Outcome of Surgery for Idiopathic Normal Pressure Hydrocephalus: Role of Preoperative Static and Pulsatile Intracranial Pressure

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OBJECTIVES: **To examine the outcome of surgery for idiopathic normal-pressure hydrocephalus (iNPH) and how outcome relates to the preoperative static and pulsatile intracranial pressure (ICP).**

METHODS: **An observational cohort study included all patients with iNPH managed at our department during the years 2002–2012 in whom overnight ICP monitoring was part of the preoperative work-up. Clinical data were retrieved from a quality registry and ICP scores from a pressure database.**

RESULTS: **The study included 472 patients, 316 in the surgery group and 156 in the nonsurgery group. Among those treated surgically, 278 (90%) showed clinical improvement (Responders) whereas 32 (10%) had no improvement (Nonresponders). Among Responders, only about one third reached the best clinical scores; moreover, the difference in clinical score between Responders and Nonresponders declined with time after surgery, particularly after 3–4 years. The surgery was accompanied by acute intracranial hematomas in 11 patients (3.5%), of whom 4 (1.3%) died. Survival (age at death) was significantly greater among the Responders than in Non-responders. Although the static ICP was normal in all patients, the pulsatile ICP was significantly greater in Responders than in Non-responders.**

CONCLUSIONS: **The pulsatile ICP was greater in shunt Responders than Nonresponders. Although the clinical improvement declined over time and the majority did not experience complete relief of symptoms, shunt Responders lived significantly longer than Nonresponders. The present observations suggest that the current surgical treatment regimens for iNPH (primarily shunt surgery) address only some aspects of the disease process, in particular the aspect of brain water disturbance.**

INTRODUCTION

The so-called idiopathic *normal-pressure* hydrocephalus (iNPH) syndrome was described 50 years ago.[1] Patients with the triad of unsteady and ataxic gait, urinary incontinence, and cognitive impairment (dementia), combined with enlarged cerebral ventricles and normal lumbar cerebrospinal fluid (CSF) pressure, improved clinically after CSF diversion surgery (shunt implantation).[2] Shunt surgery (and in a few cases endoscopic third ventrciulostomy) is the treatment of choice, although the results of surgery for iNPH are still a matter of controversy.[3,4]

The pathophysiology of iNPH remains an enigma. Because symptoms improve after CSF diversion surgery,[5] it generally is accepted that a disturbance in CSF circulation is involved. The clinical improvement may be linked to improved cerebral metabolism,[6] as well as improved intracranial pressure–volume relationship.[7] Despite the term *normal-pressure* hydrocephalus, it is controversial how the intracranial pressure (ICP) becomes altered in iNPH. Further knowledge on this matter is crucial because the only current treatment for iNPH is surgical, which goal is to reduce the ICP.

Key words
- Complications
- Intracranial pressure
- Normal-pressure hydrocephalus
- Outcome
- Shunt surgery

Abbreviations and Acronyms
CSF: Cerebrospinal fluid
CT: Computed tomography
ICH: Intracerebral hemorrhage
ICP: Intracranial pressure
iNPH: Idiopathic normal-pressure hydrocephalus
MRI: Magnetic resonance imaging
MWA: Mean intracranial pressure wave amplitude

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Citation: World Neurosurg. (2016) 86:186-193.
http://dx.doi.org/10.1016/j.wneu.2015.09.067

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

In our department, we have for more than a decade monitored the static and pulsatile ICP overnight as part of the preoperative work-up in patients with iNPH. In this observational cohort study, we examined the outcome of surgery for iNPH with regard to clinical outcome, severe complications (intracranial bleeds), and survival. We further evaluated how the preoperative static and pulsatile ICP scores related to the outcome of surgery.

METHODS

Patient Materials

The study included all iNPH patients who underwent ICP monitoring as part of their preoperative work-up in the Department of Neurosurgery, Oslo University Hospital-Rikshospitalet, Oslo, Norway, during the years 2002–2012.

The study was approved by the Oslo University Hospital–Rikshospitalet as a quality study (Approval 2014/4720). The Regional Committee for Medical and Health Research Ethics of Health Region South-East, Norway, was informed in writing and had no objections to the study (reference 2014/528). Information was retrieved from Neurovascular-Hydrocephalus Quality Register (Regional Committee for Medical and Health Research Ethics Approval 11/6692).

Patient Management and Follow-Up

The department's routine for the management of iNPH is as follows: Patients with suspected iNPH usually are referred from local neurologic departments on the basis of symptoms indicative of iNPH and imaging findings of ventriculomegaly. In some patients, a tap test or infusion test has been performed before their referral. At our department, a clinical assessment is done, and ICP monitoring is performed overnight. Indication for CSF diversion surgery is based on the combination of clinical findings, the presence of comorbidity, imaging findings, and results of the ICP monitoring. Thus, patients should meet the clinical and imaging criteria for iNPH, and the ICP measurements were a final decision maker. With regard to the ICP scores, we primarily use the mean intracranial pressure wave (MWA) values and recommend shunting in patients with MWA values greater than the upper normal threshold values at night, i.e., MWA $\geq$4 mm Hg on average and $\geq$5 mm Hg in minimum 10% of recording time from 11 PM until 7 AM.[8]

A NPH grading scale (**Appendix**) is used to assess the severity of symptoms. Assessment was performed before ICP monitoring/surgery and then at intervals during follow-up. Clinical improvement was defined as an increase in clinical score on the NPH grading scale.

Imaging includes computed tomography scanning and/or magnetic resonance imaging. During the last few years, magnetic resonance imaging phase-contrast imaging also has been included. The quantitative imaging of ventricular size or other imaging indices of CSF circulation was not a part of the present study and is therefore not commented on.

The ordinary treatment is shunt surgery (ventriculoperitoneal shunt). Two types of shunt valves were used: Codman Hakim Programmable valve (Codman, Johnson & Johnson, Raynham, Massachusetts, USA), or Mietke ProGAV valve (Aesculap AG, Tüttlingen, Germany). In rare cases with questionable aqueduct stenosis, an endoscopic third ventriculostomy is performed, either soon after the ICP monitoring or some weeks later.

After surgery, the patients are followed in our outpatient clinic or they are contacted by phone. According to this department's routine, clinical control was done after 3–6 months, 12 months, and then annually. Suspected shunt failure is accompanied with either of the following: adjustment of shunt valve opening pressure, continuous overnight ICP monitoring, or shunt-revision.

The Neurovascular-Hydrocephalus Quality Register stores the clinical information, including preoperative and follow-up data. The death dates of all patients are provided from the Norwegian Folk Registry.

Preoperative Monitoring of Static and Pulsatile ICP

We have described our clinical routine for ICP monitoring previously.[8] Placement of the solid ICP sensor is done in the operating room with the patient under local anesthesia. A small burr hole is made in the frontal region, a small opening made in the dura, and the sensor placed 1–2 cm into the brain parenchyma after being tunneled subcutaneously. Most commonly, the Codman ICP MicroSensor (Codman; Johnson & Johnson) is used, and in some patients the Raumedic NeuroVent P sensor (Raumedic AG, Münchberg/Helmbrechts, Germany) is used.

The patient is transferred to the neuro-intermediate ward, the ICP sensor connects to a computerized system for continuous recording, and the monitoring is continued overnight, with real-time presentation of the continuous ICP signals. Assessment of the ICP measurements is performed by the attending doctor the subsequent morning. The continuous ICP raw data files are stored in a pressure database on the hospital server.

For the present study, the continuous ICP recordings were retrieved from the pressure database and analyzed according to a method described previously.[9] According to the automatic routine, the cardiac-induced ICP waves were identified in the signal and for every subsequent 6-second time window the static ICP is characterized as the mean ICP. The pulsatile ICP is characterized as the mean ICP wave amplitude (pressure difference from diastolic minimum to systolic maximum pressure, MWA), the mean ICP wave rise time (time difference from diastolic minimum to systolic maximum pressure), and the mean ICP wave rise time coefficient (pressure difference divided by time difference from diastolic minimum to systolic maximum pressure). To compare patients, we considered only the recordings from 11 PM until 7 AM.

Statistical Analysis

All statistical analyses were performed with SPSS software, version 22 (IBM Corporation, Armonk, New York, USA). Between-group differences for repeated measures were analyzed by the use of linear mixed models with a random intercept. In addition, independent sample *t*-tests between the 2 groups were performed at each follow-up time. Survival was assessed using Kaplan-Meier plots with using log-rank test to determine differences between groups. The ICP scores were used in decision making for shunting, and we did not determine predictive values of ICP scores for shunt response. Statistical significance was accepted at the 0.05 level.