SURGICAL MANAGEMENT OF IDIOPATHIC NORMAL-PRESSURE HYDROCEPHALUS

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OBJECTIVE: To develop evidence-based guidelines for surgical management of idiopathic normal-pressure hydrocephalus (INPH). Compared with the diagnostic phase, the surgical management of INPH has received less scientific attention. The quality of much of the literature concerning the surgical management has been limited by many factors. These include retrospective analysis, small patient numbers, analysis of a mixed NPH population, and sometimes a lack of detail as to what type of shunt system was used. Many earlier studies predated our current understanding of the hydrodynamics of cerebrospinal fluid shunts, and therefore, the conclusions drawn may no longer be valid.

METHODS: A MEDLINE and PubMed search from 1966 to the present was conducted using the following key terms: *normal-pressure hydrocephalus* and *idiopathic adult-onset hydrocephalus*. Only English-language literature in peer-reviewed journals was reviewed. The search was further limited to articles that described the method of treatment and outcome selectively for INPH patients. Finally, only studies that included 20 or more INPH patients were considered with respect to formulating the recommendations in these Guidelines (27 articles).

RESULTS: For practical reasons, it is important to identify probable shunt responders diagnosed with INPH. If the patient is an acceptable candidate for anesthesia, then an INPH-specific risk-benefit analysis should be determined. In general, patients exhibiting negligible symptoms may not be suitable candidates for surgical management, given the known risks and complications associated with shunting INPH. The choice of valve type and setting should be based on empirical reasoning and a basic understanding of shunt hydrodynamics. The most conservative choice is a valve incorporating an antisiphon device, with the understanding that underdrainage (despite a low opening pressure) may occur in a small percentage of patients because of the antisiphon device. On the basis of retrospective studies, the use of an adjustable valve seems to be beneficial in the management of INPH.

CONCLUSION: The treatment of INPH should not be considered lightly, given the seriousness of the potential complications. Within these limitations and the available evidence, guidelines for surgical management were developed.

KEY WORDS: Normal-pressure hydrocephalus, NPH, Surgical management

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RECOMMENDATIONS

Standards

There is no accepted standard for this topic.

Guidelines

Surgical diversion of cerebrospinal fluid (CSF) is recommended for idiopathic normal-pressure hydrocephalus (INPH) patients in whom there is a favorable risk-to-benefit ratio. Not every patient diagnosed with INPH is a good candidate for shunting. Factors such as coagulation status, immune incompetence, comorbidity, functional status, and advanced age should be considered. In each case, the overall risk-to-benefit ratio should be evaluated carefully in deciding whether or not to intervene.

Options

Postoperative follow-up should include a computed tomographic (CT) scan between 1 and 4 months after surgery. There are insufficient data demonstrating either an advantage

or a disadvantage of ventricular versus lumbar shunt configurations. The results of several retrospective studies suggest that adjustable ("programmable") valves offer an advantage over fixed valves, because corrections for underdrainage or overdrainage, which are encountered relatively frequently with INPH, can be performed noninvasively instead of requiring a surgical revision. Clinical studies for assessing the beneficial effects of "antisiphon" or CSF flow-limiting devices have not been performed. The use of these devices may reduce the incidence of serious overdrainage complications but also may result in underdrainage in other patients.

OVERVIEW

Compared with the diagnostic phase, the surgical management of INPH has received less scientific attention. The quality of much of the literature concerning the surgical management has been limited by retrospective analysis, small patient numbers, the analysis of a mixed NPH population, and sometimes a lack of detail as to what type of shunt system was used (see Evidentiary Data, *Table 4.1*). Many earlier studies predated our current understanding of the hydrodynamics of CSF shunts, and therefore, the conclusions drawn may no longer be valid.

The importance of making the proper diagnosis of INPH arises from the fact that the only method of treatment, surgical diversion of CSF, carries significant risks. Some have argued that compared with the percentage of patients who make an excellent improvement with a shunt, the overall morbidity experienced by the remaining patients warrants a very cautious approach when considering treating an INPH patient (52). With this in mind, every effort should be made to achieve an accurate diagnosis (see Part II) and minimize the risks associated with treating INPH. This requires an understanding of the factors that should be considered before recommending an operation, the in vivo hydrodynamic behavior of shunt systems, and the optimal postoperative management. The management-related issues addressed in this Guidelines section include indications for surgical management, shunt-related complications, choice of shunt configuration, and valve type and/or setting selection.

PROCESS

A MEDLINE and PubMed search from 1966 to the present was conducted using the following key terms: *normal-pressure hydrocephalus* and *idiopathic adult-onset hydrocephalus*. Only English-language literature in peer-reviewed journals was reviewed. The search was further limited to articles that described the method of treatment and outcome selectively for INPH patients. Finally, only studies that included 20 or more INPH patients were considered with respect to formulating the recommendations in these Guidelines (27 articles).

SCIENTIFIC FOUNDATION

Indications for Surgical Management of INPH

Not every patient diagnosed with probable or possible INPH should undergo a CSF shunting procedure. Although there is no doubt that selected patients can make a remarkable and prolonged improvement after the placement of a shunt, others may not. For any individual patient, an assessment must be made with respect to risk-to-benefit ratio. The various factors that must be considered include the following. What is the probability of improvement with a shunt? How much improvement will occur? If improvement occurs, how long will it last? What is the natural history if conservative management is chosen? What is the probability of neurological deterioration as a result of the shunt? Does the current level of INPH-related disability warrant the risks of a shunt?

Consideration of Risk-to-Benefit Ratio

Estimating the probability of improvement with treatment is not synonymous with making the diagnosis of INPH. From a medical decision-making perspective, the probability of shunt responsiveness is a more important parameter because the patient and his or her family seek an improvement in functionality, not only a diagnosis. The patient must compare the risks of no treatment against proceeding with the shunt procedure. In addition to estimating the probability of improvement, patients want to know how much they will improve. Another guideline article (see Part III) addresses the issue of estimating the probability of shunt responsiveness. With regard to estimating how much improvement may be expected, this issue has not been adequately addressed in the literature (see Part V). The 72-hour external lumbar drainage test may give some indication, because it is in a sense a "temporary shunt." It is important to consider that patients who are likely to improve only minimally may receive no practical benefit from treatment. In such cases, the risks of treatment may be too high, even though some might consider these patients "shunt responders."

An issue that occasionally arises with regard to the management of INPH is that of systemic anticoagulation. Standard neurosurgical precautions should be taken, including stopping antiplatelet medications for the required period before surgery and not restarting them immediately. There are no studies or expert consensus addressing whether or not restarting full anticoagulation with warfarin is a contraindication to a CSF shunt for INPH. In general, the improvement anticipated from shunting should be greater in such cases to justify the added hemorrhagic risks in an anticoagulated patient.

What is to be expected if the patient decides against the shunt procedure or wishes to postpone the decision indefinitely? Is there a penalty for delaying treatment? The "natural history" of untreated INPH has not been studied well. There is no published documentation on INPH patients returning to normal without treatment. Conversely, there are no published reports demonstrating that INPH is invariably a progressive

TABLE 4.1. Evidentiary data[a]

Series (ref. no.)	Type of study	Class	n (INPH)	Shunt type	Valve type	Comments	Complication rate
Boon et al., 1998 (7)	Prospective, randomized, multicenter, mixed NPH	II	85	VP	Low versus medium DPV, no ASD	85 of 96 INPH patients. Results not segregated by cause. Trend ($P = 0.06$) in outcome favoring the low DPV over the medium DPV. Incidence of subdural hygromas higher with low DPV (71%) to medium DPV (34%, $P = 0.0002$).	Complication incidence not segregated out by cause.
Meier et al., 2004 (40)	Prospective, mixed NPH	II	70	Not specified	Dual-switch valve	Results not segregated by cause. Overall 63% improvement rate.	Complication incidence not segregated by cause.
Malm et al., 2000 (35)	Prospective, all INPH. Outcome was compared with an age-matched group of 84 healthy subjects and 84 patients with first-ever ischemic strokes	II	42	Not specified	Not specified	Improvement in the NPH group was seen in 64 and 26% of patients at 3 mo and 3 yr, respectively. The case-fatalities for stroke and NPH patients were similar. NPH patients were 3.3 times more likely to die than healthy individuals.	SDH 5%, shunt failure 14%, CVA 10%, and shunt-related death 2%.
Børgesen, 1984 (8)	Prospective, mixed NPH	II	40	VA	Medium DPV, no ASD	Only patients with low CSF conductance were shunted. Improvement was 42% at 1 yr for INPH.	Complication incidence not segregated out by cause.
Malm et al., 1995 (33)	Prospective, all INPH	II	35	VP	Orbis-Sigma, various DPV with no ASD	Improvement at 3 mo was seen in 72% of cases.	Not stated.
Malm et al., 1995 (34)	Prospective, all INPH	II	34	VP	Orbis-Sigma, various DPV with no ASD	A reduction in upright ICP was documented with the differential pressure valve compared with baseline ($P < 0.0001$) but not with the Orbis-Sigma valve. The postoperative supine ICP, which was not different between the two valves, correlated with MMSE score.	Not stated.
Raftopoulos et al., 1994 (46)	Prospective, all INPH with "high waves," ICP >9 mm Hg	II	23	VA	Medium DPV, no ASD	96% improvement rate at 1 yr.	SDH 17%, asymptomatic subdural effusions 30%, revision 13%.
Raftopoulos et al., 1996 (47)	Prospective, all INPH and "high ICP waves"	II	23	VA	Medium DPV, no ASD	5-yr follow-up. 61% reduction in ventricle size at 1 yr. Majority of subdural effusions and all SDHs occurred within 2 mo.	SDH 17% (all within 2 mo), chronic subdural effusion 43%, revision 21%.

TABLE 4.1. Continued

Series (ref. no.)	Type of study	Class	n (INPH)	Shunt type	Valve type	Comments	Complication rate
Zemack and Romner, 2002 (56)	Retrospective mixed NPH	III	147	VP (90%), VA (10%)	Programmable DPV, no ASD	138 adjustments performed in 72 patients. Reason for adjustment was overdrainage (26%), underdrainage (54%), SDH (20%). A beneficial effect was found in ≈50% of adjustments.	SDH and hygroma 9.5%.
Vanneste et al., 1992 (52)	Retrospective, multicenter, mixed NPH	III	127	VP, VA	Various DPV, no ASD	Improvement was noted in 31% (marked 15%). The benefit-to-harm ratio was 1.7.	Severe complications 17% (9% permanent).
Vanneste et al., 1993 (53)	Retrospective, mixed NPH	III	91	Not stated	Not stated	Results not segregated out by cause.	Complications not segregated out by cause.
Greenberg et al., 1977 (21)	Retrospective, all INPH	III	73	VA, VP	Low, medium DPV, no ASD	This mainly pre-CT-era study included delayed follow-up of an earlier report. Initial improvement at 10 mo of 64% of patients decreased to 42% at 3 yr. For all patients, 45% improved.	SDH 3%.
Black, 1980 (4)	Retrospective, all INPH	III	62	VP, VA	Various DPV, no ASD	This mainly pre-CT-era study reported a 47% improvement rate.	Not stated.
Laws and Mokri, 1977 (31)	Retrospective, mixed NPH	III	56	VA, VP, VPL	Not stated	Typical INPH had a 74% improvement rate at mean 19-mo follow-up. Atypical 38%. Overall 50%.	Overall complication rate 44%, symptomatic subdural fluid collection 9% (14% overall incidence), obstruction 18% per patient (32% total), seizures 11%.
McQuarrie et al., 1984 (37)	Retrospective, mixed NPH	III	47	VP, VA	Medium, low DPV, some with ASD	The improvement rates for low and medium pressure valves were 80 and 50%, respectively, although the ASDs were not segregated out.	Complications not segregated out by cause.
Petersen et al., 1985 (44)	Retrospective, all INPH	III	45	VP, VA	Various DPV, no ASD	This mainly CT-era study reported a 75% improvement rate.	Overall complication rate 31%.
Krauss et al., 1996 (27)	Retrospective, all INPH	III	41	VA, VP	Medium DPV, programmable DPV; no ASD	90% improvement, mean follow-up 16 mo.	Overall complication rate 5%, SDH 2%, subdural effusion 7%, ICH 3%, overdrainage headache 2%, malfunction 10%.
Benzel et al., 1990 (2)	Retrospective, all INPH	III	37	VP, VPL	Various DPV, no ASD	Improvement was reported in 70% of cases.	SDH 16% (all medium pressure valves).
Weiner et al., 1999 (54)	Retrospective, all INPH	III	37	VP	Medium, high DPV with no ASD, Orbis-Sigma	Improvement occurred in 86% of cases.	No significant difference in improvement or complication rate between the two valve systems.
Black et al., 1985 (6)	Retrospective, all INPH	III	36	VA, VP	Not stated	Improvement rate of 64% at 3 mo.	Chronic subdural effusion 28%, seizure 8%, infection 3%.

TABLE 4.1. Continued

Series (ref. no.)	Type of study	Class	n (INPH)	Shunt type	Valve type	Comments	Complication rate
Reinprecht et al., 1995 (48)	Retrospective, mixed hydrocephalus	III	32	Not stated	Adjustable DPV, no ASD	Only 12% of INPH patients had no pressure readjustment.	Complications and outcome not segregated for INPH.
Børgesen and Gjerris, 1982 (9)	Prospective, mixed NPH	III	31	VA	Medium DPV, no ASD	67% improvement for INPH.	Complications not segregated out by cause.
Hughes et al., 1978 (25)	Retrospective, all INPH. An untreated 12-patient "control" group (not case controlled) analyzed.	III	27	VA	Various	This mainly pre-CT-era study had dementia as the primary presenting symptom. Improvement was reported in 33% of cases. Of the 12 nontreated patients, 6 were unchanged with follow-up ranging from 7 mo to 3 yr.	SDH 16%, seizure 3%.
Larsson et al., 1991 (30)	Retrospective, mixed NPH	III	26	VP	Various	Improvement was reported in 73% of patients with INPH.	Complication incidence not segregated out by cause.
Magnaes, 1978 (32)	Retrospective, mixed	III	26	VA	Medium DPV, no ASD	The results of the INPH cases could be determined from this pre-CT-era report.	Complication incidence not segregated out by cause.
Takeuchi et al., 2000 (50)	Retrospective, all INPH	III	25	VP	Programmable DPV, no ASD	48% improvement rate. 8% required reprogramming because of underdrainage.	Not stated.
Gangemi et al., 2004 (20)	Retrospective, all INPH	III	25	ETV		72% improvement rate.	ICH 4%.
Spanu et al., 1986 (49)	Retrospective, mixed NPH	III	23	VP, VA	Various DPV, no ASD	Improvement was reported in 78% of idiopathic cases.	Not stated.
Yamashita et al., 1999 (55)	Retrospective, mixed	III	20	VP	Hakim programmable DPV, no ASD	At follow-up, the mean valve setting was 100 mm H_2O. The valve was reprogrammed a mean of 1.25 times.	Not stated.

[a] INPH, idiopathic normal-pressure hydrocephalus; ICP, intracranial pressure; VP, ventriculoperitoneal; VA, ventriculoatrial; VPL, ventriculopleural; ETV, endoscopic third ventriculostomy; DPV, differential-pressure valve; ASD, antisiphon device; CSF, cerebrospinal fluid; MMSE, Mini Mental State Examination; SDH, subdural hematoma; CT, computed tomography; CVA, cerebrovascular accident; ICH, intracerebral hemorrhage.

disorder. No studies meeting the inclusion criteria for these Guidelines have addressed the natural history of INPH. Anecdotally, one small retrospective study that included 12 INPH patients who refused shunting procedures reported that, at follow-ups ranging from 7 months to 3 years, 6 patients (50%) were neurologically unchanged (25). Given that these patients were not randomly selected, this finding may not be representative of the natural history of INPH in general.

Response to Surgical Intervention

Because the pathophysiology of INPH is not fully understood, it is not possible to ascertain when the point of "irreversibility" of brain injury occurs. It should be considered that many, if not most, INPH patients have comorbid brain conditions. Periventricular white matter ischemia is commonly seen in INPH patients. Patients with severe cerebrovascular disease do not respond as well to shunting but may still derive some benefit from the procedure (7, 27). The neurological decline sometimes seen despite shunt placement in INPH may be related to the progression of comorbid conditions. This is supported by investigations documenting the course of treated INPH (21, 35, 47). Malm et al. (35) prospectively followed 84 surgically managed INPH patients and found that the number of patients with improvement declined from 64%

at 3 months to 26% at 3 years. Similar results were reported from a smaller, older retrospective study (21). These findings suggest that a shunt may not always arrest the progression of INPH or that comorbid conditions may progress and lead to deterioration. Nevertheless, even temporary improvements ranging from 1 to 3 years may make a substantial difference in quality of life for these individuals.

Complications Associated with Shunting

When comparing the course of treated versus untreated INPH, the incidence of morbidity related to the surgical management is a key factor in determining risk-to-benefit ratio. If the morbidity is excessive, then, as a whole, treating INPH patients may not offer a better outcome compared with nonsurgical management. Assessment of the probability of complications and morbidity associated with a CSF shunt can be divided into two stages: the risks incurred at the time of the operation and the risks that occur after the procedure. Selecting the proper patient diagnosed with INPH for surgical management shares a decision-making process common to other neurosurgical operations. Operative risk assessment and medical optimization by an internist or other appropriate specialist should be considered when indicated. Other than anesthesia-related risks (such as myocardial infarction), acute intracerebral hemorrhage is the primary "procedure-related" risk. The incidence of this complication is most likely underreported for a variety of reasons, primarily inconsistent immediate postoperative CT scanning. In a retrospective study of 36 treated INPH patients, the incidence of intracerebral hematoma was 3% (6).

Delayed morbidity from a CSF shunt may arise from infection, seizures, shunt obstruction, subdural fluid collection, overdrainage headaches, and shunt underdrainage (failure to improve despite a patent shunt). From the perspective of permanent morbidity, the most important complication to consider is the subdural hematoma. The other "complications" listed above may result in prolonged or repeated hospitalizations, but in general, patients recover fully. The eventual outcome may not be negatively affected, but the treatment of INPH symptoms can be delayed.

Subdural fluid collections include both so-called "effusions" (also called "hygromas") and frank hematomas. Blurring the distinction between these two is the fact that sometimes "effusions" show mixed density on CT scans and therefore may have some component of hemorrhage. The incidence of subdural hematomas after a shunt for INPH is not known, and reported values range widely, from 2 to 17% (2, 21, 25, 27, 35, 46, 47, 56). There are several possible explanations for this variability. First, many reports do not differentiate clearly between subdural effusions and hematomas (lumping both together). A key question that has not been addressed formally in the literature is to what extent subdural effusions are a risk factor of a subdural hematoma. It has been well documented that small subdural effusions may be clinically silent (7). Conversely, the incidence of subdural effusions seems to be related to the degree of shunt drainage, because the incidence was greater in low- versus medium-pressure valves (7).

Incidence of Subdural Hematomas in Retrospective versus Prospective Studies

One factor that may logically be related to the incidence of subdural hematomas is how closely the patients were followed up after surgery. Prospective studies (7, 47) in which routine early CT scans were obtained generally document higher incidence rates of subdural effusions compared with retrospective studies (6, 27, 31, 56). The mere act of discovering these effusions may have led to a closer surveillance of the patients and in some cases, prompted proactive surgical intervention. As a result, early intervention may have prevented the conversion of an effusion into a more serious subdural hematoma. This may in part explain the relatively higher incidence of subdural hematomas in some retrospective studies (2, 25). Although prospective studies better document the true incidence of subdural hematomas, the results may be pertinent only to clinicians who implement a similar management protocol.

Influence of Valve Type on Incidence of Subdural Collection

The relationship of the shunt valve type to the incidence of subdural hematoma remains unclear. Although it is generally assumed that subdural hematoma formation may occur as a consequence of excessive or too rapid CSF drainage, the use of flow-limiting valves or antisiphon devices (ASDs) to reduce the incidence of subdural hematomas has yet to be proved. In a study of 37 INPH patients, Weiner et al. (54) did not find a difference in the incidence of complications comparing a multistage flow-limiting valve (Orbis-Sigma; NMT Neurosciences, Duluth, GA) to medium- and high-differential-pressure valves. Last, nearly all of the literature regarding complication rates for INPH predates the advent of adjustable ("programmable") valves. Adjustable valves allow more conservative treatment of subdural effusions by adjustment of valve pressure (56). However, the relationship between shunt valve set pressure and the incidence of subdural hematomas has not been well studied.

What incidence rate for subdural hematoma should neurosurgeons quote to INPH patients considering surgery? The answer probably depends on the individual management protocol used, with the reported range of incidence being between 2 and 17%. If preoperative intracranial pressure is measured routinely, valve type or pressure is selected on the basis of reasonable physiological grounds and follow-up neuroimaging studies are obtained in a timely manner, then the incidence rate of subdural hematomas presumably will be minimized.

Other Shunt-related Complications

The reported incidence of other shunt-related complications for INPH varies. The incidence rate for infection has not been

TABLE 4.2. Estimates of complication incidences for the treatment of idiopathic normal-pressure hydrocephalus

Series (ref. no.)	Complication	Approximate incidence
Black et al., 1980 (4)	Intracerebral hematoma	3%
Black, 1980 (4)	Subdural hematoma	2–17%[a]
Boon et al., 1998 (7)	–	–
Laws and Mokri, 1977 (31)	–	–
Krauss et al., 1996 (27)	–	–
Benzel et al., 1990 (2)	–	–
Zemack and Romner, 2002 (56)	–	–
Hughes et al., 1978 (25)	–	–
Zemack and Romner, 2002 (56)	Shunt infection	6%
Laws and Mokri, 1977 (31)	Seizure	3–11%
Hughes et al., 1978 (25)	–	–
Black, 1980 (4)	–	–
Raftopoulos et al., 1996 (47)	Shunt malfunction (5 yr)	20%
Malm et al., 2000 (35)	–	–

[a] Incident rate may depend on management practice.

reported consistently but seems to be low (3–6%) (6, 56). Postoperative seizure incidences ranging from 3 to 11% have been reported (6, 25, 31). One prospective study that followed up patients for 5 years postoperatively documented a 21% shunt revision rate (47). Malm et al. (35) reported a shunt-related mortality rate of 2% in a prospective study. Many other studies have reported patient deaths but attributed the deaths to existing comorbid conditions. Additional complications caused by shunting may include hearing loss, tinnitus, oculomotor palsies, and headache, all of which may persist, resolve spontaneously, or be relieved by an adjustment in the shunt setting. *Table 4.2* summarizes reasonable estimates of complication incidences for the treatment of INPH on the basis of current literature.

Choice of Shunt Configuration

The most common shunt configurations used for INPH are ventriculoperitoneal (VP) and ventriculoatrial (VA) shunts. No prospective or retrospective study has been performed comparing these two shunt configurations for INPH, and consequently, no standard or guidelines can be formulated with regard to which is preferable. With regard to complication rates, a retrospective study of 128 adult hydrocephalus patients (NPH not specified), Lam and Villemure (28) found no differences in the rate of distal shunt complications.

Certain complications that occur with VP shunt configurations are related to how well, or at what backpressure, the abdominal cavity accepts CSF. A careful history should be obtained to determine whether there has been a history of peritonitis or peritoneal adhesions from multiple previous abdominal operations, because underdrainage may occur because of absorption incompetence. Severe constipation or truncal obesity may be other reasons to avoid a VP shunt configuration. These drawbacks to the VP configuration are obviated by VA shunt configurations, because distal pressure elevations are of less concern. Excellent response rates have been reported using VA shunts, and this configuration is preferred for INPH by some experts (22). The rare syndrome of shunt nephrosis, caused by a long-standing undiagnosed low-grade shunt infection (typically but not limited to VA shunts), has not been reported in INPH patients.

In a patient with a preexisting seizure disorder or other relative contraindication for a ventricular shunt, a lumboperitoneal shunt can be considered. There are no reports in the literature (meeting the inclusion criteria for these Guidelines) detailing the experience of lumboperitoneal shunts for INPH. Lumboperitoneal shunts can be effective but possibly more problematic because of mechanical malfunctions. In addition, fewer options are available with respect to valve type in this configuration.

Ventriculopleural shunts were historically more popular, but, owing largely to the incidence of pleural effusions with this configuration, they are typically used only when no other option is available or if maximum CSF drainage is desired. There has been recent renewed interest in ventriculosuperior sagittal sinus shunts, but long-term results are still pending (10).

Endoscopic third ventriculostomy may play a role in the treatment of selected INPH patients. Gangemi et al. (20) reported a 72% neurological improvement rate in 25 INPH patients treated with endoscopic third ventriculostomy. Small retrospective studies, not meeting the criteria for Guidelines recommendations here, have suggested that endoscopic third ventriculostomy procedures may be beneficial in NPH pa-

tients who demonstrate high ventricular CSF outflow resistance in combination with low lumbar CSF outflow resistance (38, 41). The study by Gangemi et al. (20), although intriguing, is somewhat counterintuitive in the face of communicating hydrocephalus and therefore may require confirmatory studies at other institutions before inclusion in the formal Guidelines.

Valve Type and/or Setting Selection

Valve selection has long been considered one of the more important management decisions for the treatment of INPH. There may be a tradeoff between efficiency of drainage and the occurrence of overdrainage-related complications. Retrospective and prospective studies have attempted to address this question (7, 29). First, the general principles of valve design and function will be briefly discussed so that the results of these studies can be put into context. For simplicity, valve designs will be divided into three categories: 1) differential-pressure valves, 2) valves incorporating gravity-compensating devices, and 3) valves with flow-limiting mechanisms. Each valve and accompanying shunt assembly can be further characterized by pressure and flow traits.

Simple Differential-pressure Valves

The differential-pressure valve opens if the pressure difference across the valve mechanism exceeds a set value. This "opening pressure" is typically given in units of millimeters of water (equivalent height of a column of water). The actual mechanism is typically either a spring-loaded ball check valve or opposed leaves of a slit valve. Valves were originally operationally categorized into low-pressure (≈20–40 mm H_2O), medium-pressure (≈50–90 mm H_2O), and high-pressure (≈100–140 mm H_2O) ranges. In its original conception, the differential-pressure valve was designed to mimic the sinus venous valves that modulated the intracranial pressure at a constant level. It was soon realized, however, that the valve pressure settings were relatively small compared with the negative intracranial pressures developed by a hydrostatic column of CSF draining to the peritoneum in the upright position (often referred to as "siphoning") (11, 19). In vitro, differential-pressure valve systems allow high CSF flow rates when the valve mechanism is open (although in vivo, mean CSF flow rates may be significantly lower because the valve mechanism is closed a significant proportion of the time) (43).

A special note regarding "distal slit" valves is warranted, because these shunt systems seem to have the greatest propensity for overdrainage, on the basis of in vitro tests documenting CSF flow rates greater than 3000 ml/h (1). Although there is no literature concerning the use of distal-slit valves for INPH, expert opinion strongly recommends against their use for INPH because of the high risk of overdrainage complications.

Antisiphon Devices

When the phenomenon of "siphoning" (overdrainage attributable to the hydrostatic column produced by the shunt catheter) became evident, add-on mechanisms were developed to counteract gravity-dependent drainage. These devices are generally called ASDs. The ASD is situated in series immediately distal to a standard differential-pressure valve. Although it is somewhat misleading, valve systems containing ASDs are often characterized solely by the differential-pressure valve opening pressure. From the standpoint of in vitro and in vivo hydrodynamics, a clear distinction should be made between sole differential-pressure valves and ASD systems. Valve systems with ASDs are effective in preventing postural intracranial hypotension and therefore are not equivalent in function to shunt systems containing only a differential-pressure valve. In a study of hydrocephalic patients (not specifically INPH), Chapman et al. (11) showed that ASDs have a significant effect on postoperative intracranial pressure that was distinctly different from shunt systems with equivalent valve pressure settings. It is important to consider that for INPH, siphoning has not been proved to be harmful. In patients in whom the baseline intracranial pressure is truly normal (including the lack of frequent B waves), placing a shunt with an ASD that is aimed at producing a normal intracranial pressure may be ineffective (3).

Flow-limiting Valves

The third type of valve mechanism (or total shunt system) is the so-called flow-limited valve. There are several currently marketed, with different design strategies. One design, shared by the NMT Orbis-Sigma and Phoenix (Biomedical Corp., Valley Forge, PA) valves, is multistage differential-pressure valves that, in at least one operating mode, limit the CSF flow rate by narrowing the aperture through the differential-pressure valve mechanism. Conceptually and theoretically, these valves are designed to operate in the flow-rate-limiting mode under "normal" conditions and then switch to a high flow rate under conditions of high intracranial pressure. Although designed primarily to prevent overdrainage complications, nontraumatic subdural hemorrhage formation has been reported anecdotally in NPH patients in whom these valves were used (37, 54).

A second design approach to achieve CSF flow restriction has been to incorporate a high-flow-resistance tube that does not have a differential-pressure check-valve mechanism. The Codman FloGuard valve (Codman/Johnson & Johnson, Raynham, MA) is a recently introduced valve that adds in series a dual-stage flow-limiting device to an adjustable differential-pressure valve (see discussion below regarding adjustable valves). It is designed to prevent gravity-dependent overdrainage by selectively reducing high CSF flow rates when the patient is the upright position (13). An advantage of flow-restricted valve designs for INPH has not been established prospectively.

Dual-stage Differential-pressure Valve Designs

The Miethke dual-switch valve (Christoph Miethke GmbH and Co., Potsdam, Germany) uses a dual-stage differential-

pressure valve design to counteract or prevent overdrainage complications. High-density tantalum spheres move within the valve in response to gravity so that the supine and upright positions have low-pressure or very-high-pressure (400 mm H_2O) differential-pressure valve settings, respectively. The effectiveness of the Miethke dual-switch valve for INPH has not been established. One study, by Meier and Kintzel (39), suggested a lower incidence of subdural hematoma formation with the Miethke dual-switch valve as compared with the Orbis-Sigma and simple differential-pressure valves. This study, which was purported to be prospective, was not randomized and did not specify as to what percentage of NPH patients treated (total, 116) were idiopathic (therefore not included in the Evidentiary Data, *Table 4.1*). Meier et al. (40) also reported their experience using the Miethke dual-switch valve in 128 NPH patients (70 with INPH). The results, not segregated by INPH versus secondary NPH, demonstrated a 63% good outcome rate, a 2% overdrainage, and a 5% underdrainage complication rate.

Adjustable ("Programmable") Valves

As noted above, nearly all valve designs incorporate a differential-pressure valve mechanism as the core component. Because all valve designs have been susceptible to either underdrainage or overdrainage, several adjustable valves have been designed and marketed that allow for the opening pressure of the differential-pressure valve mechanism to be changed noninvasively. The Sophy (Sophysa, Orsay, France) and Codman-Medos valves were introduced in the late 1980s, and the latter was approved for use in the United States in 1998. More recently, valve designs incorporating an ASD (PS Medical Strata valve; Medtronic PS Medical, Goleta, CA; essentially an adjustable Delta valve) or a flow-restricting device (Codman FloGuard valve; a Codman-Medos valve combined with a flow-restricted helical chamber) have been introduced. An advantage of the use of adjustable differential-pressure valves for INPH has not been established in a prospective manner. One large prospective, randomized study of primarily pediatric hydrocephalus patients (including a very small number of NPH patients) did not demonstrate an advantage of the Codman Medos valve compared with other (nonadjustable) valve designs (45).

With regard to INPH, retrospective studies have been reported describing the use of adjustable valves (5, 12, 43, 48, 55, 56). The most significant of these is one by Zemack and Romner (56), who reported their experience with the Codman Medos adjustable valve in 147 patients with INPH. For the initial valve setting at implantation, they chose a high opening pressure (140–180 mm H_2O) for older patients (>75 yr) or patients with "low" lumbar puncture opening pressures. In patients with "high" lumbar pressures, they began with valve pressures ranging from 90 to 130 mm H_2O. Given this strategy for the initial settings, a total of 138 adjustments were performed (average, 0.94 and maximum, 8 adjustments per patient). The reasons for adjustment were overdrainage, 24%; underdrainage, 54%; and response to subdural fluid collection, 9%. Approximately 50% of the valve adjustments (typically ≈30 mm H_2O) were deemed clinically beneficial. The average "final" valve setting was 130 mm H_2O (range, 40–200 mm H_2O). In another retrospective study including 32 INPH patients, 88% of the patients required at least one setting readjustment (48). These studies are remarkable with regard to the heterogeneity of pressure hydrodynamics in shunted INPH patients, judged by the sheer number of required adjustments and the extraordinary range of opening pressures ultimately settled on.

Valve Comparison Studies

Several studies have compared different valve pressure settings for the treatment of INPH. The first study, by McQuarrie et al. (37), was a retrospective study that included 47 INPH patients treated with either low- or medium-pressure valves. Unfortunately, some valves with ASDs were included, and the results of ASD versus no ASD were not segregated out. Although the improvement rate was better for low- compared with medium-pressure valves (80 versus 50%, respectively), the methodology used makes the results inconclusive.

The Dutch NPH study was designed, in part, to determine the effect of valve selection for the treatment of NPH. This study, reported by Boon et al. (7), included 85 INPH patients who were randomly selected to receive either a low- or medium-pressure differential-pressure valve (no ASD). The Dutch NPH study, which included mostly INPH patients (85 of 93), demonstrated that there was no difference in outcome between these two valve settings.

One retrospective study, by Weiner et al. (54), compared the outcome results between the Orbis-Sigma valve and shunt systems using either medium- or high-pressure differential-pressure valves. This study of 37 INPH patients found no significant difference between these two groups.

On the basis of our current understanding of both the in vitro and in vivo behavior of shunt systems (1, 3, 12, 14–18, 23, 24, 26, 36, 39, 42, 51), several comments are warranted in regard to the above valve comparison studies. The study by McQuarrie et al. (37) is limited by an incorrect assumption that in vivo shunt hydrodynamics are equivalent for the same valve opening pressure with or without an ASD. For the Dutch NPH study (7), the two valve pressures selected were on the lower end of the spectrum (low, 30–40 versus medium, 50–90 mm H_2O). On the basis of the results of the Dutch NPH study, one could argue that valve pressure selection does not make a difference in NPH and therefore extrapolate this finding to conclude that there is no evidence suggesting the usefulness of an adjustable (programmable) valve. This assertion may not be valid or reasonable, given the reported experience with adjustable valves for INPH, in which the much higher valve pressures than those used in the Dutch NPH study were optimal for the management (56). In addition, one could alternatively argue that the valve pressures used in the Dutch NPH study were too low given the high incidence of subdural

effusions. If the Dutch NPH study had instead compared 30 versus 200 mm H_2O valve settings, it is possible that a statistically significant difference might have been found with regard to complications, etc. Therefore, it is premature to conclude that valve pressure setting is inconsequential with regard to outcome with INPH.

SUMMARY

In summary, because there are no Class I studies that have addressed the question of comparing operative versus conservative management of INPH, there is insufficient evidence to establish the surgical management of INPH as a standard. It is included here as a guideline on the basis of a preponderance of the evidence, including well-conducted Class II prospective studies demonstrating acceptable risk-to-benefit ratios. The risk-to-benefit ratio must be individualized for each patient with the following issues in mind: 1) shunt-responsive INPH exists with reasonable certainty, 2) there are low surgical risks related to comorbidities, and 3) the degree of INPH-related morbidity warrants the shunt-related risks.

Patient Selection

For practical reasons, it is important to identify probable shunt responders diagnosed with INPH. If the patient is an acceptable candidate for anesthesia, then an INPH-specific risk-benefit analysis should be determined. In general, patients exhibiting negligible symptoms may not be suitable candidates for surgical management, given the known risks and complications associated with shunting INPH. The treatment of INPH should not be considered lightly, given the seriousness of the potential complications.

Type of Shunt

The two most commonly used configurations are the VP and VA shunts.

Valve Selection

The choice of valve type and setting should be based on empirical reasoning and a basic understanding of shunt hydrodynamics. The most conservative choice is a valve incorporating an ASD, with the understanding that underdrainage (despite a low opening pressure) may occur in a small percentage of patients because of the ASD. On the basis of the results of retrospective studies, the use of an adjustable valve may be beneficial in the management of INPH because of the ability to manage both underdrainage and overdrainage problems nonoperatively.

KEY ISSUES FOR FUTURE INVESTIGATION

If we are ever going to be certain that surgical management of INPH is the appropriate recommendation, a better understanding of the natural course of untreated INPH is needed. Because the patient population is elderly (frequently with other medical problems, including ischemic brain disease) and the progression of INPH is variable, this is an important issue. From a practical standpoint, it is not clear whether a suspected INPH patient would accept being randomized into a conservative management arm, and therefore, such a study may never be performed. The question of optimal valve selection requires further study as well. With the advent of adjustable valves, there is no longer a question of whether one pressure setting is better than another. Instead, we need improved diagnostic techniques and improved preoperative methods for determining the optimal valve type for individual patients. There is clearly a need for prospective randomized studies to help resolve many of the issues raised in this report.

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Schematic of the first clinically successful regulatory valve for control of hydrocephalus, introduced by Nulsen and Spitz in 1949.