

FOREWORD

Guidelines for Management of Idiopathic Normal Pressure Hydrocephalus

Guidelines From the Guidelines Committee of Idiopathic Normal Pressure Hydrocephalus, the Japanese Society of Normal Pressure Hydrocephalus

Approved by Guidelines Committee, The Japan Neurosurgical Society

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Abstract

With the rapid aging of Japanese society, medical care of the elderly has become an important social issue. Among various disorders manifesting dementia, gait disturbance, and urinary incontinence in the elderly population, normal pressure hydrocephalus (NPH), especially of idiopathic type (iNPH), is becoming noteworthy. The Guidelines for management of iNPH in Japan are created in compliance with the evidence-based medicine methods and published in 2004. This English version is made to show the diagnosis and treatment of iNPH with reference to the socio-medical background in Japan and to promote the international research on iNPH. They propose three diagnostic levels; possible, probable, and definite. They indicate the diagnostic importance of high convexity tightness and dilated sylvian fissure with mild to moderate ventriculomegaly on coronal magnetic resonance imaging. The cerebrospinal fluid tap test is regarded as an important diagnostic test because of its simplicity to perform and high predictability of the shunt efficacy. The use of programmable valves at shunt surgeries is recommended. Flowcharts for diagnosis, preoperative assessment, and prevention for complications of shunt surgery are made to promote a wide use of them.

Key words: gait disturbance, dementia, urinary incontinence, hydrocephalus, the elderly

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CREATING THE GUIDELINES

1. Introduction

With the rapid aging of Japanese society, medical care of the elderly has become an important social issue. Among various disorders manifesting dementia, gait disturbance, and urinary incontinence in the elderly population, normal pressure hydrocephalus (NPH) has become more important.

NPH, first reported by Hakim and Adams in 1965,³⁴⁾ manifests as a syndrome of clinical triad of dementia, gait disturbance, and urinary incontinence, with ventricular dilation and normal cerebrospinal fluid (CSF) pressure, and these symptoms can be reversed by CSF shunt surgery. NPH is classified into secondary NPH (sNPH) of known etiology such as subarachnoid hemorrhage and meningitis, and idiopathic NPH (iNPH) of unknown etiology. In contrast to sNPH, iNPH is difficult to distinguish from parkinsonism and vascular dementia, and aggravation of symptoms due to shunt complications including subdural effusion and hematoma have been reported with fairly high incidence. Therefore, iNPH has not attracted as much attention as sNPH, for which CSF shunt surgery is more successful with fewer shunt complications. However, there are patients with iNPH in which CSF shunt surgery is clearly effective. Therefore, the selection of patients where CSF shunt surgery is effective is important. Another important issue is to maintain the long-term efficacy of the CSF shunt surgery.

In 1996, iNPH was first selected as a main research subject by the Committee for Scientific Research on Intractable Hydrocephalus, the Japanese Ministry of Health and Welfare of Japan (Chairman: Professor Koreaki Mori, then at Department of Neurosurgery, Kochi Medical School) during a long history of the hydrocephalus research. In consideration of its continuing social importance, the Japanese Society of Normal Pressure Hydrocephalus was established in 2000 for the purpose of continuing research. At the 3rd board meeting of the Japanese Society of Normal Pressure Hydrocephalus in 2002, it was decided to establish Guidelines for the diagnosis and treatment of iNPH. Members specializing in the fields of neurosurgery, neurology, psychiatry, and clinical epidemiology met and discussed this matter. Although, as mentioned above, iNPH has not attracted a great deal of attention and there are few studies on this syndrome that contain a high level of evidence, the current Guidelines were created for this syndrome in Japan due to its social importance.

2. Purpose of these Guidelines

The Guidelines for the management of iNPH were created to allow more accurate diagnosis of iNPH in the elderly, to select appropriate patients for whom CSF shunt surgery would be effective, and to maintain the long-term effect of shunt surgery. The Guidelines will be useful for neurosurgeons, neurologists, and psychiatrists, who often treat neurological disorders in the elderly, and also for general practitioners. The Guidelines may also be useful for paramedical staff including nurses, and physical and speech therapists. The Guidelines were published in Japanese in May 2004. This English version has been produced to illustrate the diagnosis and treatment of iNPH with reference to the socio-medical background in Japan and to promote internation-

Table 1 Bibliographic search standards and results in diagnosis from MEDLINE

Search	Most recent queries	Result
#25	Search #3 AND #23 Field: All Fields, Limits: All Adult: 19+ years, Publication Date from 1965 to 2002/6/30	517
#24	Search #3 AND #23	695
#23	Search #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4	1163694
#22	Search mmse	1346
#21	Search apath*	1669
#20	Search abulia	61
#19	Search depressi*	157665
#18	Search neuropsychiatr*	9744
#17	Search incontinen*	22193
#16	Search gait	12683
#15	Search working memory	7610
#14	Search executi*	16210
#13	Search attenti*	106629
#12	Search frontal lobe	26968
#11	Search frontal function	26008
#10	Search neuropsychologi*	27583
#9	Search cogniti*	85859
#8	Search amnes*	16243
#7	Search dementi*	41791
#6	Search "neurologic manifestations" [MESH]	421930
#5	Search "behavioral sciences" [MESH]	112600
#4	Search "mental disorders" [MESH]	477766
#3	Search #1 AND #2	1823
#2	Search hydrocephal*	16020
#1	Search (normal pressure) OR normotensive OR (low pressure)	117087

Table 2 Bibliographic search standards and results in treatment from MEDLINE

Search	Most recent queries	Result
#8	Search #1 AND #2 AND #6 Field: All Fields, Limits: All Adult: 19+ years, Publication Date from 1965 to 2002/7/30	585
#7	Search #1 AND #2 AND #6	915
#6	Search #3 OR #4 OR #5	39374
#5	Search shunt OR shunts OR shunting	38924
#4	Search ventriculostom*	779
#3	Search "cerebrospinal fluid shunts" [MESH]	5961
#2	Search hydrocephal*	15960
#1	Search (normal pressure) OR normotensive OR (low pressure)	116553

al research on iNPH. It is necessary to understand that these Guidelines are not intended to override the diagnosis and treatment decisions of experienced practitioners, and that they are not intended as a denial of treatment policies other than the included policies.

3. Guideline creation

The Guidelines were created in compliance with evidence-based medicine methods. Initially, all clinical questions related with this syndrome were raised, and a bibliographic search using MEDLINE carried out in order to obtain solutions to these problems. In order to minimize bias in selecting publications by investigators, a list was made in each section of diagnosis and therapy utilizing various key words: 517 publications are referenced by the diagnosis section (Table 1) and 585 by the treatment section (Table 2). Important publications other than those in this list are included at the discretion of the individual in charge of each section. This enables the inclusion of Japanese publications not listed

in MEDLINE, but such publications were designated and marked as "addition" at the end of the publication list to show that they were included in addition to MEDLINE publications. Evidence levels differ between the diagnosis and treatment sections, so the Oxford Centre for Evidence-Based Medicine classification⁹³⁾ was employed. No case reports are included. Publications dealing with iNPH were used mainly, and publications dealing with both iNPH and sNPH, or publications that did not identify these two, were considered as low level evidence. If results were not consistent and differed between publications, publications dealing with iNPH and publications with more than a certain number of cases were prioritized. Publications that did not match with the theme of the individual section but contained necessary information were adopted, with their evidence level described as "non-classifiable."

Recommendations were classified into the following 4 grades, considering the actual state and benefit in the treatment field in addition to the evidence level: Recommendation grade A, strongly recommended; Recommendation grade B, recommended; Recommendation grade C, insufficient reason to be recommended; and Recommendation grade D, not recommended.

The original Guidelines consisted of 3 parts, the text, evidence table, and Q & A, and were published in Japanese in May 2004. In this English version, the evidence table and Q & A are omitted due to the limitations on the text volume. Most of the parts in the original Guidelines are directly translated, but some data were added with reference to publications from 2002 to 2006, included in the list of 111 publications for diagnosis and 147 publications for therapy from MEDLINE. These publications after 2002 were also marked as "addition." Finally, 134 publications were referred in the Guidelines.

INTRODUCTION: CONCEPT AND EPIDEMIOLOGY

1. Concept of iNPH

iNPH is a clinical syndrome that includes dementia and urinary incontinence in addition to gait disturbance as major manifestations in the absence of a history of preceding disorders, such as subarachnoid hemorrhage and meningitis, but with ventricular dilation caused by impairment of CSF circulation. iNPH develops in the elderly, and symptoms usually progress slowly. The symptoms can be improved by appropriate CSF shunt surgery.

Note: The classic "definition" of NPH included

the condition that NPH symptoms improved by CSF shunt surgery. However, preoperative diagnosis is impossible by this definition, so a term of concept is used rather than a term of definition in these Guidelines, to avoid confusion with the classic definition.

2. Epidemiology — incidence rate

Symptoms of iNPH are nonspecific in the elderly, so it is likely that many cases go undiagnosed. For this reason, the incidence rate of iNPH is unknown. In 1995, the Committee for Scientific Research on

Intractable Hydrocephalus, the Japanese Ministry of Health and Welfare of Japan (Chairman: Professor Koreaki Mori, then at Department of Neurosurgery, Kochi Medical School) conducted a national survey. Intractable hydrocephalus of unknown origin in individuals above 65 years old, classified as idiopathic, accounted for 8.7% of cases of adult hydrocephalus.³⁸⁾ iNPH was diagnosed in 3.5% of 400 patients in a memory clinic.^{4C)} In a multi-center study in Amsterdam, the incidence of iNPH was 2.2

per 1 million per year. However, only 1.7 per 100 million benefited from shunt surgery because of complications caused by the procedure.^{126B)} Moreover, the pathological findings of iNPH classified as meningeal changes in the base of the skull and the brain surface, or the choroid plexus fibrosis, accounted for 1.3% of cases of dementia diagnosed at autopsy.⁴⁰⁾ A nationwide survey or cohort study based on the appropriate diagnostic criteria is necessary.

CHAPTER 1: DIAGNOSIS

I. Clinical Symptoms

1. Characteristics of gait disturbance

The characteristic triad of gait patterns in iNPH is short-stepped gait, magnet gait, and broad-based gait.^{110A,111)} Patients with iNPH walk slowly and unstably. The foot rotation angles are increased and the strides are variable during walking. The strides become shorter in turning than in walking straight.^{71A)} The patients become unstable and sometimes fall, particularly if they are standing up or changing directions.^{7A,55)} There is little effect of external cues, including verbal commands or visual markings such as lines, on gait improvement in iNPH, in contrast to patients with Parkinson's disease.¹¹¹⁾ Gait improvement after CSF removal is characterized by increased stride length and decreased number of steps in turning.^{71A,110A)} No improvement is seen in leg elevation and instability.^{110A)} Gait in iNPH is sometimes expressed as ataxic^{7A)} or apraxic gait.⁴⁶⁾

2. Characteristics of cognitive impairment (dementia)

Frontal lobe-related functions, such as attention, psychomotor speed, verbal fluency and executive function, and memory impairment are observed in patients with mild iNPH.^{10,36B,105,121,129A)} Concerning memory impairment, recognition memory is relatively preserved compared with recall.^{129A)} Patients with severe iNPH exhibit overall cognitive impairment.^{36B)} The impairment of attention, psychomotor speed, literal fluency, and executive function is disproportionately severe, whereas the impairment of memory and orientation is disproportionately mild in patients with iNPH compared with Alzheimer's disease.^{80,88)} Clumsiness and writing difficulty were also noted.¹⁰⁵⁾ The impairment of verbal memory and psychomotor speed of iNPH appears more likely to respond to shunt surgery,¹²⁰⁾ whereas overall cog-

nitive impairments in severe cases tend not to improve after shunt surgery.¹²⁰⁾

3. Characteristics of urinary impairment

There have been no studies on urinary impairment in patients with limited to "iNPH" patients. In NPH patients, bladder hyperactivity is seen on cystometry, and positive findings are reported in the Bors ice water test.¹⁾

4. Incidence of the classical triad

There have been no community-based studies examining the incidence of the triad of iNPH. In a study, 94.2% of 120 cases revealed gait disturbances, 88.3% revealed cognitive impairment, and 76.7% revealed urinary impairment.^{84B)} In another study, 100% of 65 cases revealed gait disturbances, 98% revealed cognitive impairment, and 83% revealed urinary impairment.⁵¹⁾ Among 400 cases who visited an outpatient memory clinic, 13 cases were diagnosed as iNPH, and 100% of these 13 cases with iNPH revealed gait disturbances, 69% revealed cognitive impairment, and 54% revealed urinary impairment.^{4B)}

5. Other clinical symptoms

Besides the gait disturbance, hypokinetic motor deficits of upper extremities are also found.^{59,62)} When the patients grasp objects to lift, the build-up of fingertip forces causes slow lifting movement. CSF removal improves the lifting movement and reduces the grip force overshoot.^{86,87)} Neurologically, bradykinesia, hypokinesia, paratonic rigidity, glabellar reflex, snout reflex, and palmomental reflex are exhibited with high frequency.^{57,62)} The combination of akinesia and tremor at rest is observed to a greater degree in iNPH than in sNPH.⁵⁰⁾ Psychiatric symptoms are seen in 88% of cases of iNPH,⁵⁹⁾ with easy fatigability, impatience, emotional instability, and drowsiness, and a tendency

toward lethargy and decreased initiative are seen with high frequency.⁶²⁾ Forced crying and laughing, delusions, hallucination, and epilepsy are rarely encountered.^{7A)} Hypertension might be involved in the pathophysiological mechanism promoting iNPH.⁵¹⁾

II. Diagnostic Imaging

1. Computed tomography (CT), magnetic resonance imaging (MRI)

Morphological brain imaging by CT and MRI are essential for screening and clinical diagnosis of iNPH. MRI is suitable for detecting morphological changes, and coronal sections are particularly useful in evaluating the condition of sulci over the high cerebral convexity.

A. Shape and size of ventricles and sulci, and cerebral atrophy

CT and MRI reveal ventricular dilation.^{20,35,44,127)} An Evans index (the ratio of the maximum width of the frontal horns to the maximum width of the inner table of the cranium) of greater than 0.3 is a historical hallmark of hydrocephalus. Dilation of the sylvian fissures and the sulci may be regarded as cerebral atrophy. However, if accompanied by narrowing of sulci and subarachnoid spaces over the high cerebral convexity, iNPH should be highly suspected^{44,127)} (Fig. 1, Recommendation grade B). In some patients with iNPH, one or more sulci over the medial surface and convexity were elliptically dilated in isolation⁴⁴⁾ (Fig. 2). Cerebral atrophy may be present in some cases, but its existence does not rule out iNPH. Hippocampal atrophy¹⁰²⁾ and widening of the parahippocampal sulci³⁵⁾ are mild compared with Alzheimer's disease, which is useful to differentiate iNPH from Alzheimer's disease.^{44,127)} Examples of MRIs are shown in Fig. 3 as a reference for the differential diagnosis of both disorders. The diameter of the midbrain is reportedly decreased in iNPH, and negatively correlated with the severity of gait disturbance^{60,81)} (Recommendation grade C).

B. Periventricular and deep white matter changes

MRIs reveal periventricular and deep white matter changes (leukoaraiosis) more often and more severe in patients with iNPH than in healthy elderly individuals, but these changes are not requisite signs for iNPH.^{19,48,53,54A)} Although white matter changes are reportedly correlated with symptoms,⁵³⁾ the relationship has not been established. The existence of severe white matter changes does not necessarily imply poor shunt responsiveness^{24,123)} (Recommendation grade C).

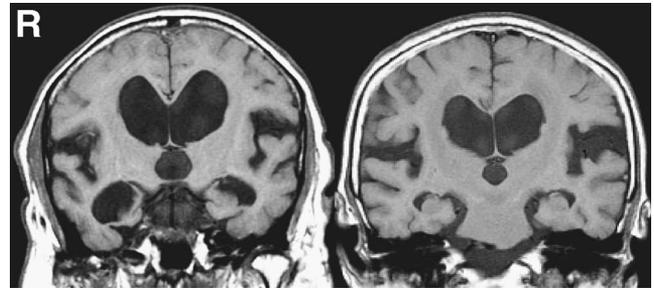


Fig. 1 Magnetic resonance imaging (coronal section): Examples of ventriculomegaly and dilation of the sylvian fissures, and narrowing of sulci and subarachnoid spaces over the high cerebral convexity.

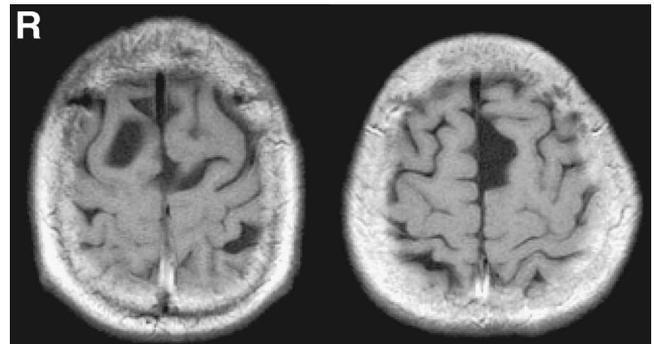


Fig. 2 Magnetic resonance imaging (axial section): Examples of narrowing of sulci with focal dilation of sulci.

C. CSF flow void by MRI, and CSF flow rate by phase contrast MRI

Although CSF flow void in the aqueduct and the adjacent ventricles is detected on MRI with similar prevalence in both iNPH and healthy individuals,²⁰⁾ its degree is greater in iNPH.^{18,39,52)} CSF flow rate measured by phase contrast MRI is reportedly greater in iNPH.⁶⁵⁾ However, the diagnostic values of CSF flow void and flow rate have not yet been established. Whether these indices predict shunt responsiveness is also controversial^{17,18,24,33,52)} (Recommendation grade C).

D. Magnetic resonance spectroscopy (MRS)

A study of MRS reported a peak of lactic acid in the lateral ventricle of iNPH, but such a peak was not seen in control subjects and patients with Alzheimer's disease.⁴⁵⁾ However, its diagnostic value remains undetermined (Recommendation grade C).

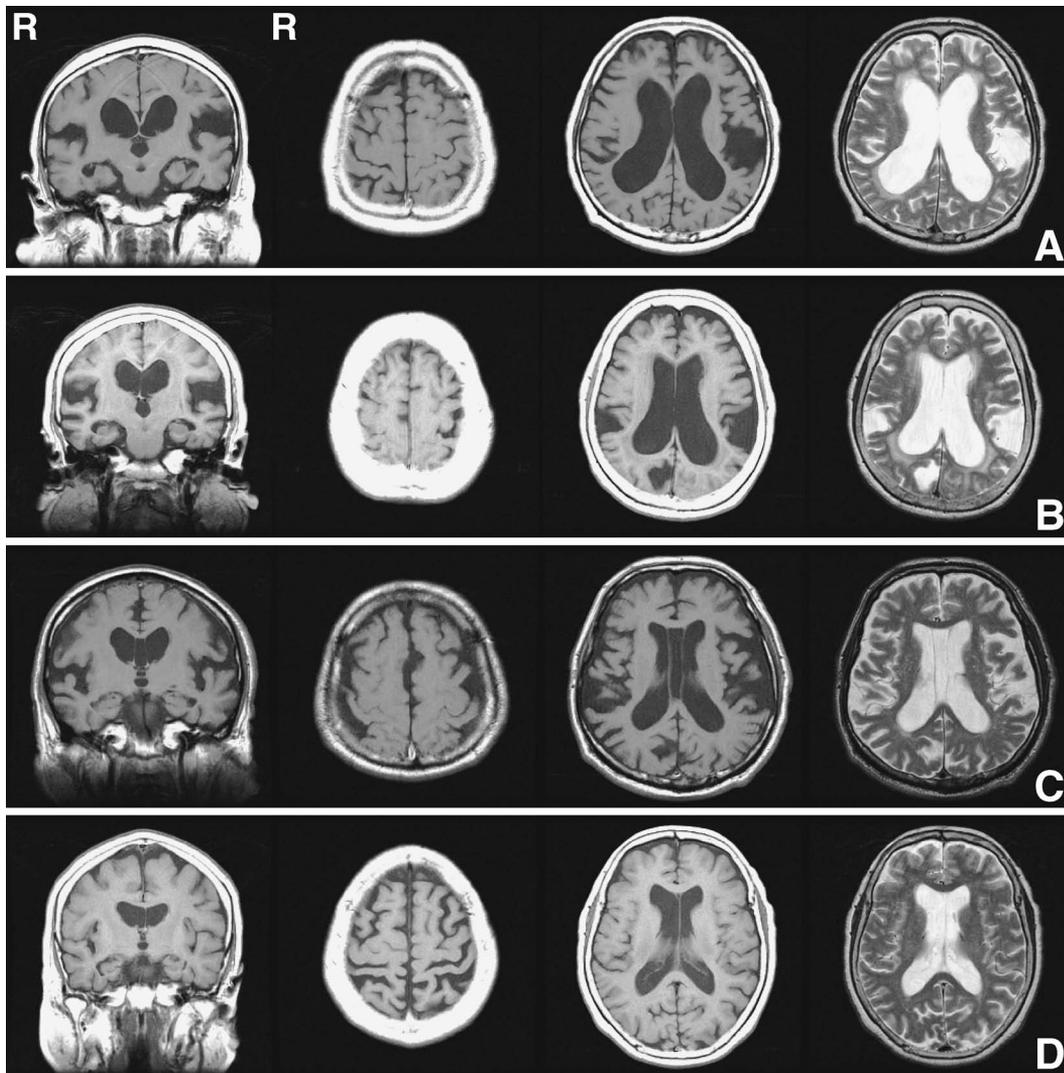


Fig. 3 Magnetic resonance imaging (coronal and axial sections): comparison between idiopathic normal pressure hydrocephalus (iNPH) (A, B, and C) and Alzheimer's disease (D). Each row contains a coronal T₁-weighted image, a dorsal horizontal T₁-weighted image, a horizontal T₁-weighted image, and a horizontal T₂-weighted image from a single patient. A and B show severe ventriculomegaly and sylvian fissure dilation. The sulci and subarachnoid spaces are narrowed over the high convexity, but not on the ventral surface. Narrowing of the high-convexity sulci and subarachnoid spaces can be clearly detected on coronal sections. T₂-weighted images show a mild- to moderate-degree of periventricular hyperintensity. B shows focal dilation of the left parieto-occipital sulcus. C shows moderate ventriculomegaly and sylvian fissure dilation. Sulci and subarachnoid spaces are dilated on the ventral surface, but are markedly narrowed over the high convexity. Periventricular hyperintensity is not evident. D is Alzheimer's disease as a comparison with iNPH. In Alzheimer's disease, ventricles, sulci, and subarachnoid spaces are evenly dilated. The gyri on the convexity are atrophic, and narrowing of sulci and subarachnoid spaces is absent.

2. Cerebral blood flow (CBF)

Measurements of CBF in NPH, including patients with iNPH, have been conducted by the inhalation method or single photon emission computed tomography (SPECT) utilizing radio-labeled materials in-

cluding xenon-133,^{70,74-76,117} technetium-99m hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO),^{54B} nonradioactive xenon-CT,¹¹⁸ and positron emission tomography (PET) with [¹⁵-O]H₂O.^{82,90} In a study measuring CBF in 31 patients of suspected

iNPH with ^{99m}Tc -HMPAO SPECT,^{54B)} reduced blood flow over a wide area, especially in the cortex and subcortical white matter of the frontal and temporal lobes (expansion of central low-flow area), is seen. These findings are supported by other studies.^{57,70,74,76,117,128)} A PET study reported the mean CBF decreased in the cerebrum and cerebellum with regional decrease in the basal ganglia and thalamus but not in the white matter.⁸²⁾ There are few studies supporting the correlation between reduced flow and degree of symptoms.⁵⁷⁾ There are many studies showing an association between improved symptoms and increased CBF after shunt procedure,^{54B,70,74,118,128)} but the contradictory result has been reported.¹²⁸⁾ CSF tap test reveals no changes in CBF in normal controls, but some studies show an increase of CBF in NPH including iNPH.^{70,114)} A voxel-based analysis study reported a significant CBF increase in the bilateral dorsolateral frontal and left mesiotemporal cortices after the tap test.²⁵⁾ No increase of CBF after the tap test was also reported.^{54B)} The involvement of autoregulatory impairment is still controversial.^{70,74,82,118)} Thus, CBF measurements can show diffuse or regional decrease of CBF in NPH, but they are insufficient for the definite diagnosis of iNPH and also insufficient for the indication of shunt surgery (Recommendation grade C). However, CBF studies are useful in differentiating iNPH from other disorders of dementia, including Alzheimer's disease.

3. Cisternography

Radioisotope (RI) or CT cisternography has been considered to be important for the diagnosis of NPH, whose typical findings are intraventricular reflux and stagnation on the brain surface of RI and contrast media.^{56,116)} They are mainly derived from studies of sNPH, although its diagnostic significance is of some doubt even in sNPH.¹²⁵⁾ A study of iNPH reported improvement of symptoms in 55% of all cases with normal findings on RI cisternography.^{7B)} Another study reported improvement of symptoms in 69% of patients showing ventricular stasis at 48 hours after injection, and in 58% of patients showing no ascent to the brain surface.⁵⁾ Although cisternography is useful in identifying CSF circulation disturbance, it is difficult to conclude that cisternography is a reliable examination for the diagnosis (Recommendation grade C).

III. CSF Tap Test, Intracranial Pressure (ICP) Test, and Other Tests

1. CSF tap test (CSF removal test)

The CSF tap test, which is performed to examine

improvement of clinical symptoms after CSF removal by lumbar tap, is one of the useful methods for the diagnosis of NPH. In a study in which 50 ml CSF was removed twice on 2 successive days, patients with improvement of gait showed a high rate of symptomatic improvement after shunt procedure.¹³¹⁾ Various methods have been employed for the tap test, depending on the number of taps,⁸⁹⁾ amount of CSF removal, and final CSF pressure.⁸³⁾

As for a response to the CSF tap test, gait disturbance is a most simple and useful indicator. The improvement is sometimes noted immediately and usually within a few days.²²⁾ Among various components of the gait, walking speed and stride are improved.^{110B)} Many studies show that the CSF tap test is useful for the prediction of shunt efficacy,^{41,100,129)} although a contradictory report is known.^{69B)} It is important that the clinical responses are different in each patient, so that attention should be paid to even minor or short improvements.

Comparing the sensitivity and positive predictable value (PPV) between the CSF tap and drainage tests,^{129B)} the CSF tap test showed a sensitivity of 28% against the drainage test's 50%, with a PPV of 100% for the former and 87% for the latter. Similarly, in a study comparing the CSF tap test and CSF dynamic test,⁴¹⁾ the former revealed a sensitivity of 42% while the latter showed 82%, with a PPV of 94% for the former and 80% for the latter. Thus, when the CSF tap test was positive, the probability of shunt efficacy is high. Additionally, it is easy to perform and use at any facility. Therefore, the CSF tap test is recommended as a key step for the diagnosis in patients of suspected iNPH (Recommendation grade A). To minimize discomfort in the elderly, CSF was drained once only and the volume removed was 30 ml or until the final pressure was 0 in these Guidelines.

A drawback in the CSF tap test is that there are false negatives in which the shunt procedure is effective although the patient does not show improvement in symptoms after the tap test. Therefore, the usefulness of the CSF tap test is sometimes questioned. In patients who do not show improved symptoms after the initial tap test, it is worthwhile to repeat the procedure if the symptoms progress.

2. CSF drainage test (continuous CSF drainage test)

In a study of iNPH in which continuous CSF drainage is done for 5 days and a shunt procedure was performed, the patients with positive response showed the efficacy of the shunt was maintained for 1 year, whereas the patients with a negative response showed no improvement of symptoms in

the follow up.²¹⁾ A study for continuous CSF drainage for 5 days in patients with negative response to the CSF tap test shows that the shunt is effective for all patients with positive response and was ineffective for all patients with negative response.³²⁾ Another study with a similar protocol revealed a CSF tap test sensitivity of 28%, PPV of 100%, and negative predictive value (NPV) of 32%, whereas in the patients with a negative response, CSF drainage test showed a sensitivity of 50%, PPV of 87%, and NPV of 36%.^{129B)} A recent report of 3-day external lumbar drainage for suspected iNPH showed a sensitivity of 95%, specificity of 64%, PPV of 90%, and NPV of 78%.^{71A)} As these facts suggest, the CSF drainage test has higher accuracy on prediction of the shunt efficacy than the CSF tap test. However, there are problems involving infections and the invasiveness of leaving a drainage tube in the elderly patient for long periods of time. No clear standards regarding the amount to be drained and period of drainage have been established. However, it is desirable to perform the CSF drainage test in patients if the CSF tap test shows negative results (Recommendation grade B).

3. ICP monitoring, CSF dynamic tests, and other tests

A. Pressure and condition of CSF

The condition of CSF is colorless, watery, and clear. Many studies have reported the normal upper limit of CSF pressure to be 200 mmH₂O⁷⁰⁾ or 180 mmH₂O.⁸⁾ The possibility of iNPH cannot be denied even in cases with higher pressure, but it is also necessary to rule out other diseases, such as benign intracranial hypertension or meningitis carcinomatosa. There are few descriptions of lower limits of CSF pressure in the elderly.

B. ICP monitoring (continuous measurement of ICP)

The measurement period for ICP is approximately 12–48 hours, measured mainly at night.^{8,37,47,94,96)} Lumbar subarachnoid pressure is the most frequently measured,^{3,8,37,47,78,94)} but other studies measured intraventricular pressure⁹⁶⁾ and epidural pressure.^{99,115)} ICP monitoring can measure mean CSF pressure, pressure waves, and CSF pulse pressure. The mean CSF pressure tends to be higher within the normal range in the shunt-effective patients.^{3,8,37,47,99)} The incidence of B-wave (repeats the temporary elevation of pressure at a certain cycle) is high during sleep, especially during rapid eye movements.⁴⁷⁾ A higher incidence of B-wave (more than 15% of all records) indicates a more effective shunt procedure.^{8,96,99,115)} B-waves may express the ability of the CSF system to reallocate and store,

rather than absorb liquid.⁶¹⁾ The pulse wave with high amplitude is reported to show high predictability of shunt efficacy, although the value varies among reports.^{3,96)} Pulse wave analysis can be available even in the short-term and may be superior to long-term ICP monitoring.^{26A)} However, there is also a negative study when all these items were present.^{26A)} High predictability for the shunt efficacy is also reported for increased ICP on acetazolamide loading during ICP monitoring⁷⁸⁾ (Recommendation grade B).

C. CSF dynamic tests (CSF space volume loading tests)

These tests examine the CSF circulation dynamics by injecting normal saline solution into the CSF space. Values vary depending on speed of injection (constant infusion^{11,15,41,69C,99)} or bolus injection^{71B,115)}, or the site of CSF pressure measurement (lumbar subarachnoid pressure^{11,15,41,69B)} or epidural pressure^{99,114)}.

These tests can measure CSF outflow resistance (Ro) and CSF outflow conductance (Cout). The Ro values were significantly higher (10–20 mmHg/ml) in shunt-effective cases (PPV 75–92%).^{11,41,99,114)} Because the Ro values were not constant among institutes, each institution should have its own data for deciding on shunt surgery with reference to the literature. No correlation is noted between Ro values and degree of postoperative improvement.²³⁾ Cout is significantly low in shunt-effective patients.^{15,69B,99)}

As described above, ICP monitoring and CSF dynamic tests are reported to be useful for predicting the shunt efficacy (Recommendation grade B). However, long-term ICP monitoring including overnight is fairly invasive for elderly patients with some degree of dementia. Non-standardization of Ro or Cout measurements is another drawback. For these reasons, ICP monitoring with Ro or Cout measurements is regarded as an optional test in the Guidelines (Recommendation grade B).

4. CSF and serum biochemical tests

A. CSF tau protein, monoamine, and neuropeptide

Amyloid beta peptide 1–42⁶³⁾ in CSF is reported to be low in NPH patients and combined measurements of total tau protein can contribute to the differential diagnosis of NPH from Alzheimer's disease or vascular dementia.

CSF immunoactive myelin basic protein,¹¹³⁾ neurofilament triplet protein light subunit (NFL),¹²⁴⁾ glial fibrillary acidic protein,¹²⁴⁾ and tumor necrosis factor-alpha (TNF-alpha)¹¹⁹⁾ show high values in CSF of iNPH patients. In particular, the high values of NFL are well correlated with the severity of the sym-

ptoms, and the high values of TNF-alpha significantly correlate to the overall improvement after shunt surgery. Thus, NFL and TNF-alpha can be markers of the reversibility of neuronal damage.^{119,124} Neuropeptides including delta-sleep-inducing peptide, peptide YY and somatostatin,¹³² monoamine and lactic acid,⁶⁸ and cholecystokinin²⁸ show low values in iNPH.

B. Serum apolipoprotein, alpha-1-antichymotrypsin, and brain oxygen extraction fraction (OEF)

ApoE4 allele, a genotype of apolipoprotein E, is reported to show high values in neurodegenerative disease and iNPH.⁸⁵ Alpha-1-antichymotrypsin correlates with amyloid deposits, and contradictory results were reported in iNPH patients.^{86,115} Mild increase of OEF is also noted in iNPH, which suggests chronic ischemia.⁷⁷

The CSF and serum biochemical markers may be useful for diagnosis or prediction of shunt efficiency in iNPH patients in the future. However, the evidence level of CSF and serum biochemical markers in diagnosis of iNPH remains low at present (Recommendation grade C).

IV. Differential Diagnosis

Both characteristic clinical symptoms and imaging are critical for the diagnosis of iNPH. A careful differentiation between diseases is required: diseases affecting the elderly and causing dementia; diseases causing gait disturbance; diseases causing both dementia and gait disturbance; and diseases causing ventricular dilation on images. Differences in the clinical symptoms, including cognitive impairment and gait disturbance, are useful for differential diagnosis.

Clinically, it is especially necessary to differentiate iNPH from Alzheimer's disease, vascular dementia including multiple lacunar infarction and Binswanger's dementia, a mixture of Alzheimer's disease and vascular dementia, Lewy body dementia, Parkinson's disease, progressive supranuclear palsy, vascular parkinsonism, multiple system atrophy, and frozen gait of unknown causes.^{4B,29,36A,111} Cognitive impairment is of particular importance to differentiate iNPH from Alzheimer's disease. Impairment of attention, thinking speed, reaction speed, operating speed, and verbal memory is characteristic of iNPH, whereas impairment of the frontal lobe-related functions is minimal in mild Alzheimer's disease.^{36A} In patients with Alzheimer's disease, both recall and recognition memories are

impaired, whereas impairment of recognition memory is mild in iNPH, which is also useful. As for gait disturbance, it is important to differentiate iNPH from Parkinson's disease or parkinsonism. Walking in iNPH resembles that in Parkinson's disease, but the gait is improved by external cues in Parkinson's disease, whereas external cues are not effective in iNPH.¹¹¹ Patients with iNPH do not respond to antiparkinsonism agents, including levodopa, which is also useful for differential diagnosis.

As for imaging, it is necessary to differentiate iNPH from sNPH, obstructive hydrocephalus, and cerebral atrophy. For the differential diagnosis of sNPH, in addition to diseases occurring in succession in acute clinical conditions, including subarachnoid hemorrhage, head injury, or acute meningitis, relatively rare chronic and latent conditions, such as tuberculous meningitis, fungal meningitis, neurosyphilis, meningeal carcinomatosis, and Paget's disease, should be taken into consideration. It is possible to differentiate many of these conditions from iNPH by examining the CSF. In obstructive hydrocephalus, there are cases of latent symptoms which are found incidentally in adults by imaging, and cases that manifest symptoms in adulthood. In both cases, aqueductal stenosis may be noted, which is differentiated from iNPH by imaging. In order to differentiate iNPH from cerebral atrophy, it is useful to examine the existence of narrowing of cerebral sulci and subarachnoid spaces over the high cerebral convexity on coronal MRIs. On the other hand, other diseases, including Alzheimer's disease and Parkinson's disease, may coexist with iNPH.^{13,31,102} In such cases, the efficacy of the shunt procedure may be limited.^{13,31,102} Improvement of gait by tap test was reported in patients diagnosed as having vascular parkinsonism.^{89A} Therefore, a diagnosis of iNPH should not be excluded even in patients with other coexisting diseases.

V. Diagnostic Criteria

In the present Guidelines, iNPH is classified into 3 diagnostic levels: preoperatively "possible" and "probable," and postoperatively "definite." Probable iNPH is necessary to meet the diagnostic criteria of possible iNPH. The shunt procedure is indicated for probable iNPH, not for possible iNPH. Definite iNPH is defined as improved symptoms after a shunt procedure. The diagnostic criteria of iNPH are shown in Table 3.

Table 3 Diagnostic criteria of idiopathic normal pressure hydrocephalus (iNPH) in these Guidelines

Diagnostic criteria	Supplementary notes
<p>Possible iNPH</p> <p>1: Individuals who develop symptoms in their 60s or older.</p> <p>2: More than one of the clinical triad: gait disturbance, cognitive impairment, and urinary incontinence.</p> <p>3: Ventricular dilation (Evans index > 0.3).*</p> <p>4: CSF pressure of 200 mmH₂O or less and normal CSF content.</p> <p>5: Above-mentioned clinical symptoms cannot be completely explained by other neurological or non-neurological diseases.</p> <p>6: Preceding diseases possibly causing ventricular dilation are not obvious, including subarachnoid hemorrhage, meningitis, head injury, congenital hydrocephalus, and aqueductal stenosis.</p>	<p>1: Small stride, shuffle, instability in walking, and increase of instability on turning.</p> <p>2: Symptoms are slowly progressive; however, sometimes an undulating course, including temporal discontinuation of development and exacerbation, is observed.</p> <p>3: Other neurological diseases including Parkinson's disease, Alzheimer's disease, and cerebrovascular diseases may be coexist; however, all such diseases should be mild.</p> <p>4: Narrowing of sulci and subarachnoid spaces over the high convexity and midline surface, and dilation of the sylvian fissure and basal cistern are often observed.</p> <p>5: Periventricular lucency or periventricular hyperintensity is not essential.</p> <p>6: Measurement of CBF is useful for differentiation from other dementias.</p>
<p>Probable iNPH</p> <p>1: Meet requirements for possible iNPH</p> <p>2: Meet one of the following:</p> <p>a) Improvement of symptoms after CSF tap test.</p> <p>b) Improvement of symptoms after CSF drainage test.</p> <p>c) Abnormality in Ro measurement and ICP monitoring.</p>	
<p>Definite iNPH</p> <p>1: Improvement of symptoms after the shunt procedure.</p>	

*Evans index: the ratio of the maximum width of the frontal horns to the maximum width of the inner table of the cranium. CBF: cerebral blood flow, CSF: cerebrospinal fluid, ICP: intracranial pressure, Ro: cerebrospinal fluid out-flow resistance.

CHAPTER 2: TREATMENT

I. Shunt Procedure

Surgical intervention is the main treatment for iNPH. Although some patients exhibit an improvement in symptoms after repeated CSF removal by lumbar tap, long-term efficacy cannot be expected.

1. Surgical procedures for iNPH

The surgical procedures for iNPH are the same as those for other types of communicating hydrocephalus: ventriculo-peritoneal shunt,^{7B,12,48,69C,84C,91,130} ventriculo-atrial shunt,^{7B,48,91} and lumbo-peritoneal shunt.^{84C,92,103} As an historical change in treatment of hydrocephalus, ventriculo-atrial shunt was often performed for patients with iNPH in the past, whereas the ventriculo-peritoneal shunt is currently preferred. There have been no studies to compare these surgical procedures in the efficacy of treatment for iNPH. However, approximately 50-

80%^{7B,12,48,69C,84C,91,92,103,130} of cases are reported to improve after these shunting operations, and there seems to be little difference between these surgical procedures in the management of iNPH (Recommendation grade B). Nevertheless, ventriculo-atrial shunt is not indicated in patients with cardiovascular disease. In addition, lumbo-peritoneal shunt is not preferred for patients with severe lumbar canal stenosis or decubitus in the lumbosacral area (Recommendation grade C).

Endoscopic third ventriculostomy is a possible treatment option,³⁰ although the evidence is not good enough.⁶⁴

2. Shunt systems

Shunt systems include fixed differential pressure valves (DPVs; largely at low and medium pressure), flow-regulated valves, adjustable or programmable valves (PVs), and gravity assisted valves. Antisiphon

devices (an all-in-one type with valve is also available) may be added as an auxiliary device to prevent excessive removal when sitting and standing.

A. Fixed DPVs

The flow of fluid is regulated by the difference between the inflow and outflow sections of the valve. Fixed DPVs are characterized by a simple mechanism and low cost. Low-pressure (20–50 mmH₂O) or medium-pressure (55–85 mmH₂O) valves are used for iNPH.^{12,72} One study reported that the low-pressure valve was superior to the medium-pressure valve concerning the rate of improvement of dementia and gait disturbance in early-onset cases,⁷² whereas another study reported no differences in the long-term efficacy between low- and medium-pressure valves.¹² The low-pressure valve is superior in reducing ventricle size after shunt procedure.^{12,72} However, subdural effusion often develops in patients treated with the low-pressure valve. Care must be paid to select the valve for safety (Recommendation grade C).

B. Flow-regulated valves

Flow-regulated valves have a function of internal resistance changing automatically with pressure. Although their advantages are theoretically useful for iNPH, no differences have been demonstrated in improvement rate, infection rate, functional failure rate of shunt procedure, and incidence of subdural effusion between this valve and the fixed DPVs.^{67,130} Therefore, there is not enough evidence for this valve to be the first choice for iNPH treatment (Recommendation grade C).

C. Adjustable valves or PVs

These valves have become popular in recent years. The major advantage of these valves is that the pressure can be adjusted after installation. Readjustment of the pressure setting is reported in 36–75% of patients with this valve,^{98B,104,133B,134} in particular more frequently in iNPH.^{98B} For iNPH, it is better to adjust to the appropriate pressure gradually with this valve.^{84C} It is desirable to use this type of valve at present (Recommendation grade B). Attention is required for possible change in the set pressure during MRI^{133B} and mechanical breakdown.^{98B}

D. Gravity-assisted valve

Gravity-assisted valve is a position-sensitive valve and it contains two systems of CSF flow in the horizontal position and the vertical position. In-bread ball and spheres make possible to change automatically to regulate physiological drainage in-

dependent of the physical position of the patient. This valve is reported to be useful for patients of NPH.⁷³

E. Antisiphon devices

Excessive flow (overdrainage) occurs during sitting or standing with the CSF shunt system. Antisiphon devices prevent the siphon phenomenon, and are classified mechanically into three types: membranous, gravity-ball, and flow-sensitive types. Care is needed for the location of the device if the membranous or gravity-ball type is used. Although the use of antisiphon devices reportedly reduces the incidence of subdural effusion, complete prevention cannot be obtained.^{107,108} Further, underdrainage of flow may occur. Whether these devices can be recommended for routine use in iNPH is still unsettled (Recommendation grade C).

II. Postoperative Management and Complications

1. Postoperative management

An important issue in the postoperative management of patients with iNPH is to start gait training as early as possible, because most patients are elderly and gait disturbance is a major symptom. Another important issue for reducing complications and improving the outcome is appropriate valve pressure settings, especially in the early postoperative period. Although no ideal method for the initial pressure setting on the PV has been established, the generally accepted method is to start with a high pressure setting and subsequently lower the pressure gradually according to symptoms in order to prevent CSF overdrainage complications which predominantly occur in the sitting or standing position due to the siphon effect^{6,58,66,98B} (Recommendation grade B).

To date there have been several studies aimed at developing a method for adjusting the initial pressure setting of the PV, primarily based on the results of the CSF circulation dynamic tests (e.g., Ro) or measurements of ICP. However, all of these studies have shown a high incidence of readjustment (incidence: 39% and average number of readjustment of 1.2 times/patient,^{133B} 78% and 0.9 times/patient,¹²² 36% and 0.5 times/patient,¹⁰⁴ and 49% and 0.94 times/patient¹³⁴), which leaves some doubt as to the validity and efficacy of these proposed strategies. A quantitative method for setting the initial pressure of the PV based on the pressure environment in the upright position, considering the patient's physique, revealed a 17% pressure readjustment rate and 0.2 times/patient.⁷⁹ This method is designed to choose the setting of the Codman-Hakim programmable

valve[®] (CHPV; without antisiphon mechanism; Codman, Johnson & Johnson Co., U.S.A.) which provides a sitting ICP between -70 and -140 mmH₂O in reference to the external auditory meatus, measuring the ICP by puncturing the reservoir of the CHPV in the sitting position. According to this method, the initial pressure setting is determined based on the pressure environment of the upright condition in which shunt flow is expected to be a maximum and, therefore, the resultant pressure setting becomes relatively higher than previously considered. Evidence supporting this approach is available in several studies: One study showed improvement in symptoms in all subjects after setting the Sophy valve[®] (SV; Sophysa, U.S.A.) at a high pressure,⁵⁸⁾ another study found that the final setting in more than 80% of patients with CHPV was approximately 150 mmH₂O.^{98B)}

If symptoms due to overdrainage develop in patients treated with conventional fixed-type valves, patients are advised to maintain a recumbent position and then allowed a gradual transition to the upright position. However, the efficacy of this strategy is questionable in elderly patients with low brain compliance. Moreover, due to a delay of recovery followed by long-term bed rest and the consequent increases in medical expenses due to extended hospital stay, this method is considered to be relatively medico-economically inefficient.

In general, it is advisable to conduct follow-up CT over a period of one year at the following intervals: immediately after operation; 1–2 weeks after operation; and at 1, 3, 6, and 12 months after operation, as well as if aggravation of symptoms emerges. The gait and level of activity gradually improves after the operation, but the risk of falling may increase inversely until the gait becomes stabilized. In particular, postoperative patients are at high risk for subdural hematoma due to falls, so that appropriate care and preventative measures should be taken.

2. Complications

Postoperative shunt complications include shunt infection, shunt failure, headache, and subdural effusion and hematoma due to CSF overdrainage. According to a study in Japan, the incidence of shunt-related complications is relatively high (18.3%),⁸⁴⁾ perhaps due to treating elderly patients. Postoperative shunt infection rates have been reported to be between 4.4%^{98A)} and 8.6%^{133A)} in patients using CHPVs, and between 4%¹²²⁾ and 15%⁶⁶⁾ in patients using SVs, which are comparable to the rates in patients using DPVs. In addition, a study reported that the infection rate is reduced from 8.5% to 5.6% by the use of antibiotics during the perioperative

period.^{133A)}

Patency rates of shunts at 1 year after operation have been reported to be 75% for CHPVs^{133A)} and 62% for Orbis-Sigma valves (OSVs),¹³⁰⁾ suggesting a slight superiority in efficacy of CHPVs. The incidence of shunt obstruction ranged from 2%¹⁰⁷⁾ to 30%¹³³⁾ for CHPVs, 4% for SVs,¹⁰⁴⁾ 5% for the dual-switch valves[®] (DSVs; B Braun, Germany),¹⁰⁷⁾ and 10% for the DPVs.^{69A)} Although it is difficult to make a direct comparison of these valves due to differences in the observation period, in general, there seemed to be no differences between them.

Although the reported incidences of subdural effusion and hematoma have ranged from 6% to 12% for CHPVs^{98A,133A)} and 14.5% for SVs,¹⁰⁴⁾ a direct comparison cannot be made due to differences in background factors such as variations in the initial pressure settings. Most of these complications resolved after readjusting the pressure to a higher level, and reoperation reportedly ranged from 1.4% to 2.7%^{98A,133A)} for patients with CHPVs, and 1.4% for patients with SVs.¹⁰⁴⁾ In patients treated with shunt valves with antisiphon devices, transient subdural effusion occurs in 3% of patients and no cases requiring reoperation with DSVs,¹⁰⁷⁾ and 7% of patients experienced subdural hematoma requiring operation with OSVs.¹³⁰⁾

3. Long-term management

Although there have been no studies on the long-term postoperative management, the pressure setting is recommended to be readjusted to changes in the patient's body weight because this would have a significant effect on the pressure condition of the shunt.^{42,80,112)} Pressure setting is particularly important due to the low brain compliance with narrow acceptable ICP range. PVs are useful for controlling postoperative complications. In addition, it is necessary to monitor for transient worsening in the patient's symptoms, which can be caused by constipation¹¹²⁾ and other maneuvers that increase the intra-abdominal pressure.

Finally, even when patients have become bed-ridden, it is recommended that patients spend as much time in the sitting position as possible in order to avoid CSF underdrainage. If patients are unable to maintain an upright position, the pressure setting must be readjusted lower.

III. Outcome

The outcome at 3 months and up to 5 years after surgery has been reported. According to the studies, the efficacy of the shunt procedure is maintained for the short term, ranging from 3 months to 2 years, in

31–100% of the patients,^{2,5,14,48,96,126B,130} and for the long term, ranging from 3 to 5 years, in 61–91% of the patients.^{7B,48,69C,91,101} Because of the advanced age of the patients, some dropped out due to other diseases during the follow up. However, it is reported that the efficacy in the activities of daily living (ADL) is maintained for 5 years in 72%,¹⁰¹ and some improvement persists in 91%.⁹⁷ There is also a study reporting that the efficacy did not last more than 1 year after the procedure in 15 out of 34 shunt-responders.⁹¹

The best improvement is noted in gait disturbance, ranging from 58% to 90%.^{5,48,69C,101,130} The improvement rates in dementia differ with the evaluation scale used, but the symptom improves in 29–80% of the patients.^{48,69C,91,130} Urinary incontinence reportedly improved in 20–78%.^{48,69C,91,130} Patients with the classical triad showed a high rate of improvement, ranging from 65% to 74%.^{7B,126A} A prospective study comparing the ADL of patients with and without the shunt procedure showed that the rate of independence is higher in the former than

in the latter until 5 years.¹⁰¹ As for improvement in the classical triad,⁹⁶ gait disturbance showed improvement in 90% of patients within 2 months of the procedure, and in 95% of patients by 1 year after the procedure. Urinary incontinence improved in 90% of patients within 1 week of the procedure. On the other hand, dementia gradually improved, and an improvement rate of 66.7% is reported for patients at 1 year after the procedure.

There are many scales for evaluation. The Stein-Langfitt grading scale for functional impairment,¹⁰⁹ one of the classical scales for NPH, underestimates the effect of the shunt procedure.¹⁴ A comparison between the modified Rankin scale and the NPH scale for the classical triad shows that improvement rate differs depending on the evaluation scales, revealing 63.1% on the modified Rankin scale and 75.8% on the NPH scale.¹⁴ Various outcome measures have been used in previous studies, so that it is difficult to compare their results directly. Standardized measures are awaited.

CHAPTER 3: FLOWCHARTS OF THE DIAGNOSIS AND TREATMENT

1. Flowchart of diagnosis

These supplementary notes expand on the flowchart in Fig. 4.

1) Patients with iNPH often develop both gait disturbance and dementia, but some patients may have only gait disturbance, and other patients may have parkinsonism.

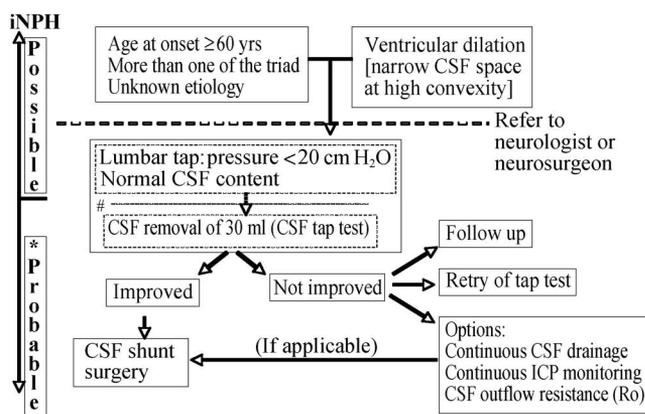


Fig. 4 Flowchart of diagnosis. #: Cerebrospinal fluid (CSF) tap test is available if CSF is watery and clear. *: Probable idiopathic normal pressure hydrocephalus (iNPH) if tap test or optional tests are positive. ICP: intracranial pressure.

2) The degree of ventricular dilation is usually greater than that in cerebral atrophy due to Alzheimer's disease. If sulcal narrowing in the high convexity is present, iNPH should be highly suspected. Coronal section images are useful for detecting sulcal narrowing (see: Chapter 1, II-1. CT, MRI).

3) It is important to suspect iNPH based on both symptoms and CT/MRIs.

4) CSF examination by lumbar puncture is important in differentiating iNPH from other neurological diseases. The CSF tap test can be conducted at the same time.

5) Volume of CSF removal by lumbar puncture is around 40 to 50 ml in many reports, but these Guidelines recommend removal of 30 ml of CSF in consideration of possible complications with excessive removal. Some studies indicate CSF removal twice on successive days, but these Guidelines recommend once in consideration of invasiveness for the elderly. CSF leakage at the puncture site may also contribute to improvement in symptoms, so the needle for puncture should be thick (recommended: 19 gauge or larger).

6) Symptomatic improvement is seen within a few days. Gait is an easy and accurate index of the improvement.

7) For the CSF shunt procedure, a ventriculo-peritoneal shunt or lumbo-peritoneal shunt is preferable.

8) Patients with negative tap test may respond to the shunt procedure. Therefore, for these patients, there are 3 choices: conduction of the optional test(s); retry of the CSF tap test; and follow up.

9) Continuous CSF drainage, continuous ICP monitoring, and Ro measurement are listed as options. The CSF drainage test requires continuous removal between 100 and 150 ml of CSF per day for several days. Ro measurement and ICP monitoring are useful in predicting the efficacy of the shunt procedure, but their thresholds differ depending on methods and facilities.

10) Retry of the CSF tap test should be conducted after more than 1 week. It is desirable to drain an amount of CSF greater than that at the initial test. If symptomatic improvement is noted at the second tap test, the shunt procedure is performed.

11) Observation may be also a good option because the CSF tap test may become positive months or years after the initial CSF tap test.

2. Flowchart for probable iNPH

These supplementary notes expand on the flowchart in Fig. 5.

1) Assessment of patient's background: Carefully examine the general status of the patient, and decide whether general anesthesia is suitable for the patient. Improvement would be seen in greater than 80% of cases for which surgery is indicated, but the efficacy is limited to severe cases. The decision for surgery should be made in consideration of the preoperative severity. Long-term follow up and adjustment of the pressure of the PV are required according to the clinical symptoms. Therefore, it is im-

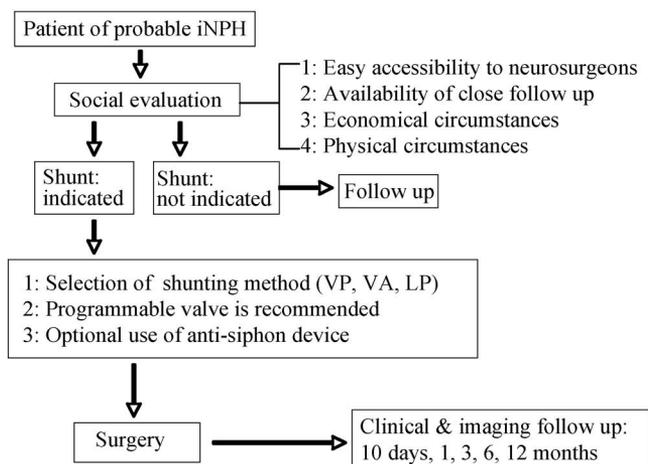


Fig. 5 Flowchart for probable idiopathic normal pressure hydrocephalus (iNPH). LP: lumbo-peritoneal, VA: ventriculo-atrial, VP: ventriculo-peritoneal.

portant for patients to reside close to the neurosurgical clinic.

2) Follow up: Non-operated patients due to any obstacles should be reexamined to assess the possibility of surgery in the future.

3) Performing shunt procedure: Before performing the surgery, the following conditions should be examined. a) Choose the shunt method that is routinely conducted at the facility. Ventriculo-peritoneal, lumbo-peritoneal, and ventriculo-atrial shunts have both advantages and disadvantages. b) As the valve pressure needs to be adjusted in response to the clinical symptoms, the use of a PV is recommended. c) There is no evidence concerning whether an anti-siphon device should be implemented initially.

4) Postoperative clinical symptoms and imaging assessment: Check intracranial lesions immediately after the surgery, and follow-up clinical symptoms and imaging at 10 days, 1 month, 3 months, 6 months, and 12 months.

3. Flowchart for problems after shunt procedure

These supplementary notes expand on the flowchart in Fig. 6. If the expected results are not achieved after the surgery, check whether the shunt flow is excessive or insufficient based on neuroimaging as well as clinical symptoms.

1) Excessive shunt flow (overdrainage): Postural headache and subdural effusion are seen on CT. Subdural hematoma may develop and require urgent surgical treatment.

2) Adjusting the pressure setting: If overdrainage is suspected, valve pressure should be adjusted to a higher setting. Most of the signs and symptoms are expected to disappear after the adjustment.

3) Addition of an antisiphon device: If the signs and symptoms of overdrainage are not resolved by set-

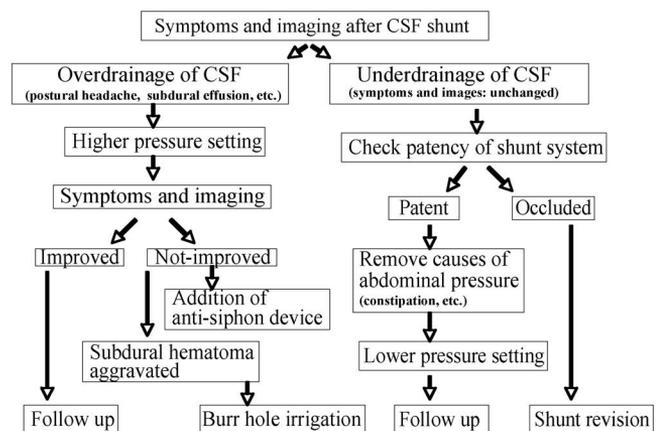


Fig. 6 Flowchart for problems after shunt procedure. CSF: cerebrospinal fluid.

ting the valve pressure maximally at 200 mmH₂O in the CHPV, addition of an antisiphon device should be indicated. If subdural hematomas associated with neurological worsening develop, surgical intervention is necessary.

4) If subdural hematomas are found, symptoms should be checked frequently, and if any exacerbation of symptoms is noted, hematoma irrigation is necessary.

5) If no improvement in symptoms or on imaging is seen after the shunt procedure, underdrainage should be suspected.

6) First, the patency of the shunt system should be examined. Verification of patency of the system by

valve pumping, shuntgraphy, or RI shunt flow test should be performed. If obstruction is noted, the shunt should be revised. Attention should be paid to the pressure setting, checking valve pressure by skull radiography.

7) If the shunt system is patent, constipation and weight gain, which raise abdominal pressure, should be resolved. Underdrainage may occur due to long bedrest. For prevention, semi-sitting or standing is encouraged. If such procedures yield no symptomatic improvement, valve pressure should be decreased gradually (10–20 mmH₂O at a time).

CHAPTER 4: REFERENCE MATERIALS

I. Conventional Diagnostic Criteria and Historical Transition

NPH is characterized by the classical triad with ventricular dilation and normal CSF pressure. The evaluation methods and diagnostic criteria have changed over time. Up to 1990, most studies included both types of NPH. After that, studies enrolling only iNPH cases increased gradually. Ventricular size had been evaluated with pneumoencephalography, later with CT with planimetric indices such as the Evans index and cella media index. Since the 1990s, MRI has gradually been implemented, making possible more detailed evaluation of white matter lesions and cerebral atrophy. MRI also allows volumetry which enables measurement of ventricular volume more precisely. RI cisternography is regarded as an important diagnostic tool, but its role in the diagnosis of iNPH is not established. CSF pressure measurement via lumbar puncture and continuous ICP monitoring are regarded as important diagnostic measures. Since the 1990s, the CSF tap test and infusion test have been included in the diagnostic criteria (Table 4).

Among shunt procedures, the ventriculo-atrial shunt was the most commonly employed earlier, but the ventriculo-peritoneal shunt has gradually been adopted. Of the various shunt systems, the fixed DPV has been used until the late 1980s, when systems with anti-overdrainage function such as the OSV and antisiphon devices were developed. Since the middle of the 1990s, studies using the CHPV have been published. Thereafter, advanced anti-siphon systems including CHPV with Siphon Guard™ Anti-Siphon Device and DSV have been commonly used. The improvement rate by shunt procedure was 61–76% between the 1970s and 1980s. Since

1990, the improvement rate has been 72–100%. The efficacy of the shunt procedure has increased with advances in the diagnostic measures and the devices (Table 5).

II. Evaluation Methods for the Classical Triad

It is important to evaluate the severity of the classical triad of iNPH accurately in order to determine the efficacy of the CSF tap test and shunt procedures. There are a number of evaluation methods that have been used in past. Here, only those methods recommended by this committee are described.

1. Evaluation methods recommended by this committee

This committee recommends the following methods for assessing the severity of iNPH and the response to the interventions.

A. Examination methods for gait disturbances

The most sensitive and simple indices are changes of the time and number of steps required to walk a certain distance. In iNPH patients, the impairment becomes more prominent while standing or changing direction than while walking. This committee recommends the 3 m Up & Go test,⁹⁵⁾ which measures the time and number of steps to stand up from a chair, walk 3 m, return, and sit down on the chair.

B. Examination methods for cognitive impairment

This committee recommends the Mini-Mental State Examination (MMSE),²⁷⁾ which is useful as a simple one for overall cognitive function. Other tests such as the Frontal Assessment Battery or the Trail

Table 4 Development of shunt procedures

Author (Year)	Research period	NPH type	No. of iNPH subjects	Diagnostic criteria/ Ancillary tests	Shunt procedure	Shunt system	Observation period	Improvement rate (%)
Stein and Langfitt (1974) ¹⁰⁹⁾	1971-1972	combined	33	classical triad, ventricular dilation, lumbar CSF pressure, RI cisternography, infusion test	unknown	unknown	18 mos	64
Black (1980) ⁷⁾	1959-1977	iNPH	62	classical triad, CT, lumbar CSF pressure (below 180 mmH ₂ O), RI cisternography	VA 57/ VP 5	Hakim valve (medium pressure)	36.5 mos	61
Børgesen and Gjerris (1982) ¹⁶⁾	1977-1980	combined	31	classical triad, CT, ICP monitoring, RI cisternography, Ro	VA	Hakim valve (medium pressure)	1 yr	68
Petersen et al. (1985) ⁹¹⁾	1966-1981	NPH	45	classical triad, CT, EEG, RI cisternography	VA/VP	combined	51 mos	76
Benzel et al. (1990) ⁵⁾	1982-1987	iNPH	37	classical triad, CT (ventricle size, PVL, cerebral atrophy), RI cisternography	VP	DPV (high pressure)	2 mos	70
Larsson et al. (1991) ⁵⁹⁾	1978-1989	combined	26	classical triad, CT, lumbar CSF pressure, CSF tap test, RI cisternography	VP	DPV (combined)	2.1 yrs	73
Vanneste et al. (1992) ¹²⁶⁾	1980-1989	combined	127	clinical symptoms, CT, lumbar CSF pressure	unknown	unknown	1 yr	31
Raftopoulos et al. (1994) ⁹⁶⁾	1986-1989	iNPH	23	gait disturbance and dementia, CT, lumbar CSF pressure < 200 mmH ₂ O, amplitude of ICP pulse wave > 9 mmHg	VA	DPV (medium pressure)	1 yr	96
Weiner et al. (1995) ¹³⁰⁾	1987-1992	combined	36	gait disturbance, MRI (excluding cerebral atrophy)	VP	OSV or DPV + ASD	14 mos	89
Malm et al. (1995) ⁶⁹⁾	1988-1992	iNPH	35	classical triad (mainly gait disturbance), CT, cooperative attitude, age < 80 yrs, lumbar CSF pressure, Ro, CSF tap test	unknown	OSV/DPV	3 mos/3 yrs	72
Krauss and Regel (1997) ⁴⁹⁾	1989-1994	iNPH	41	classical triad (mainly gait disturbance), MRI, CSF tap test, Ro, B wave on ICP monitoring	VA 35/ VP 6	DPV or CHPV	16 mos	90
Caruso et al. (1997) ²⁰⁾	1988-1992	iNPH	18	gait disturbance and dementia, CT or MRI, ICP 12-18 mmHg, B wave	VP	unknown	4.2 yrs	67
Boon et al. (2000) ¹⁴⁾	1990-1995	iNPH	95	gait disturbance and dementia, CT, slight cerebral atrophy, lumbar CSF pressure, Ro	VP	Hakim valve (low/medium pressure)	1 yr	76
Anderson et al. (2002) ²⁾	1999-2000	iNPH	20	classical triad, CT, CSF tap test, ventricular volumetry	VP	CHPV	17.5 mos	100
Kahlon et al. (2002) ⁴¹⁾	1996-2000	iNPH	51	classical triad, CT, MRI, infusion test or CSF tap test	VP/VA	CHPV	6 mos	84
Kiefer et al. (2002) ⁴³⁾	1996-2000	combined	91	classical triad, CT, lumbar CSF pressure, Ro	VP	DSV or CHPV + ASD	26 mos	85

ASD: anti-siphon device, CHPV: Codman-Hakim programmable valve, CSF: cerebrospinal fluid, CT: computed tomography, DPV: differential pressure valve, EEG: electroencephalography, ICP: intracranial pressure, iNPH: idiopathic normal pressure hydrocephalus, MRI: magnetic resonance imaging, NPH: normal pressure hydrocephalus, OSV: Orbis-Sigma valve, PVL: periventricular lucency, RI: radioisotope, Ro: cerebrospinal fluid outflow resistance, VA: ventriculo-atrial, VP: ventriculo-peritoneal.

Table 5 Diagnostic criteria for representative studies of idiopathic normal pressure hydrocephalus in the past

Author (Year)	Clinical symptoms	Ventricular dilation	CSF pressure	Auxiliary tests
Black (1980) ⁷⁾	dementia and/or gait disturbances	verified by CT scanning	below 180 mmH ₂ O	RI cisternography
Børgesen and Gjerris (1982) ¹⁶⁾	(1) dementia, (2) gait disturbances with an inability to rotate limb in a circular motion or blind gait, (3) urinary urgency at least once per week, incontinence, (4) duration > 3 mos	Evans index > 0.3, cerebral infarction, cerebral tumor, or other causes of hydrocephalus are not observed	intraventricular pressure at rest is below 12 mmHg, plateau wave is not observed in ICP monitoring	RI cisternography, Cout
Vanneste et al. (1992) ¹²⁶⁾	(1) gait disturbance and dementia, (2) regardless of incontinence	chronic ventricular dilation	normal lumbar CSF pressure	cisternography, CSF tap test, Cout, ICP monitoring
Raftopoulos et al. (1994) ⁹⁶⁾	(1) ataxic gait, (2) regardless of incontinence, (3) ambulatory 1 yr before	Evans index > 0.3, hydrocephalus of unknown cause	ICP, lumbar CSF pressure < 20 mmH ₂ O, pressure wave with amplitude ≥ 9 mmHg	
Weiner et al. (1995) ¹³⁰⁾	gait disturbance regardless of dementia and incontinence	disproportionate ventricular dilation on MRI		
Malm et al. (1995) ⁶⁹⁾	gait disturbance, dementia, and incontinence, communicable, MMSE > 10, age ≤ 80 yrs	lateral ventricular dilation		Barthel index
Krauss and Regel (1997) ⁴⁹⁾	gait disturbance	flattened sulci on the frontoparietal region	B wave ≥ 70%, CSF tap test	PVI, Ro
Boon et al. (2000) ¹⁴⁾	gait disturbance, cognitive impairment, mRS ≤ 2, age ≤ 85 yrs	(1) communicating hydrocephalus, (2) Evans index > 0.3, (3) ventricular index > 0.8, (4) no symptomatic cerebral lesions, (5) total of 4 major sulci diameters < 25 mm		Ro, CSF pressure

Cout: cerebrospinal fluid outflow conductance, CSF: cerebrospinal fluid, CT: computed tomography, ICP: intracranial pressure, MMSE: mini-mental state examination, MRI: magnetic resonance imaging, mRS: modified Rankin scale, PVI: , RI: radioisotope, Ro: cerebrospinal fluid outflow resistance.

Table 6 Japanese Normal Pressure Hydrocephalus Grading Scale-revised

Severity	Gait disturbance	Cognitive impairment	Urinary incontinence
0	normal	normal	normal
1	dizziness or unsteadiness only	complaint of amnesia or inattention, but no objective memory and attention impairment	pollakiuria or urinary urgency
2	unstable, but independent gait	amnesia or inattention, but no disorientation of time and place	occasional urinary incontinence (1-3 or more times per week but less than once per day)
3	walking with any support	disorientation of time and place, but no impairment of conversation	continuous urinary incontinence (1 or more times per day)
4	walking not possible	disorientation for the situation, or impaired meaningful conversation	almost or perfectly impaired bladder function

Making Test would be useful, but their clinical significances are not established.

C. Japanese NPH Grading Scale-revised (JNPHGS-R)

This committee has developed a revised version of

the JNPHGS-R (Table 6), which was originally derived from the Intractable Hydrocephalus Research Committee in Japan.⁸⁴⁾ This grading scale includes a very mild stage of the classical triad for evaluation of improvement after the CSF tap test or the shunt procedure.

(Addendum: Validation of this grading scale is published by Kubo Y, Kazui H, Yoshida T, et al. in *Dement Geriatr Cogn Disord* 25(1): 37–45, 2008.)

D. Evaluation methods of overall functions

The modified Rankin scale⁹⁾ has been used in many clinical studies to evaluate the degree of overall functions in social or daily life. This committee recommends it as a scale of the overall functions.

E. Evaluation methods for the change after shunt procedures and CSF tap test

There is no gold standard for determining the positive response to exploratory tests such as the CSF tap test, or the shunt surgery. This committee proposes that a positive response is judged by at least one of the followings: greater than 10% improvement of the time in the Up & Go test,⁹⁵⁾ greater than 3-point improvement in the MMSE, or more than one-point improvement in any of the classical triad in the JNPHGS-R.

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