Ventriculoperitoneal Shunt Complications in the European Idiopathic Normal Pressure Hydrocephalus Multicenter Study

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BACKGROUND: Ventriculoperitoneal shunt (VP-shunt) is the standard of treatment for idiopathic normal pressure hydrocephalus (iNPH). However, a thorough investigation of VP-shunt complications in this population is lacking.

OBJECTIVE: To present the analysis and the rates of complications progressively occurring during the first year after shunt surgery in the patients with iNPH included in the European multicenter (EU-iNPH) study.

METHODS: Patients (n = 142) were prospectively included in the EU-iNPH study by 13 institutions. All patients received a programmable VP-shunt. One hundred fifteen patients completed the 12-mo follow-up. Reexaminations were performed 1, 3, and 12 mo after surgery. Data regarding symptomatic over- or underdrainage, infections, malposition, subdural collections, and shunt surgery were collected and analyzed.

RESULTS: Thirty patients (26%) experienced symptoms due to shunt underdrainage. Symptomatic overdrainage was reported in 10 (9%). Shunt adjustments were made in 43 (37%). Shunt malposition was recognized as the primary cause of shunt malfunction in 8 (7%), while only 1 infection (0.9%) occurred. Subdural hematoma was diagnosed in 7 (6%) and was treated by increasing the opening pressure of the valve in 5 patients. Hygroma was diagnosed in 10 (9%), requiring surgery in 1 patient. Overall, 17 patients (15%) underwent 19 shunt surgeries.

CONCLUSION: The advances in valve technology, a careful opening pressure setting, and rigorous follow-up allow a significant reduction of complications, which can be usually managed nonsurgically within the first 3 to 6 mo.

KEY WORDS: Complication, Idiopathic normal pressure hydrocephalus, Multicenter study, Symptoms and signs, Ventriculoperitoneal shunt

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Idiopathic normal pressure hydrocephalus (iNPH) is a treatable syndrome characterized radiologically by ventricular enlargement, functionally by normal intracranial pressure (ICP), and clinically by gait disturbance, cognitive impairment, and urinary incontinence. Although some authors proposed endoscopic third-ventriculostomy, ventriculoperitoneal shunting remains the standard treatment for iNPH.[1] So far, most clinical iNPH studies have focused on the selection criteria and outcome. Some papers are available about the complications of ventriculoperitoneal shunt (VP-shunt) for iNPH patients, reporting different rates. However, the available data come from either single institution-based studies or retrospective analyses. The European multicenter study on iNPH (EU-iNPH) was designed and initiated to evaluate the sensitivity, specificity, positive and negative predictive values of the cerebrospinal fluid (CSF) tap test, and resistance to CSF outflow (Rout) in a large series of patients with clinical and radiological signs of iNPH. Data regarding the primary end-points of the EU-iNPH study and results about

ABBREVIATIONS: CSF, cerebrospinal fluid; **CT,** computed tomography; **ICP,** intracranial pressure; **iNPH,** idiopathic normal pressure hydrocephalus; **MMSE,** mini mental state examination; **mRS,** modified Rankin scale; **VP-shunt,** ventriculoperitoneal shunt

outcome in the same series of patients have already been published.[2-4]

Nevertheless, the EU-iNPH study gave us the opportunity to observe and collect evidence also about treatment complications. The aim of this article is to present the analysis and the rates of complications progressively occurring during the first year after shunt surgery in the patients with iNPH included in the EU-iNPH study.

METHODS

Thirteen centers in nine European countries were involved in the study and consecutively enrolled 142 iNPH patients (69 women and 73 men) with a mean age of 71 ± 9 (standard deviation) yr (range 30–87) over a period of 40 mo. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Patients with magnetic resonance imaging findings, symptoms, and signs compatible with iNPH were included in the study. At entry, risk factors for cerebrovascular disease were recorded and the mini mental state examination (MMSE) was administered. After inclusion, the patients underwent a CSF tap test and measurements of Rout, as previously described.[3] The included patients were diagnosed clinically and radiologically according to two sets of criteria, representing typical and questionable iNPH ($iNPH_T$, $iNPH_Q$).

Criteria for $iNPH_T$ required a gradually developed gait disturbance affecting tandem walking, turning, stride length, and width, mild to moderate cognitive impairment (MMSE scores $\geq$ 21), impaired wakefulness, slowness, and memory deficits, a symmetrical quadriventricular enlargement without cortical infarcts or other clinically relevant parenchymal lesions (except for lacunar infarcts of less than 1 ml, mild cortical atrophy, and mild leukoaraiosis), free communication between the ventricular system and the subarachnoid space, and an Evans' Index $>$ 0.30.

Criteria for $iNPH_Q$ required other cognitive symptoms (i.e. aphasia, apraxia, or agnosia) or more severe cognitive deficits (MMSE $<$ 21), moderate cortical atrophy, moderate to severe leukoaraiosis (single cortical infarcts accepted), free communication between the ventricular system, and the subarachnoid space, and an Evans' Index $>$ 0.30.

Patients were also evaluated using the modified Rankin scale (mRS) and a newly developed iNPH scale, as previously described.[2] Patients who refused to participate had a short life expectancy or had contraindications to surgery, and those later found to have an ICP $>$ 18 mm Hg were excluded. Prior to surgery, included patients underwent a combined CSF dynamic test to examine ICP, Rout, and the results of a 50 ml CSF tap test in terms of gait (number of steps and seconds needed for walking 10 m), and psychometric performance (Grooved Pegboard, Stroop's Test), compared with the results achieved before the tap test.

All patients underwent shunt surgery with a Codman-Hakim adjustable valve (Codman, Johnson & Johnson, Codman & Shurtleff Inc, Raynham, Massachusetts) with an opening pressure set to 120 mmH_2O. Patients were reexamined 1 mo, 3 mo, and 12 mo after operation in the same way as at entry (mRS, iNPH Scale and computed tomography (CT) scan). Although 142 patients were initially recruited for the EU-iNPH study, only 115 could be reexamined 12 mo after surgery. Two patients refused further participation before surgery, 3 died of causes not related to their hydrocephalus or shunt surgery, 22 were lost to follow-up, for a total of 27 drop-outs. Most iNPH patients in the participating Centers are supported after discharge in order to recognize eventual problems and to be referred to the neurosurgeon when needed. Nevertheless, 22 out of 142 patients (15.5%) were lost to follow-up. Half of these patients came from two centers that experienced administrative problems. Moreover, the dropouts were more affected at entry than those who completed the study, i.e. they had significantly lower iNPH-scale scores, higher mRS, and higher frequencies of hypertension, diabetes, cardiac disease, and previous strokes. Importantly, none of these factors contributed negatively to improvement among those who completed. Pronounced disease severity at baseline made patients less prone to complete the study.

All patients who received VP-shunt were included in the analysis of complications. We defined as "complications" all the following: malposition, infection, appearance of subdural hematoma and hygroma at head CT scan. Malposition means that either the proximal or the distal catheter was found to be positioned in a way that caused a reduction or obstruction of CSF flow. The differential between subdural hematoma and hygroma was made basing on CT appearance, which is similar, but the density of hygroma is the same as CSF. We also analyzed symptomatic underdrainage and overdrainage, although they should not be considered complications sensu stricto, as they are an expected finding when adjusting the valve opening pressure. Symptomatic overdrainage can manifest as slit ventricle syndrome or intracranial hypotension syndrome; cases with subdural fluid collections were analyzed separately. Symptomatic underdrainage is defined as persistent symptoms of hydrocephalus due to insufficient CSF drainage. Symptomatic underdrainage is normally encountered in implanted patients, as the valve opening pressure is progressively reduced during follow-up until symptoms are minimized. Symptomatic underdrainage must be distinguished from failure to respond to shunting, which is defined as persistent symptoms of hydrocephalus despite valve opening pressure adjustments. Moreover, we examined the need for further surgeries due to complications.

The local ethical committees at all participant centers approved the study (Clinical Trial ORG).

RESULTS

Symptomatic Underdrainage and Overdrainage

Thirty patients (26.1%) out of the 115 patients who could be evaluated 12 mo after surgery-experienced symptoms due to shunt underdrainage. Symptomatic overdrainage was reported in 10 patients (8.7%). Compared to overdrainage symptoms, which are usually encountered in the first 30 d, underdrainage symptoms progressively decreased over time (Figure 1).

Shunt adjustments were made in 43 patients (37.4%). In 36 cases adjustment was made for either under- or over-drainage. In 7 cases the shunt was downregulated in an effort to further optimize treatment. The number of patients requiring shunt adjustment progressively decreased over time, with the most significant decreases during the first 3 mo (Figure 2). Out of the 43 patients who had shunt adjustments, 27 were ultimately found to be shunt responders, and the remaining 16 were labeled nonresponders. It is worth noting that 19 patients failed to respond

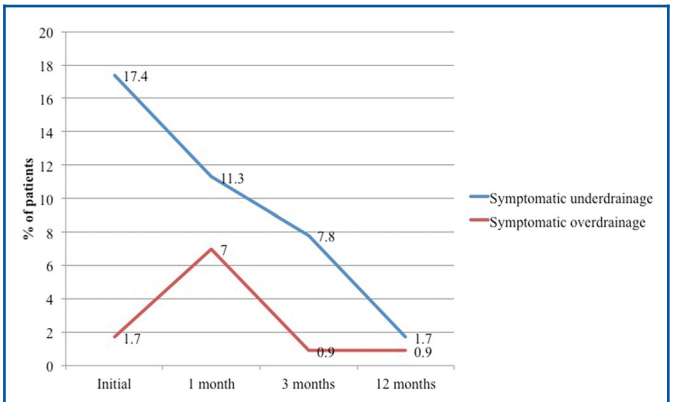

FIGURE 1. *Symptomatic underdrainage and overdrainage.*

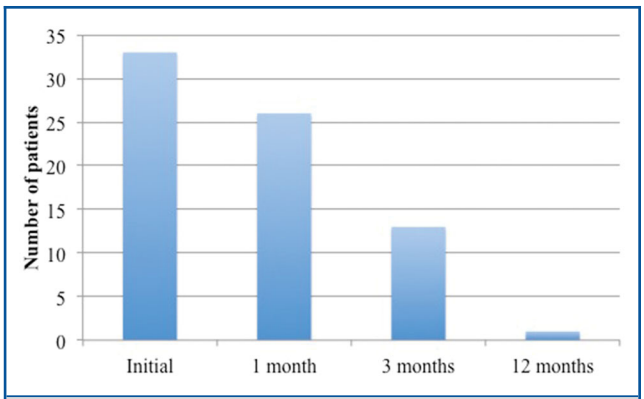

FIGURE 2. *Valve adjustments.*

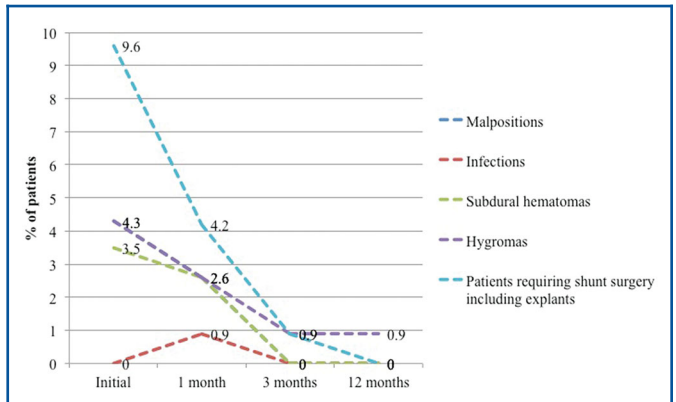

FIGURE 3. *Complications of VP-shunting.*

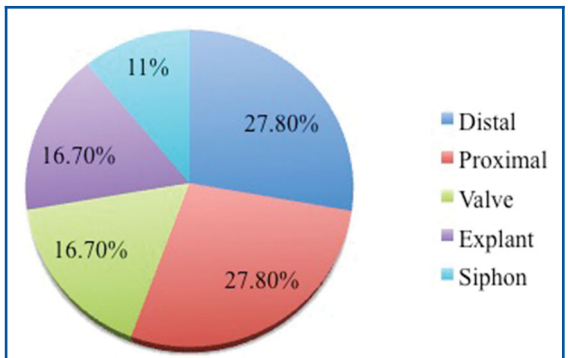

FIGURE 4. *Sites of shunt surgery.*

to shunting and their symptoms were unchanged 12 mo after surgery.

Malposition

Malposition of the shunt was recognized as the primary cause of the shunt malfunction in 8 patients (6.9%; Figure 3). In all cases surgery was required to reposition the shunt. Malposition was always diagnosed in the first 30 d after implant.

Infections

Only 1 infection (0.9%) occurred in 115 patients (Figure 3). It was diagnosed within the first month after implant, and explant of the shunt was required.

Subdural hematoma

Subdural hematoma was diagnosed in 7 patients (6.1%), all during the first month after implant (Figure 3). In 2 cases (1.7%) surgical evacuation was necessary. The 5 others were successfully treated during the first 3 mo after implant increasing the opening pressure of the valve.

Hygroma

Hygroma was diagnosed in 10 patients (8.7%). Although rarely, hygroma was detected even several months after implant (Figure 3). In 1 case (0.9%) surgery was indicated.

Shunt Surgery

Seventeen patients (14.7%) underwent 19 procedures (to replace 5 distal catheters, 5 proximal catheters, 3 valves, 2 siphons, and to perform 3 explants; Figure 4). The procedures were performed during the first 30 d in 94% of cases.

DISCUSSION

iNPH is the only form of dementia that can be satisfactorily treated with surgery, when it is properly distinguished from other neurodegenerative conditions. Although shunting is the most widely accepted surgical treatment for iNPH, and the published improvement rates after surgery are significantly high,[5] some studies warned about a potentially significant complication rate. In their review published in 2001, Hebb and Cusimano[6] reported a pooled mean shunt complication rate as high as 38% (range 5%-100%), with a 22% (range 0%-47%) risk of additional

TABLE. Literature Review on Shunt Complications in iNPH Patients

	Patients	Shunt complication rate	Symptomatic overdrainage	Malfunction	Infection	SDH/SDHy	Permanent neurological deficit/death	Additional surgery
Hebb, Cusimano[6]	1835	38% (5-100%)		8.3%	2.2%	9%	6% (0%-35%)	22% (0%-47%)
Zemack, Romner[7]	218 NPH (147 iNPH)				6.4%	7.5%/2%		23.8%
Poca et al[8]	43					4.2%/3.4%	0%	7%
McGirt et al[9]	132		15% (headache)		6.7%	2%	1%	
Marmarou et al[10]	102	9.8% major 13.7% minor	5% (headache)		3%	3%/3%		
Poca et al[5]	236	8.3%		0.8%	0.4%	2.5%	0.8%	
Khan et al[11]	164				0.6%	29%	0%	7.4%
Malem et al[12]	24					4%		
Saehle et al[13]	68	23%		4.4%	1.5%	13%		
Gölz et al[14]	147	13%			2%	1.4%		8.2%
EU-iNPH study	115		8.7%	7%	0.9%	6%	0%	15%

surgery and a 6% (range 0%-35%) combined rate of permanent neurological deficit and death. Such data, if confirmed, could be problematic and worrisome when deciding for shunt surgery for iNPH patients. However, new valve technologies have been developed over the last decades that were unavailable when some of the reported studies were published. Moreover, the majority of the reviewed articles are retrospective with a small number of cases. A thorough review of the most recent literature (studies published after 2001) clearly showed the improvement of shunt surgery for iNPH patients in terms of complication rates (Table).[5-14] Particularly, it has been demonstrated that permanent neurological deficit or shunt-related death usually occur in less than 1% of cases, and the rates of malfunction, subdural fluid collections, and additional surgery can be significantly reduced.

Besides the already published data about the predictive values of resistance to CSF outflow and the CSF tap test, and the outcome after shunt surgery, the prospective EU-iNPH study allowed the collection of important information about complications after shunting. These results are even more valuable because the onset of specific complications could be tracked over the 12-mo period of the follow-up in a continuous way. Consequently, it was possible not only to assess their rate, but also their trend. Complications after shunt surgery can be distinguished between symptomatic and asymptomatic (radiologically diagnosed), surgically and nonsurgically treated, early (appearing in the first 30 d) and late.

The most common problem with shunted patients is symptomatic under- or overdrainage. However, inappropriate underdrainage should not be considered a complication. Actually, it is the expected occurrence immediately after surgery because the initial opening pressure of the valve is intentionally set high in order to prevent excessive drainage and consequent subdural effusions. The subsequent gradual reduction of the opening pressure consistently with the clinical course allows tailoring the appropriate value for each patient. Conversely, symptomatic overdrainage can be potentially dangerous. Nonetheless, this risk (7%) is almost totally limited to the first month after surgery. Recent studies compared two groups of shunted patients. In the first group the valve setting was initially set to 20 cm H_2O and gradually reduced to 4 cm H_2O. In the second group the valve was kept at a medium level of 12 cm H_2O. No significant differences in the rate of complications were found between the two groups, although the frequency of overdrainage symptoms was significantly higher for a valve setting $\leq$12 cm H_2O compared with a setting $>$12 cm H_2O. Interestingly, improvement after surgery was the same in the two groups, irrespective of valve setting.[13,15] In our series, 9 patients (7.8%) had a final valve opening pressure higher than 120 mm H_2O. This suggests that 120 mm H_2O as initial valve setting is probably not the best option for every patient, and a tailored approach is advisable in order to minimize overdrainage symptoms.

Malposition, infection, subdural hematoma, and subdural hygroma are usually early complications. However, hygroma can appear also at a later stage. In our series, all these complications have a low incidence compared to the review by Hebb and Cusimano,[6] and our data are consistent with the majority of the most recent published series (Table). Furthermore, in some patients the presence of a thin, nonsymptomatic hygroma could be acceptable to maximize shunt benefits. Although infections represent a not-further-reducible complication, the history of shunting showed that decreasing the rate of malposition and subdural fluid collections is actually feasible. Antisiphoning and adjustable valves played a major role in lowering the amount of overdrainage-related problems. Moreover, increasing the initial

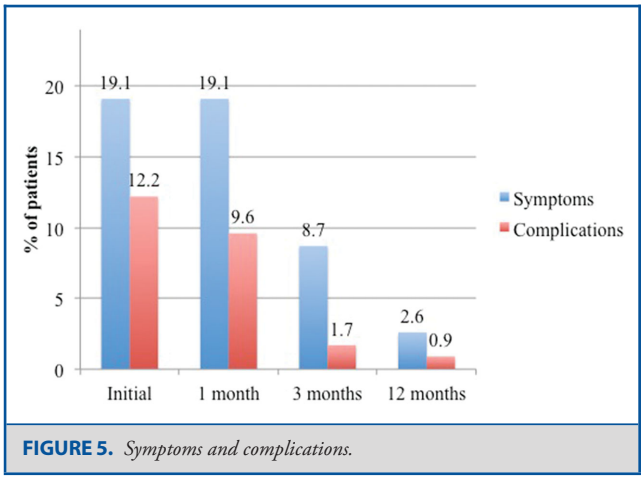

FIGURE 5. *Symptoms and complications.*

opening pressure of the valve showed to be of great value to further reduce the rate of subdural effusions. The simple valve opening pressure adjustment is very often successful in treating this condition.[16] In our series, only 2.6% of patients required surgical drainage.

About one-third of our patients underwent valve adjustments after shunt placement. It is worth noting that in the majority of cases the correct valve setting could be detected within the first 3 mo. The patient has to be informed beforehand that valve adjustments over the months following surgery are part of the current treatment of his iNPH. Nevertheless, in some cases additional shunt surgery is required when catheters are misplaced or when infection occurs requiring the explant of the system. Additional shunt surgery was necessary in 14.7% of the patients during the 12-mo follow-up. The site of surgery was more often the proximal or the distal catheter, and the risk for shunt revision is more likely to occur during the first 30 d. Although the shunt revision rate can certainly be further reduced, it is worth noting that the occurrence of this complication significantly drops over time after surgery. Of course, as always happens with implantable devices, mechanical problems can occur later than 12 mo. This complication was not analyzed by the EU-iNPH study, which was limited to a 1-yr follow-up.

The overall trend of symptoms and complications shows a significant decrease during the first 3 mo after surgery (Figure 5). A tight follow-up is therefore required especially during the first months after shunt placement in order to detect symptoms and potential complications and treat them immediately.

CONCLUSION

Besides the well-known improved outcome for iNPH patients, shunt surgery currently has an acceptably low complication rate. The advances in valve technology, a careful opening pressure setting, and rigorous follow-up allow a significant reduction of complications that can more often be managed nonsurgically. Complications can be distinguished into avoidable (for example malposition) and unavoidable (infections). The majority of complications and inadequate setting of the valve are corrected within the first 3 to 6 mo after surgery.

Disclosures

Codman, Johnson & Johnson, Raynham, Massachusetts provided financial support. The sponsor had no role in the design or conduct of this research. Dr Klinge was a medical consultant for Codman, Johnson & Johnson, at the time of the study. Dr Wikkelsø receives honoraria for lecturing and consulting by Codman, Johnson&Johnson and Likvor AB.

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