Diagnosis and management of idiopathic normal-pressure hydrocephalus: a prospective study in 151 patients

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The syndrome of idiopathic NPH was first introduced by Hakim and Adams in 1965, who described a unique triad of clinical symptoms including gait disturbance, dementia, and incontinence in patients with enlarged ventricles and occurring in the absence of raised ICP. They introduced the term “normal-pressure hydrocephalus” to describe this condition and reported that these symptoms dramatically improved on shunt placement. Although there has been significant progress in brain imaging and shunt technology during the past 40 years, correctly diagnosing the disease and selecting patients who would benefit from shunt surgery remains controversial, particularly in selecting patients for shunt insertion. The use of clinical criteria coupled with imaging studies has limited effectiveness in predicting shunt success. The goal of this prospective study was to assess the usefulness of clinical criteria together with brain imaging studies, resistance testing, and external lumbar drainage (ELD) of cerebrospinal fluid (CSF) in determining which patients would most likely benefit from shunt surgery.

Methods. One hundred fifty-one patients considered at risk for idiopathic NPH were prospectively studied according to a fixed management protocol. The clinical criterion for idiopathic NPH included ventriculomegaly demonstrated on computerized tomography or magnetic resonance imaging studies combined with gait disturbance, incontinence, and dementia. Subsequently, all patients with a clinical diagnosis of idiopathic NPH underwent a lumbar tap for the measurement of CSF resistance. Following this procedure, patients were admitted to the hospital neuropsychological service for a 3-day ELD of CSF. Video assessment of gait and neuropsychological testing was conducted before and after drainage. A shunt procedure was then offered to patients who had experienced clinical improvement from ELD. Shunt outcome was assessed at 1 year postsurgery.

Conclusions. Data in this report affirm that gait improvement immediately following ELD is the best prognostic indicator of a positive shunt outcome, with an accuracy of prediction greater than 90%. Furthermore, bolus resistance testing is useful as a prognostic tool, does not require hospitalization, can be performed in an outpatient setting, and has an overall accuracy of 72% in predicting successful ELD outcome. Equally important is the finding that improvement with shunt surgery is independent of age up to the ninth decade of life in patients who improved on ELD.

Key Words • idiopathic normal-pressure hydrocephalus • normal-pressure hydrocephalus • hydrocephalus

The syndrome of idiopathic NPH has an overall accuracy of 72% in predicting successful ELD outcome. Equally important is the finding that improvement with shunt surgery is independent of age up to the ninth decade of life in patients who improved on ELD.
Clinical Material and Methods

One hundred fifty-one patients with a clinical diagnosis of idiopathic NPH were treated at the Virginia Commonwealth University Medical Center between 1993 and 2003 according to a uniform protocol adopted in 1992 and carefully followed to the present. The clinical criterion for idiopathic NPH was ventriculomegaly demonstrated on CT or MR imaging studies combined with gait disturbance, incontinence, and dementia. All patients properly consented to all surgical procedures according to hospital regulations.

Management Protocol Summary

Patients at risk for idiopathic NPH were evaluated in an outpatient clinic after being referred by a neurologist on service or from the surrounding community. After obtaining the patient’s history and completing a physical examination, CT or MR imaging data were examined and the patient consented to routine lumbar pressure measurement. When possible, spinal MR images were analyzed to exclude spinal stenosis; in select cases, MR imaging studies were requested in patients with gait disturbance and reported lower-back pain while walking.

In all cases, the symptoms of gait disturbance, dementia, and incontinence with associated ventriculomegaly were without antecedent cause, and idiopathic NPH was diagnosed on the basis of clinical evaluation. Subsequently, all patients with idiopathic NPH underwent a lumbar tap to measure CSF resistance. Following this procedure, all patients were admitted to the hospital neurosurgical service for a 3-day ELD of CSF. A shunt procedure was then offered to patients who had experienced clinical improvement from the ELD. As time progressed, the predictive value of ELD was estimated and a shunt procedure was offered to patients who had not experienced improvement with drainage, following a careful explanation of risks and the benefits. In many cases, these patients and their families requested shunt surgery knowing that the probability of improvement was minimal.

Lumbar Pressure Measurement and Resistance Testing

Lumbar pressure measurement was performed under aseptic conditions in the outpatient clinic. Each patient was asked to lie on his or her side on the examining table, and aseptic conditions in the outpatient clinic. Each patient was asked to stop anticoagulant therapies 5 days prior to hospital admission. Shortly after admission at the patient’s bedside, an external lumbar drain was placed under sterile conditions by using a 16-gauge Tuohy needle. A catheter was passed through the needle, and the flow of CSF out the distal end of the catheter was verified before connecting it to a sterile collection bag. The patient’s bed was moved to the lowest position possible, and the bag was situated 5 or 10 cm below this level. In a few cases, the bag was lowered below 10 cm to obtain adequate CSF flow. The attending nurse was asked to open the collection bag valve each hour, to drain 10 ml, and to close the valve. No effort was made to maintain the drip at a fixed rate, and once the bag valve was opened the 10-ml CSF collection required only 3 to 5 minutes.

Cerebrospinal Fluid Collection

Each patient was asked to lie flat in bed during the 3-day check of the fluid lines to ensure that they were completely filled, the opening pressure in the patient was recorded using simultaneously the pressure monitor and the computer software, which provided an electronic stripchart of pressure that could be saved electronically.

Measurement of CSF Resistance

The resistance to CSF outflow was measured using the bolus technique. After establishing a steady lumbar pressure, a 5-ml fluid sample was obtained for analysis. This fluid was replaced by an equal amount of sterile saline to return to the initial opening pressure. When the pressure stabilized, the stopcock was turned, opening the syringe to the patient, and a 4-ml bolus of sterile saline was injected at a rate of 1 ml/second. The stopcock was immediately closed at the end of the injection, thereby opening the patient’s pressure line to the gauge and the computer. The lumbar pressure increased sharply and then gradually decreased over time. The values for initial pressure, peak pressure, and volume of injected fluid permitted calculation of the PVI according to the following equation: \( \Delta \text{volume} / \log \left( \frac{P_p}{P_o} \right) = \frac{t}{H_{9004}} \), where \( \Delta \text{volume} \) is the volume of injected fluid (in millimeters), \( P_p \) the peak pressure (in millimeters of mercury), and \( P_o \) the initial pressure before injection (in millimeters of mercury).

Similarly, outflow resistance \( R_o \) was calculated with knowledge of the PVI, and a pressure was selected on the return curve at 1, 1.5, and 2 minutes, according to the equation: \( R_o = t \left( \log \left( \frac{P_v}{P_v + \text{initial pressure}} \right) \right) \left[ \left( P_v \right) \left( P_v + \text{initial pressure} \right) \right] \), where PVI is computed as previously described, \( t \) the time (in seconds) when a pressure \( P_v \) is selected on the return curve, \( P_v \) the initial pressure before injection, and \( P_v \) the peak pressure immediately after injection. The \( R_o \) values from each of these time points were averaged to yield one \( R_o \) value for the bolus. Subsequently, the bolus injection was repeated at least three times and the \( R_o \) values for all three injections were averaged to yield the final \( R_o \) value for the patient. In the event of patient movement or disturbance, the ICP waveform fluctuated and thus these measures were not used in the calculation.

External Lumbar Drainage

Following measurement of \( R_o \), a patient was admitted to the hospital for ELD usually within 2 weeks of the outpatient clinic visit. Each patient was asked to stop anticoagulant therapies 5 days prior to hospital admission. Shortly after admission at the patient’s bedside, an external lumbar drain was placed under sterile conditions by using a 16-gauge Tuohy needle. A catheter was passed through the needle, and the flow of CSF out the distal end of the catheter was verified before connecting it to a sterile collection bag. The patient’s bed was moved to the lowest position possible, and the bag was situated 5 or 10 cm below this level. In a few cases, the bag was lowered below 10 cm to obtain adequate CSF flow. The attending nurse was asked to open the collection bag valve each hour, to drain 10 ml, and to close the valve. No effort was made to maintain the drip at a fixed rate, and once the bag valve was opened the 10-ml CSF collection required only 3 to 5 minutes.
Diagnosis and management of idiopathic NPH

drainage period and instructed to call the nurse when he or she wished to get out of bed to use the toilet. In this way, we could ensure that the valve was closed to drainage when the patient was upright. The nurse monitored the amount of fluid collected per hour on a separate form, which was later placed in the medical record. On the 2nd and 3rd days of drainage, the patient was permitted to have meals while sitting in a chair for approximately 30 minutes.

Ambulation Before and After ELD

On the day of the clinic visit, each patient was videotaped while rising from a chair and walking at a normal pace along a corridor for a distance of 10 m. The patient was then asked to turn and return to the chair. When approximately halfway, the patient was asked to tandem walk for approximately five steps. Thereafter, the patient was asked to walk to the chair, turn, and sit. The video was then analyzed by an independent observer, who classified the type of walk (for example, shuffling, or wide based gait), the ability to tandem walk (easy, difficult, or impossible), and the difficulty involved in rising from the chair (easy, difficult, or impossible). The steps per minute were calculated from an offline analysis of the videotape and entered into the patient’s record. Additionally, gait was rated as normal; mildly impaired, unsteady but unassisted walking possible; moderately impaired, inability to walk without assistance; or severely impaired, inability to walk even with assistance. A second video was obtained once the drain was removed following lumbar drainage.

Mental disturbances were evaluated using the MMSE\textsuperscript{10} and a series of neuropsychological tests\textsuperscript{20} including the Galveston Orientation and Amnesia Test, Controlled Oral Word Association Test\textsuperscript{1} and Benton Visual Retention Test–Revised.\textsuperscript{1} Digit Span Forward and Backward tasks were used to test attention and concentration.\textsuperscript{21} The Wechsler Memory Scale–Revised Logical Memory Test\textsuperscript{13} was administered to assess auditory memory. The Rey Auditory Verbal Learning Test\textsuperscript{14} was administered as a measure of verbal acquisition skills.

Memory impairment was characterized as normal; mildly impaired, testing required to demonstrate deficit; moderately impaired, difficulty noted by physician support staff or family; or severely impaired, disoriented but delirium excluded.

Bladder function was assessed and described as normal if there was no urgency, increased frequency, or incontinence. Impairment in urinary function was categorized as mild if the patient experienced increased urinary urgency; moderate if the patient had stress, urge, or overflow incontinence; and severe if the patient experienced any of the severe forms of incontinence or total incontinence.

Ventriculomegaly was determined based on an Evans Index\textsuperscript{2} equal to or greater than 0.30 or an FHI of 0.4. Note that the FHI is defined as the maximal width of the frontal horns at their extreme and the brain width along the same axis. The Evans Index is defined as the maximal width of the frontal horns measured at their extreme to the maximal biparietal diameter.

Prior to Discharge

Prior to drain removal, CSF pressure was measured by connecting the extension tubing to a strain gauge and pressure monitor (Codman). After the pressure was measured, the drain was removed and a CT scan was obtained to ensure that drainage had not resulted in a hygroma or SDH. When the CT scan was cleared by the attending physician, the patient and caregiver were given instructions to complete 10-day surveys in which they were asked to grade the patient’s daily status as improved, same, or worse. The patient was then scheduled to appear at the next clinic to discuss clinical recommendations with regard to shunt placement.

Statistical Analysis

For continuous data, two-sided t-tests were applied. For categorical data, two-sided chi-square or exact tests were applied. A level of 0.05 was considered significant. Values are represented as the means ± standard deviations.

Results

General Response to ELD Protocol

The patients tolerated the infusion study, which was usually conducted in the outpatient clinic, and the subsequent in-hospital ELD protocols. The nursing staff had no difficulty in obtaining the required volume of CSF per hour. On four occasions, the lumbar catheter was removed accidentally by the patient. When removal occurred early in the drainage cycle, the drain was replaced. When it occurred after a reasonable volume of CSF had been collected (> 300 ml), the drain was removed and the patient discharged once we had performed a postdrainage CT study, MMSE, and video.

Patient Age and Sex Distribution

The mean age of men was 74.6 years (range 59–89 years) and that of women was 75.2 years (range 61–85 years). The sex distribution was almost equal: 74 men and 77 women. In general, the older patients were in reasonably good health, although there was significant comorbidity.

Opening Pressure and PVI

The lumbar pressure measured using a conventional strain gauge transducer varied extensively; pressures as low as 2 mm Hg and as high as 20 mm Hg were observed. The mean pressure in all patients equaled 9.4 ± 4.6 mm Hg. The distribution of opening pressures is depicted in Fig. 1. Given that the infusion study required only 20 minutes or less of recording, B wave activity was observed in relatively few patients during this short interval. Pulsatile pressures also varied based on the PVI and initial pressure level and were inconsistent among patients. Both respiratory and cardiac components were present in all recordings. There was no significant difference in opening pressure between patients who did (9.4 ± 4.6 mm Hg) and those who did not improve (10 ± 4 mm Hg) on ELD. Likewise, there was no significant difference in PVI between patients who experienced improvement and those who did not following ELD.

Patient Symptoms and ELD Outcome

Among the cohort of 151 patients, 100 (66.2%) improved after ELD. It was interesting to compare the number and type of symptoms seen on initial presentation with patient
outcome following ELD. Among the 100 patients whose condition improved postdrainage, the greatest improvement was associated with patients who had not presented with the complete triad of impaired gait, incontinence, and dementia. Of 86 patients with the complete triad, only 59.3% improved compared with improvements of 88.2 and 83.9% in patients with an impaired gait only and an impaired gait plus dementia, respectively. Other patient groups were too small to draw any firm conclusions (Table 1). Based on these data, however, patients with symptoms of a disturbed gait alone and those with an impaired gait plus dementia or incontinence have significantly better outcomes after ELD compared with patients who present with the complete triad (chi-square test, \( p < 0.0006 \)).

As stated previously, patients with an impaired gait—alone or in combination with any other symptom—had a significantly better outcome after ELD compared with patients who did not have gait disturbance (chi-square test, \( p < 0.005 \)). Note that most patients with idiopathic NPH had more than one type of gait difficulty (Table 2). Most patients presented with difficulty in tandem walking and balance, although no specific type of gait disturbance was predictive of ELD outcome.

In addition to performing a clinical evaluation of gait improvement, we documented the steps per minute before and after ELD as well as the number of steps used in turning.

### TABLE 1

**Comparison of symptoms on initial presentation and ELD outcome in 151 patients with idiopathic NPH**

<table>
<thead>
<tr>
<th>Symptoms on Admission</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients</td>
<td>151 (100)</td>
</tr>
<tr>
<td>Improved</td>
<td>100 (66.2)</td>
</tr>
<tr>
<td>Not improved</td>
<td>51 (33.8)</td>
</tr>
<tr>
<td>Total no. of patients</td>
<td>151</td>
</tr>
<tr>
<td>Total no. of patients</td>
<td>151</td>
</tr>
<tr>
<td>Total no. of patients</td>
<td>151</td>
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<td>Total no. of patients</td>
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<tr>
<td>Total no. of patients</td>
<td>151</td>
</tr>
<tr>
<td>Total no. of patients</td>
<td>151</td>
</tr>
</tbody>
</table>

### TABLE 2

**Types of gait disturbance seen in 120 patients with idiopathic NPH**

<table>
<thead>
<tr>
<th>Type of Gait Disturbance with Gait Deficit</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shuffling w/ Gait Deficit</td>
<td>47 (39)</td>
</tr>
<tr>
<td>Improvement After ELD</td>
<td>36 (77)</td>
</tr>
<tr>
<td>No Improvement After ELD</td>
<td>11 (23)</td>
</tr>
<tr>
<td>Magnetic gait w/ Gait Deficit</td>
<td>20 (17)</td>
</tr>
<tr>
<td>Improvement After ELD</td>
<td>17 (85)</td>
</tr>
<tr>
<td>No Improvement After ELD</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Wide-based gait w/ Gait Deficit</td>
<td>52 (43)</td>
</tr>
<tr>
<td>Improvement After ELD</td>
<td>40 (77)</td>
</tr>
<tr>
<td>No Improvement After ELD</td>
<td>12 (23)</td>
</tr>
<tr>
<td>Difficulty in rising from chair w/ Gait</td>
<td>40 (33)</td>
</tr>
<tr>
<td>Improvement After ELD</td>
<td>26 (65)</td>
</tr>
<tr>
<td>No Improvement After ELD</td>
<td>14 (35)</td>
</tr>
<tr>
<td>Difficulty in turning w/ Gait</td>
<td>58 (48)</td>
</tr>
<tr>
<td>Improvement After ELD</td>
<td>42 (72)</td>
</tr>
<tr>
<td>No Improvement After ELD</td>
<td>16 (28)</td>
</tr>
<tr>
<td>Incontinence w/ Gait Deficit</td>
<td>102 (85)</td>
</tr>
<tr>
<td>Improvement After ELD</td>
<td>67 (66)</td>
</tr>
<tr>
<td>No Improvement After ELD</td>
<td>35 (34)</td>
</tr>
<tr>
<td>Difficulty in imbalance w/ Gait</td>
<td>112 (93)</td>
</tr>
<tr>
<td>Improvement After ELD</td>
<td>80 (71)</td>
</tr>
<tr>
<td>No Improvement After ELD</td>
<td>32 (29)</td>
</tr>
</tbody>
</table>

* Gait assessment was conducted in 120 of 151 patients; 18 patients were wheelchair bound and the remaining 13 patients did not have gait disturbance. Percentages in this column were based on the assessment of 120 patients.

180°. Before ELD, the mean number of steps per minute was 80 ± 12 (55 patients); after ELD, the mean number of steps per minute was unchanged at 79 ± 12. The mean number of turning steps before ELD was 5.6 ± 2.8; after ELD and prior to discharge, the mean number of turning steps reduced to 4.4 ± 2.3. This reduction in turning steps was statistically significant (\( p = 0.0044 \)).

**Severity of Symptoms and ELD Outcome**

Among patients whose symptoms improved following ELD, the response to drainage correlated with the severity of symptoms demonstrated on initial clinical presentation (Fig. 2). For example, patients enduring mild and moderate gait disturbance experienced significant improvement after drainage compared with those suffering from severe gait disturbance (\( p = 0.0016 \)). Similarly, patients subject to mild or moderate memory loss experienced significant improvement compared with those subject to severe memory loss (\( p = 0.0064 \)). Finally, patients initially demonstrating mild symptoms of incontinence experienced significant improvement compared with those exhibiting moderate and severe symptoms (\( p = 0.016 \)).

**Effect of ELD on Neuropsychological Performance**

We found no difference between neuropsychometric parameters assessed post-ELD and baseline levels (Fig. 3). Only one test—delayed auditory memory—showed significance (\( p < 0.05 \)). Note, however, that this finding could have been observed by chance considering the number of tests administered.

**Correlation of CSF Resistance and ELD Outcome**

The ELD outcome was compared with CSF outflow resistance (\( R_o \)) values less than and greater than or equal to 4 mm Hg/ml/min. Of 44 patients with an \( R_o \) less than 4 mm Hg/ml/min, 20 patients (45.5%) experienced improvement and 24 (54.5%) did not. This difference was not significant. Of 78 patients with an \( R_o \) greater than 4 mm Hg/ml/min, 64 patients (82%) improved with ELD and 14 (18%) did not.
Diagnosis and management of idiopathic NPH

This difference was highly significant ($p < 0.0001$). Based on these data, the ability of an $R_o$ value greater than or equal to 4 mm Hg/ml/min to predict ELD outcome has a sensitivity of 0.75 (95% CI 0.67–0.84), specificity of 0.63 (95% CI 0.48–0.78), positive predictive value of 0.82 (95% CI 0.75–0.89), and a negative predictive value of 0.53 (95% CI 0.44–0.62) and is associated with an overall accuracy of 0.72 (95% CI 0.65–0.79). An example of the ICP course in a patient with a high $R_o (\geq 4$ mm Hg/ml/min) and another with a low $R_o (< 4$ mm Hg/ml/min) is shown in Fig. 4. Because not all patients underwent shunt insertion, it was not possible to calculate the sensitivity of $R_o$ to predict shunt outcome.

**Correlation of ELD With Shunt Outcome**

Of the 100 patients who had experienced improvement post-ELD, 84 underwent shunt surgery; 76 (90.5%) of these 84 patients improved following shunt insertion. After explaining to patients whose condition did not improve on ELD (51 patients) that the probability of benefiting from shunt placement was low, 18 elected to undergo surgery. Four of these 18 patients experienced improvement, whereas 14 did not experience improvement 3 and 6 months and 1 year after shunt surgery. Of the four patients whose condition improved, three demonstrated mild improvement in gait, which was sustained for at least 1 year; the remaining patient had mild improvement in gait and incontinence, which was transient and not sustained at the 1-year follow up. The number of patients who improved on ELD and after shunt surgery compared with those who did not was statistically significant ($p < 0.0001$; Table 3). Based on these data, the use of ELD in predicting shunt outcome has a sensitivity of 0.95 (95% CI 0.84–0.90), specificity of 0.64 (95% CI 0.44–0.84), positive predictive value of 0.90 (95% CI 0.72–1.00), negative predictive value of 0.78 (95% CI 0.70–0.80), and accuracy of 0.88 (95% CI 0.83–0.93).

**Influence of Patient Age on ELD Outcome**

The mean age in the 151 patients equaled 74.9 years (range 59–89 years). We questioned whether there was an age beyond which ELD would cease to be an effective prognostic indicator and/or a percentage of patients with a positive ELD outcome that would not be reflected in an improved shunt outcome. Several interesting answers were found. First, patients with an age younger than 75 years had...

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**TABLE 3**

<table>
<thead>
<tr>
<th></th>
<th>Improvement From ELD</th>
<th>No Improvement From ELD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of Patients (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total no. of patients</td>
<td>100 (66.2)</td>
<td>51 (33.8)</td>
</tr>
<tr>
<td>shunt surgery</td>
<td>84/100 (84.0)</td>
<td>18/51 (35.0)</td>
</tr>
<tr>
<td>improvement w/</td>
<td>76/84 (90.5)*</td>
<td>4/18 (22.2)</td>
</tr>
<tr>
<td>shunt surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no improvement w/</td>
<td>8/84 (9.5)</td>
<td>14/18 (77.7)</td>
</tr>
<tr>
<td>shunt surgery</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* $p < 0.0001$, compared with patients who did not improve on ELD.

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Fig. 2. Bar graphs demonstrating the percentage of patients whose condition improved following ELD. **Upper:** Patients were classified according to the severity of gait disturbance. Although all patients shown experienced improvement, proportionally fewer patients with a severe gait disturbance improved after ELD. * $p = 0.016$, rank sum test. **Center:** Patients were classified according to the severity of dementia. Although all patients shown experienced improvement with ELD, those with mild or moderate memory loss had a greater tendency to improve with drainage compared with those patients with severe memory disturbance. **$p = 0.006$, rank sum test.** **Lower:** A greater number of patients who had mild or moderate (mod) urinary incontinence on presentation demonstrated improvement following ELD compared with patients with severe incontinence. * $p = 0.033$, rank sum test.

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a higher rate of improvement on ELD (78%) compared with patients 75 years or older (57%; Table 4). This result was highly significant \(p < 0.007\) (chi-square), indicating that proportionally fewer patients older than 75 years would likely improve on shunt surgery compared with those younger than 75 years. Second, improvement on ELD in patients younger than 75 years of age who presented with the symptom triad was significantly higher (81%) than that in patients 75 years or older (40%; \(p < 0.005\)), indicating that patients 75 years or older with the symptom triad were less likely to improve on shunt surgery. Interestingly, in patients without the triad, ELD outcome was independent of age, thus indicating that patients were more likely to improve on shunt placement during the intermediate course of NPH and prior to reaching the stage at which all three symptoms were present.

### Influence of Age on Shunt Outcome

It is conceivable that the elderly patient may improve following short-term drainage (ELD) and yet not improve after long-term drainage. We explored this idea by comparing shunt outcome as a function of age (Table 4). The greater proportion of patients who underwent shunt placement had been evaluated following ELD. Thus, the influence of age on shunt outcome also referred to patients who improved on ELD. In those who improved on ELD, there was no difference in shunt outcome in patients younger than or those 75 years of age or older. Improvement on shunt insertion was 90% or greater. Similarly, there was no significant difference in shunt outcome as a function of age in patients with the complete symptom triad or disturbed gait plus incontinence or dementia. In summary, if the patient improved on ELD, there was a greater than 90% probability of improving on shunt placement that was independent of age.

### Brain Tissue Response to Shunt Placement in the Elderly Patient

In patients whose condition improved, we occasionally observed a reduction in ventricle size, which could be easily demonstrated on CT studies or on remarkable recovery of brain tissue after shunt insertion. Example imaging studies from a 78-year-old patient with such a remarkable recovery 11 months after shunt placement are shown in Fig. 5. We analyzed the FHI in patients (27) whose condition had improved after drainage and shunt placement, and who had follow-up CT studies from within 6 months to 1 year of surgery. The FHI in this patient group before surgery equaled 0.46 ± 0.04. The FHI measured at the follow up was 0.40 ± 0.05. The reduction in ventricle size among

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**TABLE 4**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Patients w/ ELD (%)</th>
<th>No. of Patients w/ Shunt Placement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Improvement</td>
<td>No Improvement</td>
</tr>
<tr>
<td>age &lt; 75 yrs</td>
<td>52 (78)*</td>
<td>15 (22)</td>
</tr>
<tr>
<td>age ≥ 75 yrs</td>
<td>47 (57)</td>
<td>36 (43)</td>
</tr>
<tr>
<td>age &lt; 75 yrs &amp; symptom triad</td>
<td>30 (81)†</td>
<td>7 (19)</td>
</tr>
<tr>
<td>age &lt; 75 yrs &amp; symptom triad</td>
<td>22 (73)</td>
<td>8 (27)</td>
</tr>
<tr>
<td>age ≥ 75 yrs &amp; symptom triad</td>
<td>20 (40)</td>
<td>29 (60)</td>
</tr>
<tr>
<td>age ≥ 75 yrs &amp; symptom triad</td>
<td>7 (79)</td>
<td>7 (21)</td>
</tr>
</tbody>
</table>

* \(p < 0.01\), compared with ELD outcomes in patients 75 years or older.
† \(p < 0.005\), compared with ELD outcomes in patients 75 years or older with the complete symptom triad.
patients who improved was statistically significant (p < 0.001). The number of patients who did not improve after ELD and shunt placement together with a follow up between 6 months and 1 year was small (six patients). Among this group, the FHI prior to surgery equaled 0.45 ± 0.04; at follow up, the FHI equaled 0.45 ± 0.05 and there was no reduction in ventricle size. Of equal importance is the observation of no reduction in FHI before and after 3-day drainage despite the improvement in NPH symptoms.

Response to Survey Following Discharge

Most patients eagerly returned the survey at the follow up in the clinic to discuss the next step in treatment. Patients who improved following ELD reported a marked improvement in their symptoms immediately after discharge followed by a gradual return to baseline levels over a 10-day period (Fig. 6). This patient and caregiver survey was consistent. The self-evaluation by patients who believed that they did not improve after ELD agreed with the clinical assessment. Allowing the family to document the outcome of ELD gave greater assurance to patients with a positive ELD outcome that shunt surgery would be worthwhile.

Patient Complications

The complications associated with lumbar pressure measurements and infusion tests were minimal and consisted of mild to moderate headache (12 [8%] of 151), which usual-
...and it was this differentiation that allowed the
In our view, the accuracy of pre-

TABLE 5
Shunt complications in patients with idiopathic NPH

<table>
<thead>
<tr>
<th>Complication</th>
<th>Total</th>
<th>Complete Recovery</th>
<th>Partial Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>major (9.8%)</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>infection</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>SDH</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>hygroma</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>minor (13.7%)</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>headache</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>hearing loss</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

ly resolved within 12 hours. The only serious complication associated with ELD was infection, which occurred in two (1.3%) of 151 patients. Another four patients (2.6%) suffered headache, which resolved within 1 to 3 days. There were 9.8% major complications associated with shunts (Table 5), including SDH (three [3%] of 102), hygroma (three [3%] of 102), infection (three [3%] of 102), and sinus thrombosis (one [0.98%] of 102). There were 13.7% minor complications, including headache (five [5%] of 102), hearing problems (five [5%] of 102), and double vision (four [4%] of 102). The rate of recovery from these complications is shown in Table 5.

Discussion

Idiopathic NPH is readily diagnosed based on a patient’s clinical presentation and brain imaging studies. Nonetheless, determining which patient will benefit from shunt placement is more problematic. Data in the present study affirm that improvement in gait immediately following ELD is the best prognostic indicator of a positive shunt outcome, with a prediction accuracy greater than 90%. We also found that bolus resistance testing is useful as a prognostic tool that does not require hospitalization, can be performed in an outpatient setting, and has an overall accuracy of 72%. Equally important is the finding that improvement with shunt insertion is independent of age up to the ninth decade of life in patients who had improved on ELD.

Classification of NPH

In the first report of NPH in 1965, Hakim and Adams discussed the outcome of three patients, only one of whom was considered to have idiopathic NPH. This patient improved on shunt placement, and as a result a new treatment was introduced, alleviating symptoms of gait disturbance, incontinence, and dementia. Note, however, that the treatment of any patient with NPH during the next 40 years became controversial, because the outcome in many with so-called NPH was less than favorable. This result was due in part to the treatment of both idiopathic and secondary NPH as a single entity, although it became clear over time that the two must be separated. The concept of primary (idiopathic) and secondary (all known causes) NPH was introduced by Black, and it was this differentiation that allowed the specific problems associated with idiopathic NPH to be addressed. First, the disease diagnosis was confounded by the notion that if the patient at risk for NPH improved on shunt placement, the diagnosis was accurate and indeed the patient had NPH. In this report, however, we posited that idiopathic NPH may have progressed to a stage at which the patient may be refractory to treatment. With this view, there must be a clear separation between diagnostic criteria based on clinical presentation and those based on surgical outcome.

Opening Pressure in Idiopathic NPH

Based on Ekstedt’s study in 100 patients, normal pressure varies over a relatively narrow range of 8.6 to 13.1 mm Hg, with a mean pressure of 10.4 ± 1.43 mm Hg. In contrast, the ICP distribution observed in the present study in patients with idiopathic NPH extended over a much wider range of 2 to 20 mm Hg, with a mean pressure of 9.4 ± 4.6 mm Hg. Given the relatively large number of patients in this study, it was reasonable to extend the range of so-called normal pressure in idiopathic NPH to an upper limit of at least 18 mm Hg based on two standard deviations from the mean. What factors account for the higher pressure level? Considering the equation for steady-state ICP, one would expect the higher opening pressures to be associated with higher CSF resistance values, although such was not the case. Using the estimated rate of normal CSF formation of 0.35 ml/minute, an increase in CSF resistance from 2 to 10 mm Hg/ml/minute, a fivefold increase, would result in an ICP increase from only 10 to 12.8 mm Hg. Thus, the opening pressure in patients with idiopathic NPH is an insensitive indicator of CSF resistance. We posit that the ICP levels associated with idiopathic NPH are more a function of venous pressure than CSF resistance. Additional studies are necessary to clarify this issue, however.

Shunt-Responsive NPH

In the study by Vanneste and colleagues, patients predicted to be shunt-responsive based on clinical and CT criteria had an overall improvement of 58% after shunt insertion. Data from other studies have shown that favorable responses to shunt placement based on clinical and CT criteria, especially in the elderly population, which has both NPH symptoms and significant comorbidity. If all patients in our study had undergone shunt insertion based on clinical and CT criteria, we would have achieved an improvement rate of only 66% (100 of 151 cases). This rate is slightly higher than the improvement rates reported in earlier studies. The results of using ELD to predict shunt responsiveness increased our predictive accuracy to 88%. Williams, et al., studied 86 patients with NPH by using controlled lumbar drainage; however, the number of patients with idiopathic NPH was not specified. Nevertheless, among the 47 patients who underwent shunt surgery, the sensitivity of ELD was 97% and specificity was 60%—results very close to those in our study of ELD (95% sensitivity and 64% specificity).

Value of CSF Resistance Testing

All patients entered into the present study underwent both CSF testing and ELD, and as a result we had a unique opportunity to evaluate the sensitivity of CSF resistance...
testing in predicting ELD outcome. This opportunity was important because $R_c$ can be measured in an outpatient setting and could possibly eliminate hospitalization for ELD. We found that patients with an $R_c$ greater than 4 mm Hg/ml/min are most likely to have a positive ELD response ($p < 0.0001$). This value is slightly lower than the 6 mm Hg/ml/min used in posttraumatic hydrocephalus in an earlier study.\(^19\) With regard to predicting ELD outcome, bolus $R_c$ had a positive predictive value of 82% and a sensitivity of 75%. The overall accuracy of $R_c$ in predicting ELD outcome equaled 72%. We believe that $R_c$ testing is a valuable supplementary test that increases the predictive accuracy of potential shunt responders beyond that of clinical criteria alone. The fact that we tended to place shunts in only those patients who improved on ELD prevented us from evaluating the accuracy of resistance testing to predict shunt outcome directly.

Several methods can be used to determine CSF resistance, and the absolute value of $R_c$ varies with the method used. For this reason, it has been difficult to compare the results of other studies. For example, Malm, et al.,\(^18\) prospectively evaluated the predictive value of $R_c$ by using a modification of the pressure technique. They reported that the CSF resistance in the group of 35 patients with idiopathic NPH was high, measuring $8.2$ mm Hg/ml/min. Nonetheless, these authors concluded that resistance testing could not predict the outcome of gait or neuropsychological indices. In contrast, Takeuchi, et al.,\(^2\) used the bolus method to predict outcome in 25 patients who had undergone shunt surgery and reported a sensitivity and specificity of 100 and 92%, respectively. These authors used an epidural monitor, and the mean $R_c$ value in patients improving after surgery equaled $35$ mm Hg/ml/min. The study published by Boon, et al.,\(^4\) reported results in 101 patients with the objective of predicting shunt outcome based on CSF resistance. The study included a mixture of primary and secondary NPH, although most of the patients had idiopathic NPH. Using the constant-flow technique for the measurement of $R_c$, they found that $R_c$ values correlated with primary outcome measures by using linear regression methods and recommended $18$ mm Hg/ml/min as the threshold for shunt insertion. At $18$ mm Hg/ml/min, the sensitivity and specificity equaled 46 and 87%, respectively, with a calculated overall prediction accuracy of 67%. The predictive accuracy achieved using the bolus technique in our study (72%) is slightly higher than the value reported by Boon and colleagues.

In summary, CSF resistance testing is a valuable supplementary test that can be performed in an outpatient setting while measuring opening pressure with a lumbar tap.

The Non-Responder to ELD

The hypothesis underlying ELD is that the response to short-term drainage is predictive of the response to long-term drainage achieved by shunt placement. In our study, 51 patients did not improve on ELD. Studies by other investigators who used ELD vary in their results. In the retrospective study of 32 patients with idiopathic NPH by Haan, et al.,\(^11\) 10 improved after a single lumbar tap and underwent shunt placement. The remaining 22 patients, who had not improved with the tap, underwent ELD; all 22 experienced improvement. These authors concluded that ELD is a safe and effective means of predicting shunt outcome. In a prospective study of 43 patients with idiopathic NPH, Walchenbach and colleagues,\(^32\) who used the drainage method described by Haan, et al.,\(^11\) reported a positive predictive accuracy of 87% with ELD and a negative predictive accuracy of 36%. Walchenbach, et al., concluded that shunt placement in patients who improve on ELD is justified. They also concluded that patients who do not improve following drainage should be considered for shunt placement given the high percentage of patients in the present study who improved despite a negative ELD outcome.

In the study by Walchenbach and colleagues, of the 51 patients who did experience improvement on ELD, 18 requested shunt surgery despite our prediction of potential reduced benefits. Of the 18 who received a shunt, four patients showed some degree of gait improvement. These numbers are too small at present to draw accurate conclusions, but as our study continues we hope to clarify this issue further. Presently, we explain to our patients that there is an approximately one-in-five chance that they will experience improvement with shunt placement even though they received no benefit from ELD.

Comparison of ELD With the Tap Test

There are no direct comparisons between a CSF tap test and ELD in patients with idiopathic NPH. Nonetheless, in a study of combined idiopathic and secondary NPH, Wikkelso, et al.,\(^34\) who introduced the 50-ml CSF tap, reported a sensitivity of 68% and specificity of 100% in 24 patients available to follow up who had received shunts. Malm, et al.,\(^35\) could not confirm the results of Wikkelso and colleagues in their study of 25 patients with idiopathic NPH. Malm, et al., reported that only 16 of the 25 patients who improved with gait after shunt insertion showed improvement with the tap test and thus concluded that the tap test was not predictive of shunt outcome. In general, the positive predictive value of a CSF tap based on studies by Malm,\(^18\) Walchenbach,\(^32\) and Haan,\(^11\) and their colleagues ranges from 73 to 100%. In summary, a CSF tap of 45 to 50 ml is most expedient and has a high positive predictive value for shunt outcome. Nevertheless, many patients who would potentially benefit from shunt placement would be lost as a result of the tap test’s poor sensitivity, which ranges from 26 to 62%.\(^3,11,18,32\) Thus, the highest overall accuracy in terms of shunt outcome prediction, based on our study data, is provided by ELD.

Patient Response to ELD

Our assessment of ELD outcome occurred at 72 hours and consisted of both video and neuropsychological documentation and general clinical evaluation of symptoms following ELD. The improvement described on ELD was primarily based on clinical assessment of gait and balance when the 72-hour drainage protocol was completed. The 3-day hospitalization was too short to assess any change in the frequency of urination. With regard to dementia, in contrast to some reports following large volume taps,\(^18\) we found no significant improvement on MMSE or neuropsychological parameters, although there was a general sense of improvement with regard to verbalization, initiation of conversation, and responses to questions during daily rounds in patients whose gait and balance had improved. We speculate that were neuropsychological testing

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**Diagnosis and management of idiopathic NPH**
performed months after shunt placement, we would probably find a significant difference. Nevertheless, a short practical test of memory and executive function, which can be administered at the patient’s bedside or at the clinical follow up, is still lacking.

Objective Gait Analysis in the Patient With NPH

There is still a need for a simple practical test that would provide a quantitative index for the improvement of gait disturbance. We analyzed the steps per minute over a fixed length of 30 ft on the assumption that doing so would reflect both the patient’s increase in stride length as the number of steps decreased and the resulting increase in walking speed. With improvement, however, the number of steps decreased and the time required to traverse the 30-ft length decreased. Because both the numerator and the denominator decreased, the ratio remained the same. If one uses the number of steps only, the variability among patients does not lend itself to an analysis of larger patient groups. Among the scales used in quantitative gait analysis, the only significant quantitative feature was the number of steps used in turning 180°. At baseline, the patient exhibited a multistep turn; the number of steps used in turning decreased following shunt placement. More work is needed to derive a gait scale that reflects improvement following shunt insertion and that is objective and easily quantified.

Transient Effect of ELD

All patients were discharged following a routine CT study at the end of the drainage protocol to rule out the occurrence of SDH or hygroma post-ELD. It is interesting to note the gradual return to baseline function following discharge in patients who improved. Most improvement occurred immediately following discharge and returned to near baseline within 10 days. The volume of CSF removed in the study cohort was a mean of 465 ± 135 ml, and the time required to refill the original CSF volume was much shorter than 10 days. The gradual return to baseline over a longer time period was probably due to the fact that patients continued to drain through the puncture wound until the CSF leak was healed. The patient and caregiver survey was invaluable in allowing the family to document the outcome of ELD and gave greater assurance to patients with positive ELD outcome that shunt surgery would be worthwhile.

Complications and Comorbidity

Overall, ELD complications are low (1.3%), with the major complication consisting of the potential for infection. In the two cases of infection among the 151-patient cohort, both were successfully treated. No major complication occurred on resistance testing. Shunt complications were reasonably low as major complications, which included both SDH and hygroma (6%). Nevertheless, other problems with shunt insertion were not insignificant. Although troublesome, the improvement in response to shunt placement in these patients had a more significant impact than the transient complications resulting from surgery.

Conclusions

External lumbar drainage is a highly prognostic and safe procedure with a sensitivity of 92% for identifying patients with NPH most likely to benefit from shunt surgery. Cerebrospinal fluid resistance testing provides a predictive accuracy of 72% and remains useful because it can be performed in an outpatient setting. Finally, improvement on shunt placement is independent of patient age up to the ninth decade of life in those whose condition improved post-ELD.

References


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