Research paper

Normal pressure hydrocephalus: long-term outcome after shunt surgery

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ABSTRACT

Background/objective: Little is known about the long-term clinical course and management of patients with normal pressure hydrocephalus (NPH) treated by cerebrospinal fluid (CSF) shunting.

Methods: We retrospectively reviewed records of 55 patients diagnosed with idiopathic NPH (INPH) and treated with CSF shunts, all of whom were followed for more than 3 years after the original shunt surgery. At each annual follow-up visit, the patient was assessed by Folstein Mini Mental State Examination, detailed clinical evaluation of gait and assessment of headache, cognition, gait or urination, as assessed by the patient and relatives.

Results: The mean duration of follow-up was 5.9 ± 2.5 years. There was an overall sustained improvement among all symptoms. Gait showed the highest maintenance of improvement over baseline (83% at 3 years and 87% at the last analysed follow-up of 7 years), cognition showed intermediary improvement (84% and 86%, respectively), and urinary incontinence showed the least improvement (84% and 80%, respectively). Fifty-three percent of patients required shunt revisions. Indications for revision included shunt malfunction (87%), infection (10%) and change of shunt configuration (3%). Overall, 74% revisions resulted in clinical improvement.

Conclusions: Clinical improvement of patients with NPH can be sustained for 5–7 years in some patients with NPH, even if shunt revision surgery is needed multiple times. With earlier diagnosis and treatment of NPH and the increasing lifespan of the ageing population, the need for long-term follow-up after shunt surgery for NPH may be greater than it was in the past. Monitoring, identification and treatment of shunt obstruction is a key management principle.

Normal pressure hydrocephalus (NPH) is a treatable cause of dementia that may account for up to 6% of causes of dementia.[1 2] Hakim and Adams were the first to describe the symptoms and signs that include gait apraxia and imbalance, progressive memory loss, urinary incontinence and normal cerebrospinal fluid (CSF) pressure on lumbar puncture.[3 4]

NPH can be primary or secondary to other disease processes that cause inflammation within the arachnoid space, such as subarachnoid haemorrhage, traumatic brain injury or meningitis that probably interferes with CSF resorption at the arachnoid granulations.[5] In secondary NPH, often the CSF pressure is moderately elevated.[6] As many as half of patients with NPH have no identifiable risk factor, in which case it is called idiopathic NPH (INPH). The causes implicated in INPH include asymptomatic fibrosing meningitis[6] or insufficiency of the transcortical subarachnoid space leading to absorption defect. Whereas secondary NPH can present at any age, INPH usually presents in the sixth or seventh decade of life.[7–9]

The mainstay of therapy for NPH is CSF diversion via a ventriculoperitoneal or ventriculoatrial shunt. Shunting INPH is controversial because of the difficulty in distinguishing it from other neurodegenerative conditions, especially subcortical arteriosclerotic encephalopathy. Thus, accurate diagnosis of INPH is the key to successful treatment. Success is determined by long-term remission of symptoms, which requires long-term follow-up and management of shunt complications. Shunt complications usually require shunt revision surgeries. There is an ongoing debate among neurologists as to whether the benefits outweigh the risks in shunting INPH patients.[10]

Most studies of INPH outcomes have followed patients for no more than 5 years[5 11–17] with varying outcomes. To date, one of the longest studies is by Savolainen,[15] who followed 25 patients for 5 years, and showed that 47% felt their gait to be better, 29% felt their urinary symptoms to be better and 38% felt their memory to be better than in the preoperative stage. Hence, not many studies have elucidated the long-term effects of shunting in INPH patients. We report our experience with patients of INPH followed for more than 3 years and assess the predictors of outcome.

METHODS

Patient selection

We retrospectively reviewed the records of all patients referred to the Johns Hopkins Adult Hydrocephalus Program from 1 January 1993 to 31 December 2005 and identified 55 INPH patients who were followed for 3 or more years after shunt surgery.

Preoperative assessment

Our diagnostic and management algorithm, which is consistent with the 2005 NPH Consensus Guidelines,[18] has been previously published.[19] All patients who were referred for evaluation of INPH were examined clinically by both senior authors (MAW and DR) and a detailed questionnaire was completed by the patients describing their symptoms and comorbid conditions. A computed tomographic (CT) or magnetic resonance imaging (MRI) scan was obtained for all patients to assess ventriculomegaly or additional intracranial pathological features. Patients with ventriculomegaly and at least two clinical features of NPH were admitted to the hospital for 2 days of continuous CSF pressure (Pcsf) monitoring followed by a 3-day trial of controlled CSF drainage.

The spinal catheter (Codman/Johnson & Johnson, Raynham, MA, or Medtronic PS Medical, Goleta, CA) was inserted percutaneously into the lumbar subarachnoid space using a 14-gauge Touhy needle under local anaesthesia at the bedside. Physiological parameters, including Pcsf, were recorded continuously for 2 days. Abnormal Pcsf waveforms were identified only during epochs that were free from artifacts when the record indicated that the transducer was leveled properly and the patient was quiet, usually during sleep or quiet rest.

A 3-day trial of controlled continuous CSF drainage was then performed. The CSF drainage rate was controlled to approximately 10 ml/h (240 ml/d). Patients were examined clinically for their response at least once daily. Response to drainage was defined as objective improvement in gait, cognition or bladder control. Only subjects who had 3 or more years of follow-up are included in this report.

Outcome assessment

Follow-up consisted of clinical and radiological evaluation as indicated evaluation at 1, 3, 6 and 12 months after surgery and yearly thereafter. Follow-up examination was performed by one or both senior authors (MAW and DR) on all patients. At the time of follow-up, patients and their families are routinely reminded of the possibility of shunt malfunction causing return of their NPH symptoms, and are instructed to contact us if this circumstance occurs. All patients underwent the Folstein Mini-Mental State Examination[20] and Tinetti gait scores (after 2000)[21] at each follow-up visit. Patients and their families were also questioned regarding observed cognitive change at home after shunt surgery, with particular attention to functional impairment resulting from dementia. Improvement in cognitive function was defined as at least a three-point improvement in the Mini-Mental State Examination score and improvement in the patient's cognitive function from either the patient's or family's perspective. Improvement in urinary incontinence was defined as a decrease in incidence of urinary frequency, urgency or incontinence that was thought by the patient or family to have improved (often characterised by less dependence on an incontinence undergarment or pad). Improvement in gait was documented by change in detailed clinical evaluation (eg, stride length, pace, base, stability on turning, presence of shuffling or side-stepping) and also was assessed on the basis of the patient's and family's perspective, including documentation of dependence on assistive devices (eg, cane, walker, wheelchair) and comparative Tinetti scores. Symptoms were classified as improved if they resulted in an improvement in the patient's day-to-day functioning, as assessed by both examiner and patients or family members and had sustained improvement over baseline. Symptoms were also assessed in comparison to their previous follow-up.

Analysis

We tabulated the patient evaluations at 1, 3, 5 and 7 years after shunt surgery. In addition, to present an overall picture of the trend of patient response to shunt surgery, we used all available follow-up visits to classify patients into three groups. Patients who had sustained improvement over baseline in all their clinical symptoms at all follow-ups were marked as having "Sustained Improvement". Patients who had initial improvement in any of their symptoms but deteriorated later below baseline in any of these symptoms and showed no improvement thereafter were marked as having "Transient Improvement". Patients who had showed initial improvement followed by deterioration to baseline but again showed improvement in subsequent follow-up visits in any of their symptoms were marked as having "Fluctuating Improvement". Some patients in the transient and fluctuating improvement categories deteriorated/fluctuated with respect to one symptom but showed sustained improvement in other symptom(s). Hence, we also analysed the trend in each symptom separately for a comprehensive analysis of the available data.

Predictors of gait improvement at 3 years were assessed using multivariate logistic regression. Age at first surgery, sex, presence of complete INPH triad, duration of symptoms and type of valve were used as covariates. Exploratory data analysis was carried out using scatter plots for all the covariates. Missing values were excluded during the analyses, in the sense that any patient who had a value missing for any variable used in the analyses was excluded. This was a concern for two analyses. First, for bivariate analysis for increased duration of symptoms for which data was available only for 46 patients, and second in multivariate analysis in which duration of symptoms was a covariate and hence only 46/55 patients were included.

All data analysis was done using STATA 8 (College Station, TX: Station Corp LP).

Institutional review board approval

This study was approved by the Johns Hopkins Medical Institutions' Institutional Review Board.

RESULTS

Demographics and baseline assessment prior to shunting are shown in table 1. There were 55 patients treated with shunt surgery who were identified having follow-up of more than 3 years. Baseline characteristics symptoms prior to shunting are detailed in table 1.

Outcome

Mean duration of follow-up was 5.9±2.5 years (fig 1). There was an overall sustained improvement among all symptoms as shown in figure 2. Gait showed the highest maintenance of improvement over baseline and urinary incontinence showed the least.

Bivariate and multivariate analysis utilising improvement at 3 years as the outcome and age at first shunt surgery, sex, presence of complete NPH triad, duration of symptoms and use of programmable valves as the covariates revealed no significant predictors of outcome.

Table 1 Baseline characteristics (N = 55)

Part A Demographics	
	Number (%) or Mean ± SD
1. Sex (female)	28 (50.9%)
2. Age (years)	71.7±9
3. Symptom duration at time of first shunt surgery (years)	2.6±2.5

Part B Symptoms at baseline			
	Initial symptom	**Symptoms present directly prior to shunting**	**Most debilitating symptom at baseline**
1. Gait	50 (90.9%)	54 (98.2%)	51 (92.7%)
2. Urinary	2 (3.6%)	45 (81.8%)	1 (1.8%)
3. Cognition	2 (3.6%)	51 (92.7%)	1 (1.8%)
4. Headache	1 (1.8%)	12 (24.0%)	2 (3.6%)
5. Complete triad (gait, cognitive and urinary problems)	–	44 (80.0%)	–

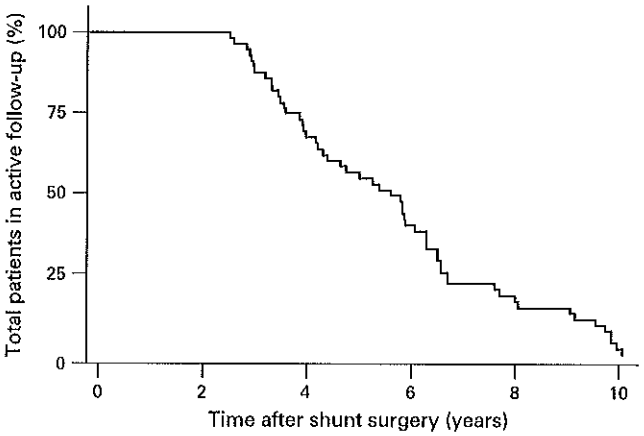


Figure 1 Kaplan–Meier curve depicting follow-up duration after shunt surgery (mean duration of follow-up = 5.9±2.5 years).

We performed survival analysis to evaluate the first episode of deterioration in patients who had shown initial improvement in their symptoms. These graphs (fig 3) represent the most likely outcome in these patients if there had been no follow-up visits after the original shunt surgery.

Shunt surgery details

Ventriculo-peritoneal shunts were used for the first shunt surgery in all patients. Adjustable valves were used in 29/55 (53%) surgeries, whereas 26/55 (47%) used fixed valves. Favourable outcome after the initial shunt surgery, as shown by improvement in any of the three cardinal symptoms of NPH, was seen in 48/55(87%) patients of the initial shunt surgery.

Twenty-nine patients (52.7%) required a total of 62 shunt revisions during the follow-up period. Indications for revision included shunt underdrainage (54/62, 87%), infection (6/62, 10%) and change of shunt configuration (2/62, 3%). Of the 29 patients, 15 (51%) required shunt revision within 12 months of their original shunt surgery. Thirteen of the twenty-nine patients had a single shunt revision and 16/29(55%) had multiple shunt revision surgeries. Of the people who required multiple shunt revision surgeries, the median was 3 surgeries (16 patients had 2 revisions, 8 patients had 3 revisions, 4 patients had 4 revisions, and 3 patients had 5 revisions)

Ventriculo-peritoneal shunts were used for 52/62(84%) revision surgeries, ventriculo-atrial shunts in 5/62(8%) surgeries, ventriculo-pleural shunts in 2/62(3%) and shunt removal was performed in 3/62(5%) surgeries. Favourable outcome to shunt surgery, as shown by improvement in any of the three cardinal symptoms of NPH, was seen in 46/62 (74%) of the revision surgeries.

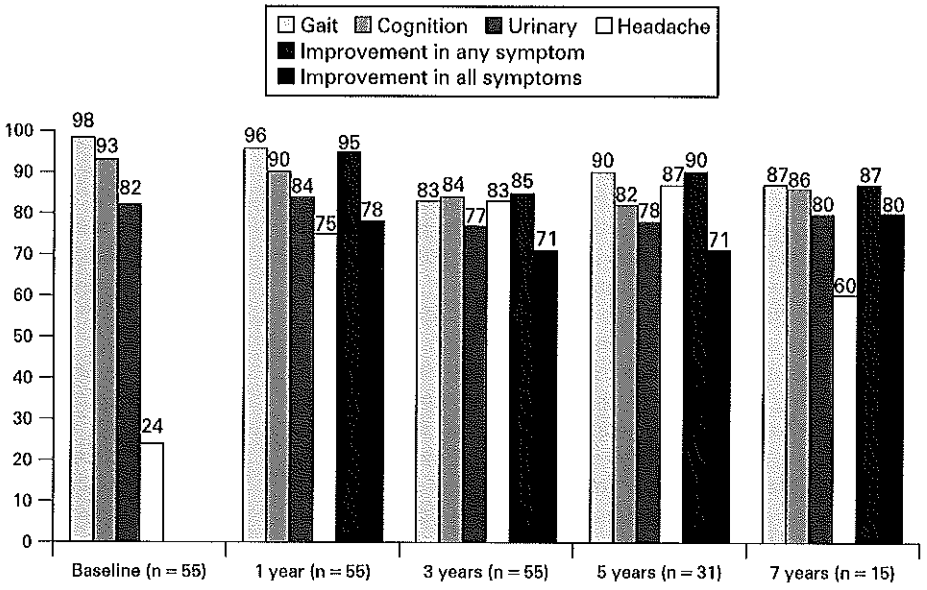
DISCUSSION

The length of response to shunt surgery for NPH is commonly perceived to be of limited duration,[22] which is a factor that physicians, patients and families may take into account when considering whether the benefit of shunt surgery outweighs the risks. The NPH Consensus Guidelines,[18] despite encouraging treatment of INPH, state, "The treatment of INPH should not be considered lightly, given the seriousness of the potential complications." In our previous work, we demonstrated a favourable benefit:risk ratio over 18 months, as 75% of 132 patients diagnosed with idiopathic NPH by our protocol improved, and the major complication rate was no more than 2%.[19] The results of our present study demonstrate that there is a subset of NPH patients who are capable of sustained improvement for as long as 7 years, with an average duration of 5.9±2.5 years, suggesting that "limited duration" of treatment effect should not be considered a major deterrent when considering shunt surgery for NPH.

Savolainen *et al.* reported approximately 50% sustained improvement for 51 patients over 5 years (15). Several studies with a 3-year follow-up have shown a rate of improvement ranging from 24% to 80%[10 11 13–17] and a recent meta-analysis demonstrated an improvement rate of 24–100% (mean 59%) in idiopathic NPH.

Unlike our previous study,[19] in which we found that gait impairment was the single most important factor predicting improvement after shunt surgery, there were no statistically significant predictors of improvement in the present study, probably because 91% of patients had gait impairment as their

Figure 2 Improvement of symptoms by duration after the first shunt surgery.



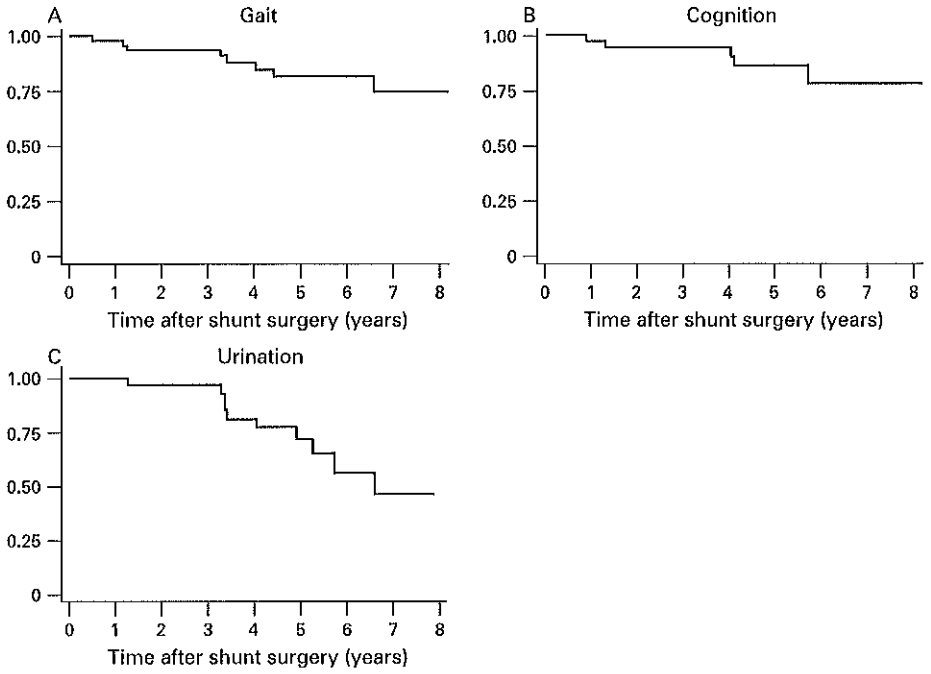


Figure 3 First episode of deterioration in patients who had shown initial improvement in that symptom after their original shunt surgery.

initial symptom and 80% had the complete NPH triad. The absence of significant predictors of improvement is consistent with the results of other studies.[10 14] However, some studies have shown that long-term outcome is influenced by life expectancy and co-morbid conditions.[1 10 22]

We attribute the high rate of success in our study to the selection criteria, which are consistent with the NPH Guidelines, and to the regular follow-up of patients to detect any malfunction of shunts, which raises the possibility that the duration of response to shunt surgery is as dependent on the follow-up strategy as it is on patient characteristics in NPH. Shunt malfunction is a frequent cause of poor outcome after shunt surgery (13, 15). The meta-analysis by Hebb *et al.*[6] showed a complication rate of 38% (range, 5–100%) and most of them were shunt revisions (22%; range, 0–47%). The NPH Guidelines estimate the rate of shunt revision at 20%.[15] In our previous study,[19] the shunt revision rate was 33%, whereas in the current study, 53% of all shunt operations were revisions, of which 87% were for shunt malfunction, and nearly 50% were in the first year after the initial shunt surgery. Shunt overdrainage, manifesting with symptoms such as headache, is routinely treated at our institution by adjustment of the shunt setting; however, data for these shunt setting changes was not collected as part of the present study. In the present study, there were no patients with fixed valves who required shunt removal because of serious overdrainage symptoms.

We believe that there are two reasons for the apparently high rate of shunt revision in the present study. First, this series of patients had one of the longest follow-up durations reported in the literature, and therefore there was more opportunity for shunt obstruction to occur, which is similar to the experience with children, who often have multiple revisions over the first 18 years of life.[23] Second, our follow-up protocol is designed to detect and treat shunt obstruction with the deliberate goal of maintaining clinical improvement for as long as possible, and therefore we may be detecting the true rate of shunt malfunction in elderly adults with NPH. Even though a large number of shunt revisions were performed, 74% of shunt revision surgeries resulted in an overall clinical improvement. Our analysis of trends in clinical response (table 2) indicate that clinical response after shunting is a dynamic process and, in patients who improve initially, a significant proportion (~25% for gait) will deteriorate (fig 3). It is highly probable that without the strategy of regular follow-up and evaluation, this deterioration would be unremitting. This trend of deterioration in initial improvement, when interpreted along with the results of revision surgery and long-term outcome (fig 3), strongly suggests that regular follow-up to detect and manage shunt malfunction can play an important role in maintaining long-term clinical improvement.

Although we have shown that long-term improvement is possible for a subset of patients with NPH, we cannot conclude that improvement of this duration is possible for all shunted patients. Nonetheless, because there are no factors yet that identify prospectively the subset who are capable of long-term improvement, we recommend treating all patients as if they have the potential for sustained improvement. Patients with NPH can have clinical deterioration either because other disease processes worsen their symptoms, or because the shunt is malfunctioning. Furthermore, the emergence of another disease process does not exclude the possibility of shunt malfunction. Thus, operationally, it is not possible to conclude that a patient is no longer capable of symptomatic improvement until either the shunt has been demonstrated to have normal flow with a shunt patency study,[24] or the patient has not improved following an additional trial of CSF drainage or has not improved after shunt revision surgery. We do not recommend shunt revision surgery without evidence that the shunt is obstructed or that additional CSF drainage benefits the patient.

There are limitations to our study. It is retrospective, and we deliberately selected patients who were followed for more than 3 years, so there is a sampling bias. Indeed, not all patients were followed for as long as 7 years. The reasons for being "lost to follow-up" cannot be determined retrospectively. Possibilities

Table 2 Trend of patient response following the initial shunt surgery (Total, N = 55)

	Overall trend (%)	Trend in gait (Number of patients affected at baseline = 54) (%)	Trend in cognition (Number of patients affected at baseline = 51) (%)	Trend in urinary symptoms (Number of patients affected at baseline = 45) (%)
A. Sustained improvement	34 (62)	43 (80)	39 (76)	27 (60)
B. Transient improvement	15 (27)	10 (19)	10 (20)	13 (29)
C. Fluctuating improvement	6 (11)	1 (1)	2 (4)	5 (11)

include death or disability from other medical conditions; inability to return to Baltimore for follow-up; failure to recognize return of NPH symptoms or seek attention for them; or failure to return because symptoms remain controlled and the patient or family felt that follow-up was not necessary.

CONCLUSIONS

Clinical improvement of patients with NPH can be sustained for 5–7 years, even if shunt revision surgery is needed multiple times. With earlier diagnosis and treatment of NPH and the increasing lifespan of the ageing population, the need for long-term follow-up after shunt surgery for NPH may be greater than in the past. Monitoring, identification and treatment of shunt obstruction is a key management principle.

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