



Effect of lumbo-peritoneal shunt surgery on neuropsychiatric symptoms in patients with idiopathic normal pressure hydrocephalus



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ABSTRACT

Introduction: Patients with idiopathic normal pressure hydrocephalus (iNPH) have neuropsychiatric symptoms that could affect patients' quality of life and caregiver burden. In this study, we assessed the effect of lumbo-peritoneal (L-P) shunt surgery on neuropsychiatric symptoms and the association between neuropsychiatric symptoms and caregiver burden after L-P shunt surgery.

Methods: We recruited 22 iNPH patients who had L-P shunt surgery and who were followed up for 3 months after surgery. Neuropsychiatric symptoms and caregiver burden were evaluated with the Neuropsychiatric Inventory (NPI) and Zarit Burden Interview (ZBI), respectively, before and 3 months after surgery. We evaluated the changes of NPI and ZBI and the association between the changes in these 2 scores and the triad symptoms.

Results: NPI total, apathy, and depression scores significantly decreased after surgery. The improvement in NPI total, apathy, disinhibition, and irritability scores after surgery were significantly and positively associated with improvement in ZBI score after surgery. Improvement in NPI apathy score was significantly associated with improvement in Frontal Assessment Battery score after surgery.

Conclusion: L-P shunt surgery was effective in reducing not only the triad symptoms but also the neuropsychiatric symptoms, and the improved neuropsychiatric symptoms might decrease caregiver burden for iNPH patients.

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1. Introduction

Normal pressure hydrocephalus (NPH), first described by Salomon Hakim in 1965, is a treatable disorder characterized by the triad symptoms of gait disturbance, cognitive impairment, and urinary incontinence [1]. NPH is classified into secondary NPH (sNPH) and idiopathic NPH (iNPH), for which there is no antecedent cause. iNPH is a common disease with a prevalence of 1.1% in Japanese [2] and 2.1% in Swedish [3] elderly community residents. iNPH is a causal disease of treatable dementia. The standard treatment of iNPH is shunt surgery. Some adjustable valve systems allow non-invasive handling of over- and under-drainage, and are thus safer and more effective than fixed valve systems [4].

Patients with iNPH have neuropsychiatric symptoms similar to other causal diseases of dementia, such as Alzheimer's disease (AD). We previously reported that 73.4% of iNPH patients had at least one neuropsychiatric symptom; apathy was the most frequent (70.3%), followed by

anxiety (25.0%) and aggression (17.2%) [5]. High prevalence of neuropsychiatric symptoms in iNPH was also found in a subsequent study [6]. In patients with dementia, both positive neuropsychiatric symptoms (e.g., delusions, hallucinations, irritability, and disinhibition) and negative neuropsychiatric symptoms (e.g., apathy) decrease the quality of life (QOL) and increase caregiver burden [7–9]. Therefore, treatment of negative neuropsychiatric symptoms, as well as positive neuropsychiatric symptoms, is important.

Apathy, depression, and disinhibition (which are common in iNPH) have been related to hypoperfusion in frontal lobe in patients with AD, frontotemporal dementia (FTD), and dementia with Lewy bodies (DLB) [10–13]. A positron emission tomography (PET) study in iNPH patients showed improvement of oxygen metabolism or cerebral perfusion in the frontal cortex and thalamus following shunt surgery [14]. Thus, shunt surgery might be shown to improve neuropsychiatric symptoms in iNPH. The effect of shunt surgery on neuropsychiatric symptoms in NPH were evaluated in some previous studies [15–17]. However, in those studies, only apathy and depression or syndromes with psychiatric symptoms, disturbance of consciousness, and cognitive dysfunction were evaluated. In addition, the subjects of the studies included both patients with iNPH and sNPH, although sNPH might differ from iNPH with regard to how symptoms progress and improvement after shunt surgery. Therefore, the effect of shunt surgery on various

Abbreviations: NPH, normal pressure hydrocephalus; iNPH, idiopathic NPH; sNPH, secondary NPH; L-P, lumbo-peritoneal; MMSE, Mini-Mental State Examination; FAB, Frontal Assessment Battery; TUG, Timed Up and Go test; ICIQSF, International Consultation on Incontinence Questionnaire—Short Form; iNPHGS, iNPH grading scale; mRS, modified Rankin Scale; NPI, Neuropsychiatric Inventory; ZBI, Zarit Burden Interview.

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neuropsychiatric symptoms has yet to be assessed in a group limited to only patients with iNPH.

The effectiveness of lumbo-peritoneal (L-P) shunt surgery on the triad symptoms of iNPH was shown in a randomized controlled trial [18], and L-P shunt is more popular in Japan than ventriculo-peritoneal (V-P) shunt [19]. In our experience, patients are more willing to accept lumbar surgery than cranial surgery, because ventricular catheter placement is associated with roughly a 1% risk of symptomatic intraparenchymal hematoma [20], although shunt malfunction was more common in L-P shunts than V-P shunts [21].

In this study, we assessed the effect of L-P shunt surgery on both neuropsychiatric and triad symptoms as well as the associations between improvement of neuropsychiatric symptoms and reduced caregiver burden in iNPH patients who were recruited from a psychiatric clinic. In addition, we assessed the relationship between the changes of neuropsychiatric symptoms and the changes of the triad symptoms after L-P shunt surgery.

2. Materials and methods

This study was approved by the ethics committee of Osaka University Medical Hospital (Osaka, Japan). Written informed consent was obtained from all subjects and/or their caregivers.

2.1. Subjects

Between 2010 and 2013, 46 patients were admitted to the Department of Neuropsychiatry of Osaka University Medical Hospital for evaluation of suspected iNPH because they fulfilled the following criteria: (1) over 60 years of age, (2) presence of one of the iNPH triad symptom(s) at least, (3) presence of ventriculomegaly on magnetic resonance imaging (Evans index > 0.3), (4) clinical symptoms were not explained by other diseases, and (5) absence of known disorders that cause ventriculomegaly. All patients were subjected to a cerebrospinal fluid (CSF) tap test, in which we removed 30 ml of CSF via lumbar tap. Thirty-four patients had normal CSF pressure (<200 mm H₂O) and normal CSF contents and were CSF tap test-positive.

Among these 34 patients, 6 refused surgery, 1 died before the planned surgery, and 5 were excluded because they had no appropriate caregivers, which were defined as those who met the patients more

than once a week in 30 days and knew the patients' daily lives well. Therefore, 22 individuals with iNPH [mean age (SD) = 75.0 (5.8) years old; female = 12; male = 10] who had L-P shunt surgery were included in this study. All included patients participated in follow-ups until 3 months after L-P shunt surgery (Fig. 1).

2.2. Procedures

All iNPH patients in this study underwent the L-P shunt surgery with either of the Codman–Hakim programmable valve systems (Johnson & Johnson K.K., Tokyo, Japan) or Strata programmable valve (Medtronic, Inc., Goleta, CA, USA). After shunt surgery, we hospitalized the patients for 2 weeks for follow up, and then followed up with them at 1 and 3 months after shunt surgery in our outpatient clinic with cognitive battery, gait assessment, and neuroimaging evaluations. If there was no improvement in clinical symptoms or neuroimaging findings, we doubted shunt dysfunction and conducted shuntgraphy.

The following assessments were conducted in the patients before and 3 months after L-P shunt surgery.

2.2.1. Triad symptom assessment

We used following examinations and scales to assess the iNPH triad symptoms.

Gait disturbance was evaluated with the Timed Up and Go test (TUG) [22]. The TUG is a test of functional mobility that measures the time it takes a subject seated in an armchair to stand up, walk forward 3 m, and return to the seated position.

Cognitive impairment was evaluated with the Mini-Mental State Examination (MMSE) [23], which is a well-validated measure of general cognitive function. We also used Frontal Assessment Battery (FAB) [24] to assess frontal lobe function, as frontal lobe dysfunctions, including attention deficit, are often shown in iNPH patients.

Urinary dysfunction was evaluated with the International Consultation on Incontinence Questionnaire–Short Form (ICIQSF) [25]. The ICIQSF is a questionnaire that evaluates a patient's QOL with regard to incontinence of urine. The range of score is 0 to 21, and higher scores indicate worse QOL.

We also evaluated triad symptoms with the iNPH grading scale (iNPHGS) [26]. The iNPHGS is a clinician-rated scale to rate the severity of each iNPH triad symptom. The score of each domain ranges from 0 to

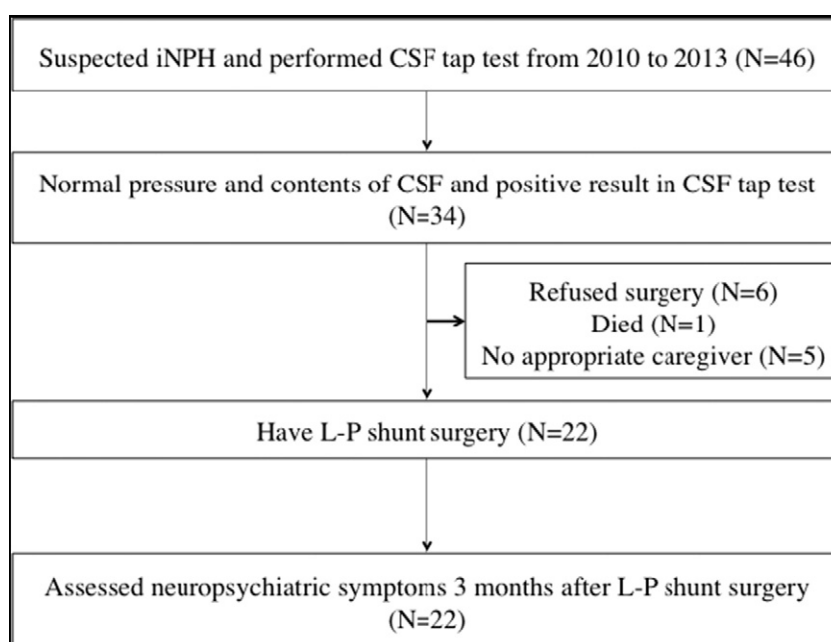


Fig. 1. Participant selection.

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