<tr>
<th>Table 1 Patterns of computed tomography (CT) cisternography</th>
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<tr>
<td>Type I No ventricular stasis at 24 hours. The convexity and parasagittal blurs are maximum at 6 hours, returning towards the baseline at 24 hours and disappearing by 48 hours.</td>
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<tr>
<td>Type II No ventricular stasis with delayed clearance of cerebral blush. No filling of the lateral ventricles at 24 hours. The convexity and parasagittal blurs are present even at 48 hours.</td>
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<tr>
<td>Type III Persistent ventricular stasis with prominent cerebral blush. Ventricular stasis at 24 hours. The convexity and parasagittal blurs are prominent, and the density on the 6-hour and/or 24-hour CT scans is not less than the density within the lateral ventricles.</td>
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<tr>
<td>Type IV Persistent ventricular stasis with diminished cerebral blush and/or asymmetrical filling of the sylvian fissures. Ventricular stasis persists at 24 hours and often even at 48 hours. The cerebral blush occasionally is distinct, but the density on the 6-hour and/or 24-hour CT is less than the density within the lateral ventricles. Non-filling of the sylvian fissure may be found, as well as decreased cerebral blushing of the ipsilateral convexity.</td>
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categorized as "favorable improvement," and patients with fair and poor outcome were categorized as "unfavorable improvement." Discussions were held with the patients' families to analyze and categorize the clinical outcome 3 months after shunting.

Values are expressed as means ± SD. Differences between groups were evaluated by one-way analysis of variance with post hoc analysis using Fisher's test. Probability values of less than 0.05 were considered significant.

Results

Table 2 shows the clinical outcome and results of CBF measurements in the 37 patients. Patients with an excellent outcome had a significantly higher mean CBF than those with a good outcome (p < 0.05), and patients with a good outcome had a significantly higher mean CBF than those with a fair outcome (p < 0.01). There was no significant difference in mean CBF between patients with fair and poor outcomes. Patients in each group showed significant reduction in mean CBF compared to age-matched controls (p < 0.005). The 20 patients with favorable improvement had significantly higher mean CBF [38.8 ± 4.6 ml/100 g/min] than the 17 patients with unfavorable improvement [31.7 ± 3.2 ml/100 g/min] (p < 0.005).

Three patients classified as type I all had poor outcomes. Four patients classified as type II had poor (1 patient) and fair (3) outcomes. Three patients classified as type III had poor (1 patient), fair (1), and good (1) outcomes. Twenty-seven patients classified as type IV had poor (1 patient), fair (7), good (8), and excellent (11) outcomes.

Figure 1 shows the relationship between CT cisternography pattern, mean CBF, and clinical outcome. Patients with excellent, good, fair, and poor outcomes are shown as open circles, closed circles, open squares, and closed squares, respectively. Patients with the type IV pattern and a preoperative mean CBF of 35 ml/100 g/min or over had favorable outcomes after shunting procedures.

<table>
<thead>
<tr>
<th>Clinical outcome</th>
<th>No. of patients</th>
<th>Mean age (years)</th>
<th>Mean CBF (ml/100 g/min)</th>
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<tr>
<td>Excellent</td>
<td>11</td>
<td>60.4</td>
<td>40.6 ± 4.6*</td>
</tr>
<tr>
<td>Good</td>
<td>9</td>
<td>67.1</td>
<td>36.5 ± 3.6*</td>
</tr>
<tr>
<td>Fair</td>
<td>11</td>
<td>71.8</td>
<td>31.7 ± 4.7*</td>
</tr>
<tr>
<td>Poor</td>
<td>6</td>
<td>67.7</td>
<td>31.8 ± 2.6*</td>
</tr>
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*p<0.005, significantly different to values in age-matched patients with alert consciousness: 44.7 ± 4.5 ml/100 g/min in 70 patients aged 60–69 years, 40.8 ± 3.9 ml/100 g/min in 28 patients aged 70–79 years.  
1p<0.05, significantly higher compared to good outcome.  
2p<0.01, significantly higher compared to fair outcome.

Fig. 1 Relationship between computed tomography (CT) cisternography pattern, mean cerebral blood flow (CBF), and clinical outcome. Patients with excellent, good, fair, and poor outcomes are shown as open circles, closed circles, open squares, and closed squares, respectively. Patients with the type IV pattern and a preoperative mean CBF of 35 ml/100 g/min or over had favorable outcomes after shunting procedures.

cisternography pattern, mean CBF, and clinical outcome. Three patients with the type I pattern had a low mean CBF (30.4 ± 2.6 ml/100 g/min) and resulted in a poor outcome. Four patients with the type II pattern also had a low mean CBF (33.0 ± 2.4 ml/100 g/min). Three patients with the type III patterns showed no correlation between the mean CBF and outcome. Among the 27 patients with the type IV pattern, the 19 patients with excellent or good outcomes had significantly higher (p < 0.005) mean CBF (39.1 ± 4.5 ml/100 g/min) than the eight patients with fair or poor outcomes (30.3 ± 2.6 ml/100 g/min). Seventeen of the 18 patients with the type IV pattern and a mean CBF of 35 ml/100 g/min or over had a favorable outcome, whereas seven of nine patients with the type IV pattern and a mean CBF of less than 35 ml/100 g/min had an unfavorable outcome.

Four patients with idiopathic NPH had a poor outcome, three had a fair outcome, one had a good outcome, and another one had an excellent outcome. The two patients with favorable improvement had the type IV pattern and high mean CBF of 33.4 ± 3.6 ml/100 g/min. The other seven patients with unfavorable improvement had a very low mean CBF of 33.4 ± 3.6 ml/100 g/min. Of these seven patients, two patients had a type I pattern, three had a type II pattern, and two had a type III pattern.
Discussion

Whether preoperative CBF is a predictor of surgical outcome is unclear. In our previous study, preoperative mean CBF was significantly reduced, and patients with a preoperative mean CBF of over 35 ml/100 g/min showed excellent or good improvement after shunting, whereas those with a preoperative mean CBF of less than 32 ml/100 g/min had little or no improvement. However, simply observation of reduced CBF is not sufficient to identify NPH in patients with ventriculomegaly because such reduction is also observed when cerebral metabolism is decreased, as in senile dementia.

In the present study, patients with a favorable outcome had a higher mean CBF than those with an unfavorable outcome. Extremely low mean CBF in patients with an unfavorable outcome may reflect irreversible tissue damage brought about by the process of NPH. In addition, patients who did not show any improvement after shunting were considered to have degenerative or atrophic dementia unrelated to NPH, and a substantial decrease in brain metabolism may have been responsible for the reduced CBF. Seven patients responded to shunting despite an extremely low preoperative mean CBF of less than 32 ml/100 g/min. In contrast, one patient did not show any response to shunting despite a preoperative mean CBF of over 35 ml/100 g/min. We cannot exactly determine which patients will respond to shunting by only the measurement of preoperative mean CBF.

The pathogenesis of NPH is believed to be due to abnormalities in the absorption of CSF into the venous sinuses. CT cisternography is an useful tool for the diagnosis of NPH. The criteria used for radioisotope cisternography have been modified to classify metrizamide CT cisternographic abnormalities. Although ventricular reflux and stasis of radioisotope or metrizamide with a diminished parasagittal blush are considered to be the most important diagnostic criteria, these findings are also seen in degenerative brain disorders with CSF dynamic disturbances. For this reason, the diagnosis of NPH is sometimes difficult to establish based on radioisotope or CT cisternography.

In our study, patients with a type IV pattern did better than those with other patterns, and all but one patient with this pattern responded to shunting. On the other hand, all patients with a type I pattern did not respond to shunting. Therefore, type IV can be considered as the typical pattern of NPH, whereas type I can be considered as the normal pattern. Five of seven patients with type II or III pattern did respond to shunting, but only one patient showed favorable improvement. We can predict an unfavorable outcome in patients with type II and III patterns, but cannot automatically exclude these patients as candidates for shunting procedures. In addition, although almost all patients with a type IV pattern responded to shunting, eight of 27 patients with this pattern had an unfavorable outcome. Therefore, patients with a type IV pattern can be considered as good candidates for shunting procedures, but we cannot exactly predict their surgical outcome only by CT cisternography.

All but one patient with the type IV pattern and a mean CBF of 35 ml/100 g/min or over had a favorable outcome. However, seven of 27 patients with a type IV pattern had an extremely low mean CBF and an unfavorable outcome. The failure of the treatment in these patients can be attributed to coexistent vascular disease or degenerative atrophy which aggravated the symptoms caused by NPH. Patients with type I, II, and III patterns and low mean CBF probably failed to achieve favorable outcomes because of degenerative brain disorders. In practice, the real problems are posed the idiopathic patients. Patients with a type IV pattern and a high mean CBF can achieve a favorable outcome. However, patients with type II and III patterns and a low mean CBF may respond to shunting but only achieve an unfavorable outcome.

Patients with a type I pattern cannot respond to shunting. Patients with type II and III patterns may respond to shunting, but it is difficult to achieve a favorable outcome. Patients showing the type IV pattern can respond to shunting, and those with a preoperative mean CBF of 35 ml/100 g/min or over can achieve a favorable outcome. Although we cannot exactly predict which patients will respond to shunting, the combination of CBF measurement and CT cisternography can improve the prediction of surgical outcome in patients with suspected NPH.

References

Commentary

Typical normal pressure hydrocephalus (NPH) usually results in gait difficulties, dementia as well as urinary incontinence. In the cases in which RI-cisternography or CT-cisternography reveals ventricular reflux, ventricular stasis or poor convexity filling of contrast medium, it is well known that a shunt operation is effective. However, in the cases in which RI-cisternography or CT-cisternography reveals nontypical findings, the decision to perform or not a shunt operation is difficult to take.

The authors chose subjects with ventriculomegaly, performed CT-cisternography, and classified them into 4 categories according to the precise calculation of their specific blood flow. The comparative study reveals very useful results, which can be used as a very useful index for suspicious NPH cases that are difficult to decide. This paper will contribute to other cases like arrested hydrocephalic condition such as myelomeningocele, ventricular hemorrhage and meningitis.

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The authors reported the prognostic value of a combination of CBF data and CT cisternography findings in patients with normal pressure hydrocephalus (NPH). The present study revealed that patients with type IV pattern of CT cisternography (persistent ventricular stasis with diminished cerebral blush and/or asymmetrical filling of the sylvian fissures) and a mean CBF of 35 ml/100 g/min or over achieved a favorable outcome. They noted favorable outcome in patients with a significantly higher CBF. However, preoperative global CBF data often failed to show a difference between good and poor responders to the CSF shunting operation. Although many parameters such as CT cisternography, CSF conductance and CBF have been reported to be useful for the prediction, no single parameter predicted the outcome with a high accuracy of more than 90%. The “gold standard” for predicting the outcome has yet to be established. At present, the combination of parameters as reported in this paper would be a better approach to this issue. Further study for investigating good parameters for the prediction must be continued in patients with NPH, especially of unknown origin.

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The prognostic criteria for the CSF shunting operation to treat normal pressure hydrocephalus are still not established. In this article, the authors describe the prognostic significance of combined criteria that include a low mean CBF of less than 35 ml/100 g/min and persistent ventricular stasis with diminished cerebral blushing and/or asymmetrical filling of the sylvian fissure. This seems to be important for preoperative prediction of normal pressure hydrocephalus. In order to test these criteria, the

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authors intend to carry out a postoperative CBF study to assess the hemodynamic effect of the shunt operation by comparing the pre- and postoperative CBF values.

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This article is a very interesting one which provides useful data for decision-making when the neurosurgeon is confronted with arduous indications of shunting for suspected NPH. As a matter of fact, it can be difficult to guarantee the efficacy of shunting in patients with a certain degree of cerebral atrophy, especially if there is no known favorable factor(s) in the patient’s past history. When looking at Figure 1, we can clearly make the deduction that shunting is indicated in patients with: 1) persistent ventricular stasis and diminished cerebral blush at CT cisternography and 2) CBF at SPECT superior to 35 ml/100 g/min. The cost for both explorations is largely compensated by the benefit to avoid unnecessary surgery and related complications.

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