

# Long-term 4 Years Follow-up Study of 482 Patients Who Underwent Shunting for Idiopathic Normal Pressure Hydrocephalus -Course of Symptoms and Shunt Efficacy Rates Compared by Age Group-

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## Abstract

A total of 482 operated idiopathic normal pressure hydrocephalus (iNPH) patients were divided into those aged <80 years at the time of surgery (group A: 400 cases; and male-to-female ratio, 259:141) and ≥80 years (group B: 82 cases; male-to-female ratio, 43:39) and comparatively investigated based on the following variables: (1) temporal changes in shunt efficacy rates, and (2) temporal changes in each symptom, including the patient's fall frequency and preoperative modified Rankin Scale (mRS) score and during follow-up at 3, 6 months, 1–4 years postoperatively. (1) The shunt efficacy rates at 3 months and 4 years postoperatively were 93% and 82%, respectively, in group A and 92.3% and 70.7%, respectively, in group B. This demonstrates a decrease in shunt efficacy at 4 years postoperatively, regardless of the persistence of shunt function or adjustments in setting pressure. This trend was particularly observed in group B. In group A, 41 (9.8%) cases had decreased efficacy rate, compared with 21 (25.6%) cases in group B, which occurred due to complications with an extracranial or intracranial disease. (2) Gait disturbance (*G*) and urinary incontinence (*U*) showed signs of improvement in the early postoperative stage, while dementia (*D*) and mRS score began to gradually improve from 6 months postoperatively. Patient's fall frequency tended to become higher until 6 months postoperatively than the preoperative rate. In group A, symptom improvement was comparatively maintained until 4 years postoperatively, while in group B, all symptoms and mRS tended to gradually deteriorate beginning at 3 years postoperatively.

Key words: normal pressure hydrocephalus, idiopathic, long-term follow-up, shunt operation

## Introduction

Follow-up studies demonstrated that the treatment effects of shunting for idiopathic normal pressure hydrocephalus (iNPH) slowly decline with time.<sup>1,2)</sup> However, all of them have made judgments based only on fragmentary shunt efficacy rates from a certain time period, and long-term follow-up studies that performed the temporal observation of each symptom are not yet conducted. In this study, the patients, based on those with iNPH who underwent shunting treatment and the possibility of 4-year postoperative follow-up survey, into two age groups and comparatively investigated the preoperative and

postoperative symptom course and shunt efficacy over time.

## Patients and Methods

A total of 482 cases (age: 57–96 years; mean age, 74.2 years; male-to-female ratio, 302:180) diagnosed with iNPH and treated with shunting who can be possibly followed up for 4 years postoperatively were included in this study. Cases of mortality in the postoperative course were excluded. Patients were divided into those aged <80 years at the time of surgery (group A: 400 cases; mean age, 69.7; and male-to-female ratio, 259:141) and ≥80 years (group B: 82 cases; mean age, 83.8; and male-to-female ratio, 43:39). Shunt treatment was determined as effective if even only one of the symptoms from the Japanese Normal Pressure Hydrocephalus Grading Scale-revised (JNPHGS-R)<sup>1,2)</sup> improved by one or more points. Patients were comparatively investigated based on

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the following variables: (1) classification of postoperative improvement in symptoms, (2) classification of shunting method, (3) temporal changes in shunt efficacy rates and their causes, and (4) temporal changes in each symptom, including the patient's fall frequency and preoperative modified Rankin Scale (mRS) score and during the follow-up period (3, 6 months, 1–4 years postoperatively).

**Results**

- 1) Classification of postoperative improvement in symptoms  
The number of cases with improved symptoms (gait disturbance [G], dementia [D], and urinary incontinence [U]) at 3 months postoperatively in group A was 365, 226, and 312, respectively, whereas in group B was 79, 56, and 64, respectively. In both groups, the symptoms that improved from most to least frequent were G, U, and D.
- 2) Classification of the shunting method  
The number of cases that used ventriculo-peritoneal (V-P), lumbo-peritoneal (L-P), and lumbo-subarachnoid-lumboepidural (L-L),<sup>3,4)</sup> shunting methods in group A was 317, 82, and 1, respectively, whereas in group B was 62, 13, and 7, respectively. In both groups, the frequency of each shunting method from

most to least common was V-P, L-P, and L-L. In older adults, the frequency of L-L, which is performed under local anesthesia, was higher in only one case (0.3%) in group A and seven cases (8.5%) in group B.

- 3) Temporal changes in shunt efficacy rates and their causes  
The shunt efficacy rates at 3 months and 4 years postoperatively were 93% (372/400) and 82% (328/400), respectively, in group A and 92.3% (76/82) and 70.7% (58/82), respectively, in group B. This demonstrates a decrease in shunt efficacy at 4 years postoperatively, regardless of the persistence of shunt function or adjustments in setting pressure. This trend was particularly observed in group B (Fig. 1). In group A, 41 (9.8%) cases had decreased efficacy rate, compared with 21 (25.6%) cases in group B. In all cases, the iNPH did not deteriorate; however, complications due to other pathologies such as 29 extracranial diseases (cancer, 4; chronic obstructive pulmonary disease, 4; heart disease, 5; diabetes mellitus, 7; kidney disease, 3; liver disease, 2; trauma, 2; ulcerative colitis, 1; pancreatitis, 1), 18 intracranial diseases (intracranial tumor, 2; intracerebral hemorrhage, 2; infarction, 4; degenerative disease, 4; arteriosclerotic ischemia, 2; head injury, 2), 10 age-related changes, and five

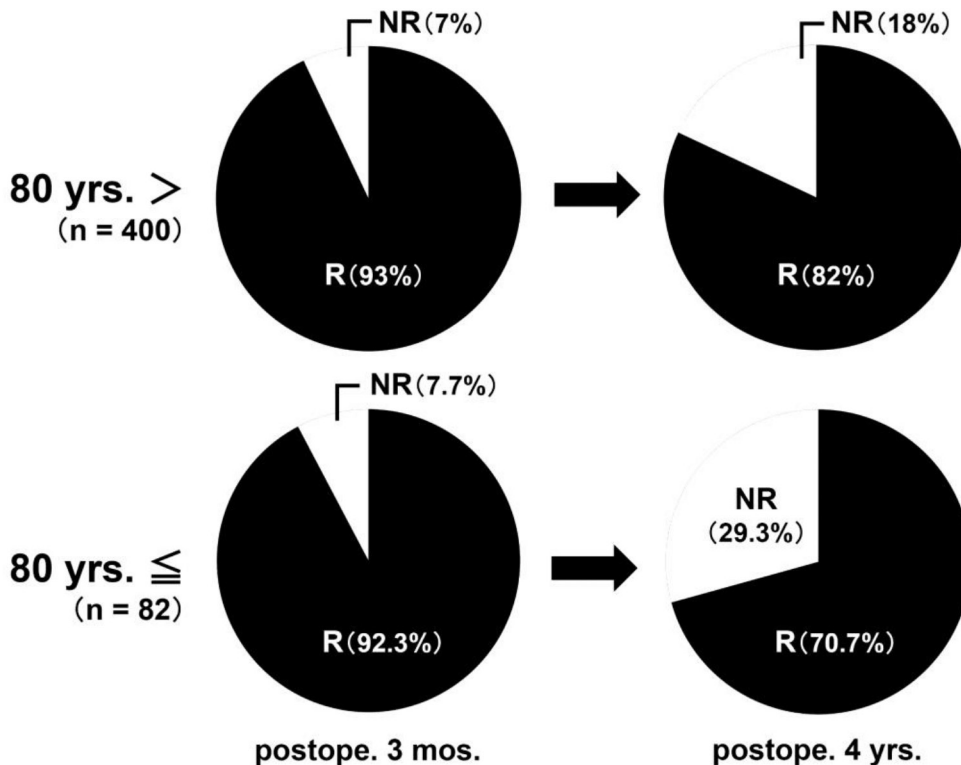


Fig. 1 Postoperative shunt efficacy rates at 3 months (left) and 4 years (right) after the operation. R: shunt responder, NR: shunt non-responder. Upper: <80 years, lower: ≥80 years.

abdominal membrane malabsorption were found in two cases in group A and three cases in group B, respectively. Group A had higher rates of extracranial and intracranial diseases (Group A: 87.8%, group B: 52.4%), whereas group B had higher rates of age-related changes (Group A: 7.3%, group B: 33.3%). In five cases with abdominal membrane malabsorption were supposed reason why the symptoms improved in three cases performed one case of ventriculoatrial (V-A) shunt and two cases of L-L shunt.

4) Temporal changes for each symptom, patient's fall frequency, and mRS scores in the preoperative and follow-up periods

\*The mean values for *G* (3 min timed up and go test: s)<sup>1)</sup> preoperatively and during the follow-up periods were 18.3, 15.0, 14.7, 12.9, 11.8, 12.6, and 13.1 in group A and 22.2, 16.3, 15.8, 14.7, 13.6, 15.9, and 18.4 in group B. In both groups, a reduction in seconds was observed beginning immediately after the surgery. However, at 3 years postoperatively, the value tended to lengthen once again. This tendency was particularly observed in group B (Fig. 2).

\*The mean values for *D* (MMSE: points)<sup>1)</sup> preoperatively and during the follow-up periods were 17.2, 18.6, 23.5, 21.8, 24.0, 23.1, and 22.7 in group A and 15.1, 15.9, 21.2, 20.8, 22.3, 16.8, and 15.3 in group B. In both groups, a marked increase in points was not observed immediately following the surgery, but the MMSE score tended to gradually increase at 6 months postoperatively. However, at 3 years postoperatively, the MMSE score tended to decline once again. This tendency was particularly observed in group B (Fig. 3).

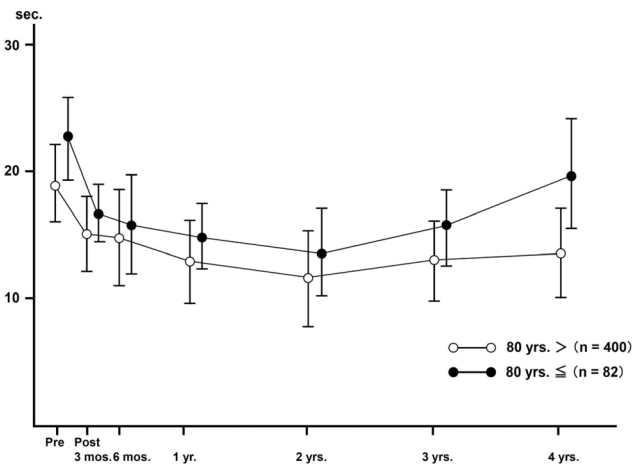


Fig. 2 Clinical course of symptoms pre and postoperatively (*G*: gait disturbance evaluated by 3 min timed up and go test<sup>1)</sup>). White: <80 years, black: ≥80 years.

\*The mean values for *U* (JNPHGS-R: grade)<sup>1)</sup> preoperatively and during the follow-up period were 3.0, 2.4, 2.2, 1.7, 1.8, 1.9, and 2.0 in group A and 3.3, 2.6, 2.4, 2.0, 2.3, 2.4, and 2.6 in group B. In both groups, the grade declined immediately after the surgery, which is similar to *G*. However, as expected, beginning at 3 years postoperatively, the grade tended to increase once again. This tendency was particularly observed in group B (Fig. 4).

\*The mean values for patient's fall frequency (number of incidents) preoperatively and during the follow-up period were 50.4, 60.3, 58.3, 51.6, 52.8, 53.4, and 52.7 in group A and 53.3, 65.1, 62.2, 53.8, 57.7, 62.8, and 64.1 in group B. In both groups, the fall frequency actually increased

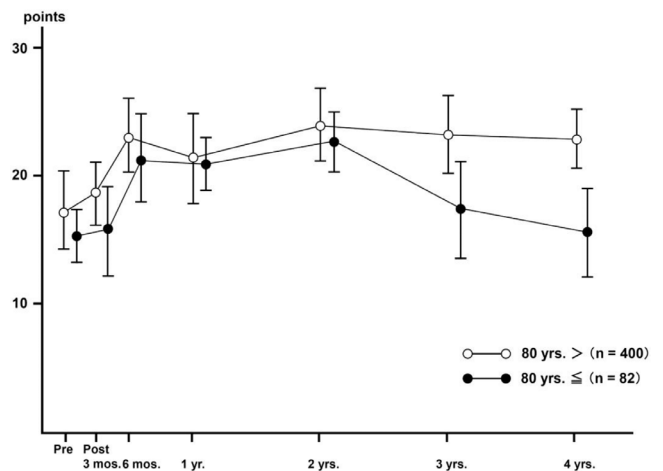


Fig. 3 Clinical course of symptoms pre and postoperatively (*D*: dementia evaluated by MMSE<sup>1)</sup>). White: <80 years, black: ≥80 years.

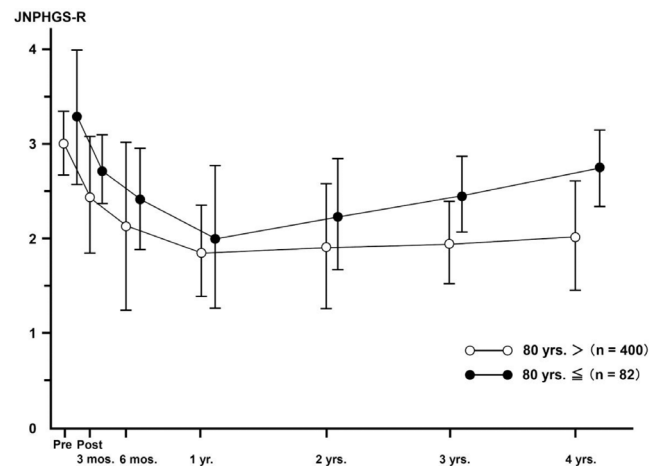


Fig. 4 Clinical course of symptoms pre and postoperatively (*U*: urinary incontinence evaluated by JNPHGS-R<sup>1)</sup>). White: <80 years, black: ≥80 years. JNPHGS-R, Japanese Normal Pressure Hydrocephalus Grading Scale-revised.

until 6 months postoperatively compared with the preoperative rate. Then, the frequency tended to gradually decline; however, in group B, the frequency increased at 3 years postoperatively once again.

\*The mean values for mRS (grade)<sup>1)</sup> preoperatively and during the follow-up period were 3.7, 3.5, 2.8, 2.9, 3.0, 3.2, and 3.2 in group A and 3.9, 3.8, 3.0, 3.1, 3.2, 3.5, and 3.7 in group B. Similar to *D*, a marked decrease in grade was not observed immediately after the surgery in both groups; however, the grade tended to decrease beginning at 6 months postoperatively. However, at 3 years postoperatively, the grade tended to gradually increase once again. This trend was particularly observed in group B (Fig. 5).

## Discussion

The three most typical signs of iNPH are *G*, *D*, and *U*, with *G* as the most common initial symptom.<sup>1,2,5-10)</sup> The characteristics of each symptom are as follows: for *G*, wide bases, short steps, and compass-like gait when turning<sup>1,9-13)</sup>; for *D*, delayed psychomotor reactivity and decreased voluntary<sup>9,10,14)</sup>; and for *U*, urge incontinence, reduced urine flow, increased residual urine, and decreased bladder volume.<sup>15)</sup> iNPH is diagnosed based on a positive DESH (disproportionately enlarged subarachnoidspace hydrocephalus) sign on MRI (or CT) and symptom improvement with a lumbar tap test (LTT).<sup>1,2)</sup> The symptom improvement in LTT most markedly affects *G* and is identified according to expanded stride width and reduced number of strides and speed.<sup>1,16,17)</sup>

In this study, patients were divided, based on cases with iNPH who underwent shunting treatment

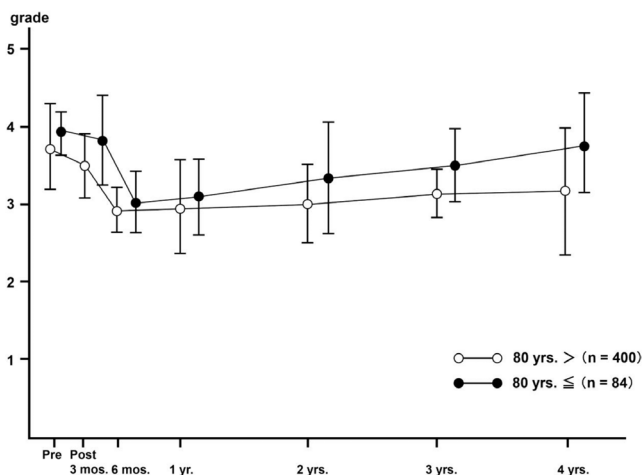


Fig. 5 Course of modified Rankin Scale<sup>1)</sup> pre and postoperatively. White: <80 years, black: ≥80 years.

and followed until 4 years postoperatively, into those aged <80 and ≥80 years, and the frequency of improvements in each symptom, temporal changes in each symptom and mRS, and the course of shunt efficacy persistence at 3 months postoperatively were comparatively investigated. In both groups, symptom improvement from most to least frequent was *G*, *U*, and *D*. Although *G* tended to be highest in previous reports, differences were noted depending on the researchers.<sup>8,18,19)</sup> Similar to previous reports,<sup>10,20-22)</sup> the temporal changes for each symptom in both groups showed that *G* and *U* improved immediately after the surgery, but *D* tended to gradually improve beginning at 6 months postoperatively. The course of mRS changes over time was the same as that of *D* in both groups. However, the temporal changes after this revealed no significant differences in either group. In other words, all symptoms and mRS scores tended to gradually worsen once again beginning at 3 years postoperatively in both groups, and this tendency was clearly more observed in patients aged ≥80 years. With respect to the persistence of shunt efficacy, previous studies observed the fragmentary efficacy rates at each follow-up period (6 months, 1 year, 3-5 years)<sup>1,18,23-25)</sup>; reports that clearly note temporal changes were extremely limited. We believe that this study, which investigates temporal changes by age group, will be extremely useful. Further, the cause of repeated deterioration of symptoms was not worsening of the iNPH condition, but was clearly due to complicating diseases other than iNPH, such as extracranial diseases, intracranial diseases, age-related changes, and peritoneal malabsorption. Regarding the frequency of complicating diseases by age group, extracranial and intracranial diseases were found to be more common in those aged <80 years, while age-related changes were more common in those aged ≥80 years.

This study also investigated fall rates in patients pre and postoperatively. The patient fall rate is actually higher at 6 months postoperatively than preoperatively. This may be because many cases had improved *G* and *U* at 6 months postoperatively, but dementia did not improve. Therefore, the patient's range of daily activities expanded due to the postoperative improvement in *G*; however, as family members were only aware of the preoperative range of activities, their care and supervision were insufficient. Further, as dementia had been hypothesized to be unimproved, falls may occur due to the patient's own insufficient awareness and confirmation in the environment. The fact that fall frequency worsened in those aged ≥80 years at 3 years postoperatively is hypothesized to be due to decreased physical strength due to aging.

We previously reported that post-shunting efficacy is favorable when the period from onset to hospital visit is short with the cut-off point of 1.5 years from onset.<sup>9,10</sup> Consistent with this research results, it is thought that in addition to the extreme importance of early detection and treatment of iNPH, shunting should be performed.

### Conclusion

- 1) iNPH symptoms generally improve after shunting; however, they begin to gradually recur beginning at 3 years postoperatively. This tendency is particularly observed in those aged  $\geq 80$  years.
- 2) The cause of symptom deterioration is not only related to worsening of the iNPH condition alone but also related to complications from other pathologies.

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### Conflicts of Interest Disorder

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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