Predictors of outcome in patients with normal-pressure hydrocephalus

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Summary

From 1982 until 2000 we examined 200 patients diagnosed with normal-pressure hydrocephalus (NPH) in a prospective study. From the patients who were surgically treated by a shunt implantation we could re-examine 155 (78%) at a mean time interval of 7 months after the operation. NPH differed in severity according to the results of the intrathecal infusion test in an early state NPH (without brain atrophy) and late state NPH (with brain atrophy).

In our study, we focused on the possible predictors: patient age; length of disease; clinical signs including gait ataxia, dementia, and bladder incontinence; idiopathic vs. secondary origin; implanted valve type and the resistance of the valve to cerebrospinal fluid outflow. In 80 patients without cerebral atrophy and a short course of disease (<1 year), a slight amount of dementia and an implanted Miethke Dualswitch-Valve were significant predictors for a positive postoperative outcome. The outflow resistance measured in the intrathecal infusion test showed only minimal relevance for outcome. Seventy-five patients with cerebral atrophy had a better outcome when dementia was not present, outflow resistance was above 20 mmHg/mL/min, the CSF tap-test was positive, and a Miethke Dualswitch-Valve was implanted.

Keywords: Hydrocephalus; outflow resistance; Miethke Dualswitch-Valve; shunt.

Introduction

This reappraisal of the clinical features of normal-pressure hydrocephalus (NPH), which was first described by Hakim and Adams [1, 17] in 1965, is based on physiological and pathophysiological findings pertaining to cerebrospinal fluid dynamics, various diagnostic methods for the detection and characterization of NPH, as well as clinical findings. The classic therapeutic approach, which is to implant a shunt that siphons excess cerebrospinal fluid, is associated with a host of complications. Consequently, indications for surgery need to be reevaluated and reliable predictors of postoperative improvement need to be defined. A review of the literature indicates that, despite improved shunt valve technology, treatment outcomes have not improved to any significant degree, and the prognosis of NPH is still associated with unsatisfactory treatment outcomes. Nonetheless, an increased rate of improvement in the clinical course of NPH can still be achieved through careful preoperative diagnosis, individualized and appropriate therapies, and preoperative modeling of valve characteristics and properties.

Materials and methods

Two hundred patients with proven NPH were treated with shunt surgery and evaluated prospectively over 12 years (1982–2000) in the Department of Neurosurgery at the Berlin-Friedrichshain Hospital and the Neurosurgery Clinic of the Unfallkrankenhaus, Berlin. The workup consisted of clinical examinations, computed tomography and/or magnetic resonance imaging studies, intrathecal infusion tests (measurement of resistance to cerebrospinal fluid outflow [Rout] and intracranial compliance), and cerebrospinal fluid tap tests. In the intrathecal infusion test, intracranial pressure (ICP) is measured continuously, while defined changes are made in cerebrospinal fluid volume [13, 41]. Our patients were classified as early stage or late stage cases of hydrocephalus in accordance with the results of the intrathecal infusion test [21–28]. While no cerebral atrophy was detected in the patient group with early stage NPH (n = 80), cerebral atrophy was noted in patients with late stage disease (n = 75), a sign of advanced disease for this group. At the time of the investigations, the mean age of the 122 men and 78 women was 52 years.

Predictors and statistics

In 155 cases (78%), a follow-up examination as well as an analysis of predictors of prognosis was performed 7 months postoperatively. The following potential predictors of prognosis were evaluated dur-
ing the study: age, length of case history, idiopathic vs. secondary origin, gait difficulty, dementia, urinary incontinence, level of Rout, level of compliance, results of the cerebrospinal tap test, type and pressure level of implanted valve, possible valve infections, and postoperative changes in ventricular size. The predictors of prognosis were compared statistically to the course of the disease using Pearson’s $\chi^2$ test.

**Clinical grading**

The results of the follow-up examinations of 155 patients were evaluated 7 months postoperatively using the Black Grading Scale for Shunt Assessment [2] and Kiefer and Steudel’s Clinical Grading Scale for NPH [19]. The graduated study results were divided into 3 groups as follows: The group with a positive and very good clinical course (NPH recovery rate of $\geq 5$ points); the group with a satisfactory clinical course (NPH recovery rate of $\geq 2$ points); the group with a poor clinical course (NPH recovery rate of $< 2$ points).

**Results**

Figure 1 summarizes the clinical course, as indicated by the NPH recovery rate, for the 155 NPH patients who underwent a follow-up examination. Overall improvement rate was 81%. In patients with early stage NPH (i.e., no cerebral hypertrophy), a case history of less than 12 months duration was associated with a more positive clinical course ($p = 0.01$) than a history extending over more than 12 months.

The level of Rout was a key predictor in classifying our patients as early stage or late stage cases of hydrocephalus (Fig. 2). In the group as a whole ($n = 155$), patients with Rout $> 15$ mmHg/mL/min showed a significantly better clinical course ($p = 0.01$) than did patients with lower Rout. Although patients in the early stage NPH group ($n = 80$) manifested Rout exceeding $15$ mmHg/mL/min and had a better prognosis following shunt surgery, this difference was not statistically significant ($p = 0.1$). Patients with late stage NPH ($n = 75$) (i.e., patients with cerebral atrophy) in whom Rout $> 20$ mmHg/mL/min was recorded on an intrathecal infusion test, showed a significantly better prognosis ($p = 0.05$) following shunt surgery than did patients with lower Rout (Fig. 2). In neither patient group were the results of the cerebrospinal fluid tap significant predictors of postoperative therapeutic outcome. This was also true of the working pressure of the implanted valve (above vs. below $100$ mm H$_2$O), postoperative decrease in ventricular dilatation (as measured with the Evans index), and adequate treatment of infections. On the other hand, the presence ($p = 0.01$) and severity ($p = 0.01$) of dementia constituted significant predictors of prognosis for both patient groups. The prognosis for patients with no memory deficit was more favorable than for patients with short-term memory deficit, whose prognosis, in turn, was more positive than for patients with acute dementia.

Hydrostatic valves constitute an advance in valve technology. Patients with a Miethke Dualswitch-Valve (Christoph Miethke GMBH & Co. KG, Berlin, Germany) (M-DSV; $n = 61$) showed a more favorable clinical course than did patients with Cordis standard valves ($n = 76$) (Cordis Corporation, Miami, FL) or Cordis Orbis Sigma valves ($n = 18$) (Cordis Corporation, Miami, FL). This trend was evident in the group as a whole ($n = 155$) and in the patient group with late stage NPH ($n = 75$). In both of these groups, the prognosis following placement of an M-DSV was more favorable ($p = 0.01$) than was the case with the other implants (Fig. 3). This same phenomenon was also noted ($p = 0.05$) in patients with early stage NPH ($n = 80$). Thus, the type of valve implanted (M-DSV) has predictive value for the postoperative prognosis of patients with NPH (Fig. 3).
Discussion

Review of the literature revealed that no data on the incidence and prevalence of NPH has been published to date. Clarfield [7] evaluated 32 studies with a total of 2889 patients in whom the clinical features of dementia were observed, but only 1.6% of these patients had NPH. A number of studies have found NPH to be more prevalent in males. There is little data available for age distribution in NPH. An analysis by Dauch and colleagues [8] revealed that the oldest NPH patients are in the seventh decade, but that 25% are under 50 years of age. In other words, NPH can occur in adults at any age. Several authors have published reports on NPH in children and teenagers, although its existence in these age groups is disputed [14, 20, 31–33].

Outcomes

The overall improvement rate in patients with NPH ranges from 31% to 96% (mean: 53%) [15, 34, 39]. One multicenter study of 166 patients with NPH [38] found that in the long-term, 36% of patients showed permanent clinical improvement while 21% had only moderate remission of symptoms following shunt placement. The overall improvement in our own patients following shunt placement was 81% (Fig. 1). A recent meta-analysis [18] demonstrated an improvement rate of 24% to 100% (mean = 59%) in idiopathic NPH and improved outcome in a significant mean of 29% of cases (range 10% to 100%). These results are consistent with the positive clinical courses observed in our patient group as a whole (mean 39%).

Length of case history

The mean age of our patient cohort was 52 years, making this a relatively young group for NPH. This may be attributable to the referral criteria used by our colleagues and to a relatively large proportion of patients (48%) with secondary hydrocephalus. In contrast to the findings of other authors [32], the clinical picture of the NPH we saw was not primarily that of a morphological disorder occurring mostly in older patients, but was instead a functional disorder that can easily develop as a secondary disorder at any age. One review of the literature [28] found that NPH is twice as prevalent in males as in females. No published data is available pertaining to duration of symptoms that could be used for comparison with our own patient groups. Thus, there is no basis for comparing the more positive postoperative prognosis in early stage NPH patients whose case histories are less than 1 year in duration.

Resistance to outflow (Rout)

In our patients, all Rout of <10 mmHg/mL/min was categorized as physiological, whereas Rout measuring between 10 and 13 mmHg/mL/min was classified as a limit value, and all Rout measuring >13 mmHg/mL/min was classified as pathological. The disproportionately low normal values for Rout obtained by Ekstedt [11], Fuhrmeister [13] and Shapiro et al. [34] should be reevaluated in the light of recent studies. Our own assessment criteria were confirmed by the results obtained in 1993 by Morgan et al. [30], which were consistent with the findings of Børgesen and Gjerris [6] as well as Tans and Poortvliet [36]. Boon et al. [5] demonstrated that the positive predictive value of Rout increases as Rout rises, which is consistent with our data (Fig. 2). These authors propose that Rout of 18 mmHg/mL/min be adopted in order to avoid reducing measurement sensitivity of the intrathecal infusion test. We found that classifying patients into an early or late stage NPH group allowed more individualized values for Rout as predictors of prognosis.

Dementia

The presence and acuteness of dementia constitutes a significant predictor of clinical outcome for all groups of NPH patients with shunts. Dementia has
been reported in 80% of cases of NPH [3, 8, 12, 15, 35]. Although acute dementia is more prevalent in late stage NPH and in older published reports is characterized as the cardinal symptom of this disorder, dementia is nonetheless of little relevance in reaching a differential diagnosis of NPH. In the literature, gait difficulty occurs in 86% of cases of NPH [3, 8, 12, 15, 35]. In our own experience, this symptom has proven to be the most reliable sign for the diagnosis of NPH [26]. It is not, however, a valid predictor of therapeutic outcome following shunt placement.

Valve mechanisms

No overdrainage complications were observed in our early stage NPH patients in whom Cordis standard valves were implanted. In addition, prolonged bench testing [37] has shown the Cordis standard valve to be stable, although some have reported overdrainage problems with this valve. The results of a Dutch multicenter study [4] revealed a better clinical course for NPH patients with Cordis standard low-pressure valves than for patients with Cordis standard medium-pressure valves; however, this advantage came at the cost of a high overdrainage rate (71%) for the low-pressure valves as compared with 34% for their medium-pressure counterparts. These postoperative complications had no clinical repercussions for either of the groups studied, although the rate of complications was disproportionately high. The Cordis standard valves are relatively inexpensive, but even a single complication resulting from overdrainage can result in burdensome expenditures, thereby negating any potential savings.

In terms of ensuring a positive prognosis for patients with early stage NPH, the M-DSV is the treatment of choice (Fig. 3). In our own patients with late stage NPH, predominantly Orbis Sigma valves, Cordis standard valves, and the Medos Hakim valve (Codman & Shurtleff, Inc., Raynham, MA) were implanted, and more recently, the M-DSV. Unlike the Cordis standard valves, the Orbis Sigma valves provide flow-based drainage utilizing physiological cerebrospinal hydrodynamics within a range of pressure gradients. In patients with hydrocephalic atrophy, this is particularly important in preventing overdrainage. In the Orbis Sigma valves, overdrainage occurred in 5 patients (25%), 3 of whom (15%) also presented with subdural hematoma. These results are consistent with another study [40] in which subdural hematoma was found to be a sign of overdrainage following placement of Orbis Sigma valves in patients with NPH. On the other hand, Decq et al. [9] observed a lower rate of overdrainage with Orbis Sigma valves relative to conventional differential pressure valves; however, as this study was not confined to patients with NPH, it is of limited relevance. It remains to be seen whether the Orbis Sigma II valve will deliver better postoperative results than its predecessor.

The Cordis Orbis Sigma valve is not suitable for implantation in patients with NPH owing to its association with high rates of overdrainage and subdural hematoma. The disadvantage of the Cordis standard valves for patients with late stage NPH is that if the patient stands or sits up abruptly, the valve responds accordingly, thereby inducing a siphoning effect in the already atrophic brain. An anti-siphon device would theoretically alleviate this problem, but the flow resistance of the entire valve system would then increase. In a randomized pediatric study, Drake et al. [10] noted no significant change in therapeutic outcome following implantation of either Delta, Orbis Standard, or Sigma valves. This study generated considerable controversy, but it is not relevant to the specific clinical features of NPH. Overdrainage was seen in 3 of our patients (6%) in whom the Cordis standard valve was implanted. Two of these patients (4%) manifested the clinical signs associated with this complication.

With its 2 different closure mechanisms that operate in parallel, the M-DSV [20, 29] constitutes an important step forward in solving the problems associated with the position of the patient’s craniospinal axis. In our own series, implantation of the M-DSV has thus far resulted in only 2 cases (5%) of chronic subdural hematoma. In 1 of these patients, the hematoma was resorbed within 1 month, and a revision operation had to be performed on the other patient. The post-implantation results obtained with the M-DSV demonstrate its high degree of suitability for the management of NPH in general, and late stage NPH in particular. For the latter disorder, the valve is highly reliable and safe due to the fact that problems of overdrainage are rarely seen (Fig. 3).

Conclusions

– NPH should be the suspected differential diagnosis in patients who present with dementia (cardinal symptom: gait ataxia) [16].
– A case history of less than 1-year duration, as well as
relatively mild dementia or the absence of memory deficit, should be regarded as predictors of a positive prognosis following shunt therapy in patients with NPH.

- The prognosis is positive for early stage NPH patients in whom the intrathecal infusion test shows Rout in excess of 15 mmHg/mL/min, or in late stage NPH patients (with cerebral atrophy) with Rout greater than 20 mmHg/mL/min on the intrathecal infusion test.
- In view of the superior therapeutic outcomes, hydrostatic valves should be implanted in patients with NPH [20, 28].

References


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