Advances in Diagnosis and Treatment of Idiopathic Normal Pressure Hydrocephalus: A Systematic Review (2019–2024)

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Abstract:

Background
Idiopathic Normal Pressure Hydrocephalus (iNPH) is a neurological disorder primarily affecting the elderly. Gait disturbances, cognitive decline, and urinary incontinence characterize it. Diagnosing iNPH is challenging because its symptoms overlap with those of other conditions, such as Alzheimer's Disease and Parkinson's Disease. Accurate and timely diagnosis is crucial for improving patient outcomes.

Methods
A systematic literature review was conducted using PubMed from January 2019 to June 2024. Search terms included "normal pressure hydrocephalus," "idiopathic normal pressure hydrocephalus," and "ventriculoperitoneal shunt (VPS)." Of the 1643 initial results, 103 papers were selected for review based on their relevance to iNPH diagnosis, treatment, and clinical outcomes.

Results/Discussion
Several diagnostic tests were evaluated, with the iNPH Radscale showing the highest sensitivity (100%) and specificity (96%) in diagnosing iNPH. For treatment, the ventriculoperitoneal shunt (VPS) has demonstrated significant efficacy in improving symptoms, particularly when surgery is performed within two years of symptom onset. The results emphasize the importance of early intervention and specific diagnostic tools in predicting treatment success.

Conclusion
Diagnosing iNPH requires a combination of clinical assessments and imaging techniques, with the iNPH Radscale being the most reliable. VPS is the preferred treatment, offering substantial symptom relief, mainly when performed early. Future research should focus on improving diagnostic protocols and exploring alternative treatment strategies to enhance patient outcomes.

Keywords: iNPH, VPS shunt, iNPH Radscale

Introduction

Normal Pressure Hydrocephalus (NPH) is a neurological disorder characterized by a triad of symptoms: impaired gait, urinary incontinence, and cognitive decline caused by an abnormal accumulation of cerebrospinal fluid in the brain's ventricles.[1] NPH is classified into two categories: idiopathic NPH (iNPH) and secondary NPH (sNPH), with the latter having an

[1] da Rocha et al., "Serial Tap Test of Patients with Idiopathic Normal Pressure Hydrocephalus: Impact on Cognitive Function and Its Meaning."

identifiable cause such as head trauma or infection.[2] Current diagnosis methods include the Cerebrospinal fluid (CSF) tap test, a procedure in which CSF is collected and tested for disease, and MRI imaging. Nevertheless, due to the high rate of misdiagnosis, there have been calls for improved diagnostic protocols within the field, particularly for iNPH, a subtype of NPH with no identifiable cause. [3]

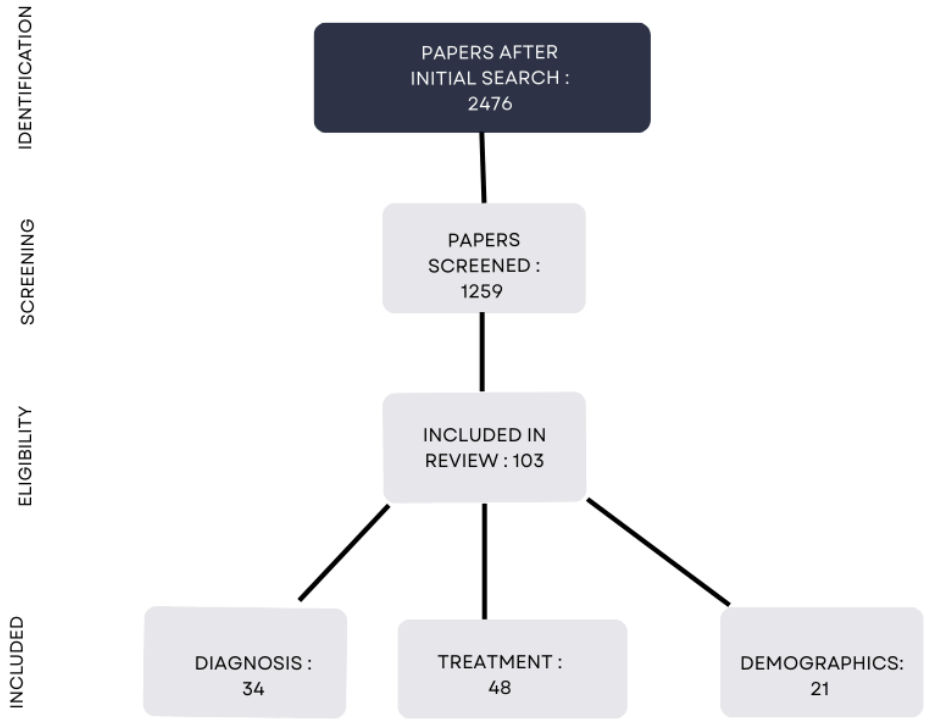
Predominantly affecting the elderly population, NPH is frequently misdiagnosed or mistaken for neurological diseases involving cognitive decline, such as Alzheimer's disease. This misdiagnosis often leads to NPH patients receiving delayed treatment, decreasing the likelihood of improvement in symptoms[4].

The most popular treatment option for NPH is the ventriculoperitoneal shunt (VPS), a plastic tube that drains excess cerebrospinal fluid (CSF) in the brain ventricles[5]. Additionally, lumboperitoneal shunts (LPS) drain excess CSF from the spine. [6] Action observation therapy also aids in impaired gait for patients who would not benefit from surgical treatment due to minimal improvement with the CSF tap test. [7] While current therapies can improve a patient's urinary incontinence and gait[8], there are concerns about the eventual decline in treatment efficacy over time.[9] Despite numerous studies on new treatment options and optimized diagnostic procedures, there is still a need for systematic reviews that consolidate the current understanding and recent advancements in iNPH research. This systematic review addresses that gap by focusing on iNPH symptoms, diagnostic procedures, and current and potential diagnosis and treatment options to enhance clinical decision-making and guide future research.

Methods

We searched PubMed from January 2019 to June 2024 for relevant articles using the keywords " normal pressure hydrocephalus" OR " idiopathic normal pressure hydrocephalus" OR " secondary normal pressure hydrocephalus" OR " NPH " OR " ventriculoperitoneal shunt (VPS)." The initial search yielded 1643 results, and after selecting papers based on their abstracts, 103 papers on idiopathic routine pressure hydrocephalus diagnosis, treatment, and etiology were chosen for review (**Figure 1**).

[2] "Normal Pressure Hydrocephalus - an Overview | ScienceDirect Topics."
[3] Acosta et al., "Protocolizing the Workup for Idiopathic Normal Pressure Hydrocephalus Improves Outcomes."
[4] de Guilhem de Lataillade et al., "Idiopathic Normal Pressure Hydrocephalus and Frontotemporal Dementia: An Unexpected Association."
[5] Popal et al., "Outcomes of Ventriculoperitoneal Shunt in Patients With Idiopathic Normal-Pressure Hydrocephalus 2 Years After Surgery."
[6] Sinha et al., "Lumboperitoneal Shunts - Patient Selection, Technique, and Complication Avoidance: An Experience of 426 Cases."
[7] Hnin et al., "Feasibility of Action Observation Effect on Gait and Mobility in Idiopathic Normal Pressure Hydrocephalus Patients."
[8] Hallqvist, Grönstedt, and Arvidsson, "Gait, Falls, Cognitive Function, and Health-Related Quality of Life after Shunt-Treated Idiopathic Normal Pressure Hydrocephalus-a Single-Center Study."
[9] Takeuchi and Yajima, "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."



Epidemiology and Clinical Presentation of iNPH

As previously mentioned, iNPH patients typically exhibit at least one of the three main symptoms: impaired gait, cognitive decline, and urinary incontinence. Understanding the epidemiology of iNPH is crucial for identifying those at risk and improving diagnostic and treatment strategies. The prevalence of iNPH ranges from 1.5% to 3.7% of the population[10], with 33% to 67.3%[11] of patients presenting with all three hallmark symptoms. Among these, impaired gait and falling are the most common, affecting 60% of patients[12], of which 50.9% experience the phenomenon of "stop talking while walking." Additionally, 3.6% to 16% of patients suffer from Freeze of Gait (FoG)[13]. Cognitive decline, including dementia, is the second most frequent symptom, affecting approximately 40% of patients[14]. Demographic factors also play a role in the

[10] Constantinescu et al., “Prevalence of Possible Idiopathic Normal Pressure Hydrocephalus in Sweden: A Population-Based MRI Study in 791 70-Year-Old Participants.”
[11] Möhwald et al., “Quantification of Pathological Gait Parameter Thresholds of Idiopathic Normal Pressure Hydrocephalus Patients in Clinical Gait Analysis.”
[12] Ishikawa, Yamada, and Yamamoto, “Agreement Study on Gait Assessment Using a Video-Assisted Rating Method in Patients with Idiopathic Normal-Pressure Hydrocephalus.”
[13] Kihlstedt et al., “Freezing of Gait in Idiopathic Normal Pressure Hydrocephalus.”
[14] Ishikawa, Yamada, and Yamamoto, “Agreement Study on Gait Assessment Using a Video-Assisted Rating Method in Patients with Idiopathic Normal-Pressure Hydrocephalus.”

incidence of iNPH. Men comprise 51%[15] to 67%[16] of patients, and most cases occur in individuals aged 76 [17] to 80[18]. Women are more likely to take more steps and have longer times in the Timed Up and Go (TUG) Test, which evaluates gait and mobility[19].

Diagnosis

A diagnostic evaluation of iNPH is essential because iNPH symptoms often overlap with other diseases, such as Parkinson's disease [20] and Alzheimer's disease[21]. Accurate diagnosis is crucial to ensure patients receive timely treatment and experience symptom improvement. The primary goals of diagnosing iNPH include assessing a patient's gait, urinary continence, and cognitive ability, and evaluating their response to the CSF tap test to determine if treatment will be beneficial.[22]

Diagnosis of iNPH involves a range of tests. The two most notable for diagnosing the triad are the iNPH Grading Scale (iNPHGS) and the iNPH Radscale (Table 1). The iNPHGS assesses the severity of symptoms in gait, urinary continence, and cognition, assigning a score out of 12, with four points each for gait, continence, and cognition. A score of 1 indicates mild symptoms, while a score of 4 indicates severe symptoms[23]. On average, patients score 6.1 out of 12, with 2.0 for gait, 2.3 for urinary incontinence, and 1.8 for cognition. While iNPHGS assesses the clinical symptoms of iNPH, the iNPH Radscale assesses the radiologic aspects of iNPH[24]. The iNPH radscale assesses components like ventricular enlargement and cortical atrophy. The rad scale scores out of 11 points, with 11 being the most severe radiologic symptoms and zero being the least severe. The rad scale is a valuable tool in diagnosing iNPH, with a sensitivity of 100%, specificity of 96%, and an overall accuracy of 98.5%. The gait domain in the iNPH rad scale is significantly higher for tap-test-positive patients[25]. Despite its ability to diagnose iNPH, the iNPH Radscale cannot identify whether a patient will respond to the CSF tap test[26].

[15] Tominaga et al., "High Prevalence of Lumbar Spinal Stenosis in Cases of Idiopathic Normal-Pressure Hydrocephalus Affects Improvements in Gait Disturbance after Shunt Operation."
[16] Constantinescu et al., "Prevalence of Possible Idiopathic Normal Pressure Hydrocephalus in Sweden: A Population-Based MRI Study in 791 70-Year-Old Participants."
[17] Morel et al., "Normal Pressure Hydrocephalus and Cognitive Impairment: The Gait Phenotype Matters Too."
[18] Lilja-Lund et al., "Dual-Task Performance in Older Adults With and Without Idiopathic Normal Pressure Hydrocephalus."
[19] Sundström et al., "The Timed up and Go Test in Idiopathic Normal Pressure Hydrocephalus: A Nationwide Study of 1300 Patients."
[20] Mostile et al., "Turning and Sitting in Early Parkinsonism: Differences Between Idiopathic Normal Pressure Hydrocephalus Associated with Parkinsonism and Parkinson's Disease."
[21] Mazzeo et al., "Alzheimer's Disease CSF Biomarker Profiles in Idiopathic Normal Pressure Hydrocephalus."
[22] Chang et al., "Dopaminergic Degeneration and Small Vessel Disease in Patients with Normal Pressure Hydrocephalus Who Underwent Shunt Surgery."
[23] Chadani et al., "Association of Right Precuneus Compression with Apathy in Idiopathic Normal Pressure Hydrocephalus: A Pilot Study."
[24] Kockum et al., "Diagnostic Accuracy of the iNPH Radscale in Idiopathic Normal Pressure Hydrocephalus."
[25] Yamada et al., "Gait Assessment Using Three-Dimensional Acceleration of the Trunk in Idiopathic Normal Pressure Hydrocephalus."
[26] Kockum et al., "Diagnostic Accuracy of the iNPH Radscale in Idiopathic Normal Pressure Hydrocephalus."

The Mini-Mental State Examination (MMSE) is another valuable tool for diagnosing iNPH and assessing cognitive function. Its scores range from 0 to 30, where 0 indicates severe impairment and 30 indicates no impairment at all. iNPH patients typically score between 21.8[27] and 22[28], indicating a mild cognitive decline.

The TUG test assesses gait and requires patients to stand up, walk 3 meters, and sit back down[29]. iNPH patients average 19 seconds and 23 steps to complete this task. The TUG test has a sensitivity of 60% and a specificity of 100%[30]. Additionally, the Tinetti and Berg Balance Scale (BBS) exams assess balance during gait. The Tinetti is scored using an ordinal scale of 0-2 for 16 items, including balance and gait, allowing a maximum score of 28, indicating the best functional mobility and stability[31]. The BBS includes 14 items assessing static and dynamic balance out of a total score of 56[32]. The Tinetti has a sensitivity of 71% and a specificity of 77%, while the BBS has a sensitivity of 85% and a specificity of 72%[33].

In addition to these physical tests, radiologic criteria, such as Evan's index (EI), provide further diagnostic insight. EI measures the ratio of the lateral ventricles in the brain, with a median value of 0.34 in iNPH patients, compared to 0.25-0.28 in non-iNPH patients.[34] EI, however, has a diagnostic accuracy of only 0.42 at an optimal threshold of 0.35[35]. Another new gait test uses a technology called Ambulatory Parkinson's Disease Monitoring (APDM) inertial sensors, which can potentially identify patients with iNPH suitable for a shunting procedure. The sensors include gyroscopes and a magnetometer to generate gait and balance analytics for a comprehensive report automatically. The sensors are placed on the bilateral wrists, feet, sternum, and fifth lumbar vertebrae. iNPH patients had decreased gait speed and impaired balance. However, there were strong correlations between Global Rate of Change (GRC) scoring for all but one parameter. GRC assesses whether a patient's condition worsens, improves, or remains unchanged[36]. The prevalence of falls in patients significantly correlates with a more significant Evans Index and a higher likelihood of iNPH. Screening elderly patients with consistent falls can potentially identify iNPH patients earlier and increase the benefits of surgical treatments[37]. Not only can motor function in the lower limbs be a sign of iNPH, but so

[27] Kockum et al.
[28] Tominaga et al., "High Prevalence of Lumbar Spinal Stenosis in Cases of Idiopathic Normal-Pressure Hydrocephalus Affects Improvements in Gait Disturbance after Shunt Operation."
[29] Kawahara et al., "Dural Sac Shrinkage Signs on Spinal Magnetic Resonance Imaging Indicate Overdrainage after Lumboperitoneal Shunt for Idiopathic Normal Pressure Hydrocephalus."
[30] Gallagher et al., "Predicting Post-Surgical Outcomes in Idiopathic Normal Pressure Hydrocephalus Using Clinically Important Changes from the Cerebrospinal Fluid Tap Test."
[31] Wu et al., "Systematic Volumetric Analysis Predicts Response to CSF Drainage and Outcome to Shunt Surgery in Idiopathic Normal Pressure Hydrocephalus."
[32] Mori et al., "Useful Outcome Measures in INPH Patients Evaluation."
[33] Gallagher et al., "Predicting Post-Surgical Outcomes in Idiopathic Normal Pressure Hydrocephalus Using Clinically Important Changes from the Cerebrospinal Fluid Tap Test."
[34] Kawahara et al., "Patients of Idiopathic Normal-Pressure Hydrocephalus Have Small Dural Sac in Cervical and Upper Thoracic Levels: A Supposed Causal Association."
[35] Wu et al., "Systematic Volumetric Analysis Predicts Response to CSF Drainage and Outcome to Shunt Surgery in Idiopathic Normal Pressure Hydrocephalus."
[36] He et al., "Quantitative Evaluation of Gait Changes Using APDM Inertial Sensors After the External Lumbar Drain in Patients With Idiopathic Normal Pressure Hydrocephalus."
[37] Oike et al., "Screening for Idiopathic Normal Pressure Hydrocephalus in the Elderly after Falls."

can upper limb function, as iNPH patients experience more impaired hand function than non-iNPH patients. [38]

Another valuable tool for diagnosis is the triage index test. This test involves gathering clinical and radiological data from patients, analyzing the data with a statistical model to predict outcomes, and then if the index test results in a high likelihood of iNPH, suggesting a patient receive a computed tomography (CT) scan to confirm the diagnosis and specialists can determine if a shunt will be beneficial. This test determined that balance and gait disorders, difficulty standing on toes or heels, urinary disturbances, and ventriculomegaly, with an Evans ratio rather than the combined diagnostic threshold, strongly predict the INPH diagnosis. The triage index test had a high sensitivity of 95.2% and specificity of 91.7%[39]

Radiologic criteria can aid in diagnosing iNPH, as can structural changes visible in an MRI or CT scan. Dopaminergic degeneration, an indicator of Parkinson's disease, is significantly correlated with a poorer improvement in the iNPHGS score.[40] Another radiologic test is a fusion model, which combines features of a ventricular morphology model (LVM) and a cortical thickness model. This fusion test achieved an accuracy of 90.43%, a sensitivity of 90.00%, and a specificity of 90.1%. This test revealed the importance of cortical thickness in the right isthmus cingulate cortex and how it influences differentiating iNPH-positive and negative patients[41]. Another significant radiological image is the disproportionately enlarged subarachnoid space hydrocephalus (DESH) score, determined based on radiologic markings such as Evan's Index and Corpus Callosal Angle. The DESH score is significantly correlated with patients' improvement after surgery. For each one-unit increase in the DESH score, patients were approximately 1.77 times more likely to experience a higher category of benefit from shunt surgery[42]. Temporal horns can also indicate if a patient will respond positively to the CSF tap test, as there is a positive correlation between smaller temporal horns and CSF tap test responders[43]. A higher "colossal angle," meaning a more acute colossal angle, strongly correlates with a positive tap test response and can indicate whether a patient will respond[44]

Evan's Index and Ventricular Volume (VV) are also significant in determining if a patient will benefit from lumbar drainage. With the EI and VV having optimal thresholds of 0.39 and 110.78 cm^3, and the overall imaging parameter thresholds achieving 74% accuracy, patients with thresholds of 0.39 or higher are more likely to show improvement, especially in gait, after lumbar

[38] Shimizu et al., "Clinical Utility of Paced Finger Tapping Assessment in Idiopathic Normal Pressure Hydrocephalus."
[39] Razay, Wimmer, and Robertson, "Incidence, Diagnostic Criteria and Outcome Following Ventriculoperitoneal Shunting of Idiopathic Normal Pressure Hydrocephalus in a Memory Clinic Population: A Prospective Observational Cross-Sectional and Cohort Study."
[40] Chang et al., "Dopaminergic Degeneration and Small Vessel Disease in Patients with Normal Pressure Hydrocephalus Who Underwent Shunt Surgery."
[41] Yang et al., "Improve the Diagnosis of Idiopathic Normal Pressure Hydrocephalus by Combining Abnormal Cortical Thickness and Ventricular Morphometry."
[42] Jóhannsdóttir et al., "Idiopathic Normal Pressure Hydrocephalus: Validation of the DESH Score as a Prognostic Tool for Shunt Surgery Response."
[43] Laticevschi et al., "Can the Radiological Scale 'iNPH Radscale' Predict Tap Test Response in Idiopathic Normal Pressure Hydrocephalus?"
[44] Pyrgelis et al., "Callosal Angle Sub-Score of the Radscale in Patients with Idiopathic Normal Pressure Hydrocephalus Is Associated with Positive Tap Test Response."

drainage[45]. Twelve radiomic features were selected as the most predictive of responders and non-responders to CSF drainage. These features include DifferenceAverage, DifferenceEntropy, Contrast, ZonePercentage, SmallDependenceEmphasis, Skewness, LongRunEmphasis, RunVariance, Id, Idm, ZoneEntropy, and LargeAreaLowGrayLevelEmphasis[46]. The inferior lateral ventricle, bilateral hippocampus, and orbital cortex are positive indicators of CSF drainage responders[47]. CSF biomarkers can also predict shunt responsiveness in patients, as the prevalence of FABP3, MIF, ANXA4, B3GAT2, ITGB1, YWHAG, OLFM2, TGFBI, and DSG2 is associated with a positive response[48]. High-resolution images can also highlight the characteristics of iNPH tap test responders versus nonresponders. Volumetric analysis has shown that as granularity levels increase, the classification accuracy of responders and nonresponders also increases. The highest diagnostic accuracy of this was achieved with a sensitivity of 0.89, a specificity of 0.91, a precision of 0.84, and an accuracy of 0.90[49].

In conclusion, diagnosing iNPH requires a combination of clinical assessments, radiologic imaging, and emerging technologies to ensure accuracy. Tools like the iNPHGS, MMSE, TUG test, and imaging indices, such as the iNPH Radscale and Evan's Index, provide valuable insights into symptoms and brain changes. Emerging methods, including APDM sensors, triage index tests, and CSF biomarkers, enhance diagnostic precision and predict treatment outcomes. By integrating these approaches, clinicians can identify iNPH earlier and tailor treatments to improve patient quality of life and outcomes.

Table 1: Sensitivity, Specificity, and Accuracy of Diagnostic Tests for iNPH

Test	Sensitivity	Specificity	Accuracy
iNPH Radscale	100%	96%	98.5%
Triage Index Test	95.2%	91.7%	N/A
Fusion Model (LVM+CT)	90.0%	90.1%	90.43%
Volumetric Analysis	89%	91%	90%
EI & VV Parameters	N/A	N/A	74%
Timed Up and Go	60%	100%	N/A
Tinetti	71%	77%	N/A
BBS	85%	72%	N/A

[45] Rohatgi et al., "Predicting Gait Speed Improvement in Idiopathic Normal Pressure Hydrocephalus Patients: The Role of Evans Index and Ventricular Volume."
[46] Sotoudeh et al., "The Role of Machine Learning and Radiomics for Treatment Response Prediction in Idiopathic Normal Pressure Hydrocephalus."
[47] Wu et al., "Systematic Volumetric Analysis Predicts Response to CSF Drainage and Outcome to Shunt Surgery in Idiopathic Normal Pressure Hydrocephalus."
[48] Sundström et al., "The Timed up and Go Test in Idiopathic Normal Pressure Hydrocephalus: A Nationwide Study of 1300 Patients."
[49] Wu et al., "Systematic Volumetric Analysis Predicts Response to CSF Drainage and Outcome to Shunt Surgery in Idiopathic Normal Pressure Hydrocephalus."

Treatment

The primary treatment for iNPH involves CSF shunting procedures, which aim to alleviate symptoms such as gait disturbances, cognitive impairment, and urinary incontinence. The effectiveness of treatment varies based on the surgical approach, patient characteristics, and the type of shunt used.

VPS is a surgical procedure that involves implanting a shunt to divert excess cerebrospinal fluid from the brain's ventricles to the peritoneal cavity, where it can be absorbed. This helps reduce intracranial pressure and improve symptoms associated with iNPH[50]. VPS demonstrates substantial improvements in functional and symptomatic outcomes. At three months post-surgery, 57% of patients with a waiting time of 3 months or less improved at least five points on the modified iNPH scale, compared to 52% and 46% of patients with waiting times of 3.1–5.9 months and 6 months or less, respectively ($p = 0.0115$). This highlights the importance of reducing wait time from diagnosis to surgery. At 12 months of follow-up, these improvement rates were 61% for surgeries with a waiting time of 3 months or less, 52% for surgeries with a waiting time of 3.1-5.9 months, and 51% for surgeries with a waiting time of 6 months or more ($p = 0.0536$)[51].

Another treatment option is CSF drainage via LPS, which significantly improves iNPH symptoms. LPS, which diverts CSF from the lumbar spine to the peritoneal cavity, is considered an alternative to VPS for patients who may not tolerate brain surgery. This treatment resulted in 72.9% of patients undergoing functional improvements and 90.6% reporting symptomatic relief at one year. Patients who had surgery within two years of experiencing their first symptoms were much more likely to experience improvements in function and gait. The chances of overall improvement were 24 times higher, and the chances of improved gait were about five times higher than those who had surgery later. Patients were more likely to experience improved cognitive ability if they had a lower level of disability before surgery, as measured by the modified Rankin Scale. Specifically, those with a score below four, indicating they could walk without help despite some disability, were about 3.5 times more likely to see cognitive improvements than those with more severe impairments[52]. After 12 months of surgery, gait improvements are observed in 60.4% to 78.2% of cases, dementia symptoms improve in 49.3% to 67.3%, and urinary symptoms improve in 60.2%[53] of cases[54]. Postoperative shunt adjustments are often necessary. Among patients who require adjustments, 76% do so due to persistent or reemerging symptoms, while 24% undergo adjustments due to overdrainage[55]. These findings highlight the importance of individualized valve programming and long-term

[50] Popal et al., “Outcomes of Ventriculoperitoneal Shunt in Patients With Idiopathic Normal-Pressure Hydrocephalus 2 Years After Surgery.”
[51] Chidiac et al., “Waiting Time for Surgery Influences the Outcome in Idiopathic Normal Pressure Hydrocephalus - a Population-Based Study.”
[52] Fang et al., “One-Year Outcome of a Lumboperitoneal Shunt in Older Adults with Idiopathic Normal Pressure Hydrocephalus.”
[53] Ishikawa and Mori, “Association of Gait and Cognition after Surgery in Patients with Idiopathic Normal Pressure Hydrocephalus.”
[54] Möhwald et al., “Quantification of Pathological Gait Parameter Thresholds of Idiopathic Normal Pressure Hydrocephalus Patients in Clinical Gait Analysis.”
[55] Junkkari et al., “5-Year Health-Related Quality of Life Outcome in Patients with Idiopathic Normal Pressure Hydrocephalus.”

patient monitoring. While these results show that LPS is a good treatment, it is less effective than VPS and should only be used when VPS is not safe.

Both fixed-pressure and programmable valves significantly improved neurological outcomes ($p < 0.001$), with no notable differences in overall effectiveness ($p = 0.104$). Fixed pressure valves are set at a specific, unchanging pressure, helping to drain fluid from the brain consistently. In contrast, programmable valves can be adjusted to different pressure settings, allowing doctors to customize treatment for individual patients. These valves regulate the amount of CSF drained to prevent complications such as overdrainage, which can lead to subdural hematomas, or underdrainage, which can cause persistent symptoms. Complication rates were significantly higher in the fixed-pressure valve group (52.6% vs. 10.5%, $p = 0.013$). Additionally, the mean annual treatment cost was lower for programmable valves (US$3,108 ± $553) than for fixed-pressure valves (US$3,820 ± $2,231), with a mean cost difference of US$712 (95% CI: 393–1,805)[56]. Neurological improvement was observed in 73.3% of patients with fixed-pressure valves and 88.2% of patients with programmable valves.

Patient selection before shunt placement is pivotal to ensure good outcomes and accurate patient prognosis. A cerebrospinal fluid tap test (CSF-TT), a diagnostic procedure in which a small amount of cerebrospinal fluid (CSF) is removed via lumbar puncture to assess potential improvement in symptoms of idiopathic normal pressure hydrocephalus (iNPH), is used to evaluate the likelihood of success of shunt placement[57]. Significant improvements were observed after CSF-TT; however, this response is temporary, suggesting symptom improvement following the shunt placement. Mean TUG scores decreased significantly after the first, second, and third procedures ($p < 0.001$; $p < 0.001$; $p < 0.02$, respectively). The Performance-Oriented Mobility Assessment (POMA) gait and balance scores improved significantly after the first and second procedures ($p < 0.05$ for each comparison), with balance improvements persisting after the third procedure. Functional Ambulation Balance (FAB) and Nine-Hole Peg Test (NHPT) scores improved significantly after the first procedure ($p = 0.012$) but remained unchanged in subsequent procedures. No significant changes were noted in the MMSE Stroop test scores, or activities of daily living (ADLs)[58].

Assessing gait patterns and spatiotemporal parameters enhances the diagnostic accuracy of the CSF-TT. Significant cadence improvements were observed at 24 hours ($p < 0.01$) and 72 hours ($p < 0.001$), with total time improvements reaching statistical significance at 72 hours ($p < 0.05$)[59]. BBS exhibited the highest sensitivity (85%) among functional assessments, while TUG demonstrated the highest specificity (100%). Linear regression analysis revealed that changes

[56] Reis et al., “Treatment of Idiopathic Normal Pressure Hydrocephalus with a Novel Programmable Valve: Prospective Evaluation of Costs, Efficacy, and Safety.”
[57] Gómez-Amarillo et al., “Cerebrospinal Fluid Closing Pressure-Guided Tap Test for the Diagnosis of Idiopathic Normal Pressure Hydrocephalus: A Descriptive Cross-Sectional Study.”
[58] Isik et al., “The Outcomes Of Serial Cerebrospinal Fluid Removal In Elderly Patients With Idiopathic Normal Pressure Hydrocephalus.”
[59] Ferrari et al., “The Effects of Cerebrospinal Fluid Tap-Test on Idiopathic Normal Pressure Hydrocephalus: An Inertial Sensors Based Assessment.”

in BBS score provided the best predictive model for post-surgical improvements ($R^2 = 0.36$, $p < 0.01$)[60].

Complication rates varied across studies, with minor operation-related complications occurring in 31.8% of patients and severe complications in 7.1%[61]. Subcutaneous CSF collection, the accumulation of CSF beneath the skin, was reported in 17.2% of cases, while epidural catheter displacement was observed in 10.3% of cases. The symptoms worsened in 12% of shunt responders over a mean follow-up period of 25.1 months, though shunt function remained unchanged[62].

VPS remains the gold standard for iNPH treatment, mainly when performed within three months of diagnosis. Programmable valves are associated with lower complication rates and treatment costs than fixed-pressure valves. Functional and gait assessments reinforce the efficacy of surgical intervention and highlight the importance of early diagnosis and treatment. Further research is needed to optimize CSF-TT protocols and predictive models for improved patient outcomes.

Conclusion

iNPH is a neurological disorder characterized by impaired gait, urinary incontinence, and cognitive decline. Symptoms arise due to abnormal accumulation of CSF in the brain's ventricles and predominantly impact elderly patients. Early diagnosis of iNPH is crucial to patient outcomes. VPS and LPS shunt placement are the standard of care treatment for iNPH and have good outcomes in appropriately diagnosed and selected patients. Current diagnosis techniques are often ambiguous, and new methods with high specificity and sensitivity are required.

Figure Legends

Figure 1: Schema illustrating identifying, screening, and including studies in the systematic review. A total of 1,643 records were identified through a search of the PubMed database. After screening those who did not meet the inclusion criteria, 103 were included. The final selection included studies categorized by the number of papers after citations, with subcategories focusing on the number of papers focusing on demographics, diagnosis, and treatment.

Bibliography

[60] Gallagher et al., "Predicting Post-Surgical Outcomes in Idiopathic Normal Pressure Hydrocephalus Using Clinically Important Changes from the Cerebrospinal Fluid Tap Test."
[61] Fang et al., "One-Year Outcome of a Lumboperitoneal Shunt in Older Adults with Idiopathic Normal Pressure Hydrocephalus."
[62] Takeuchi and Kasahara, "Surgical Indications and Operative Results of Lumbosubarachnoid-Lumboepidural Shunting in 29 Patients with Idiopathic Normal Pressure Hydrocephalus under Local Anesthesia."

Acosta, Lealani Mae Y., Kassandra Stubblefield, Trisha Conwell, Kiersten Espaillat, Heather Koons, Peter Konrad, John Fang, Howard Kirshner, and Thomas Davis. “Protocolizing the Workup for Idiopathic Normal Pressure Hydrocephalus Improves Outcomes.” *Neurology. Clinical Practice* 11, no. 4 (August 2021): e447–53. https://doi.org/10.1212/CPJ.0000000000001018.

Chadani, Yoshihiro, Tetsuo Kashibayashi, Takahiro Yamamoto, Atsushi Tsuda, Ryoko Fujito, Masanori Akamatsu, Naoto Kamimura, et al. “Association of Right Precuneus Compression with Apathy in Idiopathic Normal Pressure Hydrocephalus: A Pilot Study.” *Scientific Reports* 12, no. 1 (November 28, 2022): 20428. https://doi.org/10.1038/s41598-022-23800-x.

Chang, Tze-Wei, Pao-Hui Tseng, Yi-Cheng Wang, Guo-Fang Tseng, Tsung-Lang Chiu, Shinn-Zong Lin, and Sheng-Tzung Tsai. “Dopaminergic Degeneration and Small Vessel Disease in Patients with Normal Pressure Hydrocephalus Who Underwent Shunt Surgery.” *Journal of Clinical Medicine* 9, no. 4 (April 11, 2020). https://doi.org/10.3390/jcm9041084.

Chidiac, Christine, N. Sundström, M. Tullberg, L. Arvidsson, and M. Olivecrona. “Waiting Time for Surgery Influences the Outcome in Idiopathic Normal Pressure Hydrocephalus - a Population-Based Study.” *Acta Neurochirurgica* 164, no. 2 (February 2022): 469–78. https://doi.org/10.1007/s00701-021-05085-7.

Constantinescu, Clara, Carsten Wikkelsø, Eric Westman, Doerthe Ziegelitz, Daniel Jaraj, Lina Rydén, Ingmar Skoog, and Mats Tullberg. “Prevalence of Possible Idiopathic Normal Pressure Hydrocephalus in Sweden: A Population-Based MRI Study in 791 70-Year-Old Participants.” *Neurology* 102, no. 2 (January 23, 2024): e208037. https://doi.org/10.1212/WNL.0000000000208037.

Fang, Xuhao, Yao Deng, Xinxin Xu, Weiquan Shu, Feng Tang, Shihong Li, Ting Zhu, Li Zhang, Ping Zhong, and Renling Mao. “One-Year Outcome of a Lumboperitoneal Shunt in Older Adults with Idiopathic Normal Pressure Hydrocephalus.” *Frontiers in Surgery* 9 (2022): 977123. https://doi.org/10.3389/fsurg.2022.977123.

Ferrari, Alberto, David Milletti, Giulia Giannini, Sabina Cevoli, Federico Oppi, Giorgio Palandri, Luca Albini-Riccioli, et al. “The Effects of Cerebrospinal Fluid Tap-Test on Idiopathic Normal Pressure Hydrocephalus: An Inertial Sensors Based Assessment.” *Journal of Neuroengineering and Rehabilitation* 17, no. 1 (January 16, 2020): 7. https://doi.org/10.1186/s12984-019-0638-1.

Gallagher, Ryan M., Jodie L. Marquez, Shabnam Dal, and Peter G. Osmotherly. “Predicting Post-Surgical Outcomes in Idiopathic Normal Pressure Hydrocephalus Using Clinically Important Changes from the Cerebrospinal Fluid Tap Test.” *Journal of the Neurological Sciences* 460 (May 15, 2024): 122994. https://doi.org/10.1016/j.jns.2024.122994.

Gómez-Amarillo, Diego Fernando, Luis Fernando Pulido, Isabella Mejía, Catalina García-Baena, María Fernanda Cárdenas, Lina María Gómez, Yuli Viviana Fuentes, et al. “Cerebrospinal Fluid Closing Pressure-Guided Tap Test for the Diagnosis of Idiopathic Normal Pressure Hydrocephalus: A Descriptive Cross-Sectional Study.” *Surgical Neurology International* 11 (2020): 315. https://doi.org/10.25259/SNI_380_2020.

Guilhem de Lataillade, Adrien de, Claire Boutoleau-Bretonnière, Jesus Aguilar-Garcia, Amandine Pallardy, Edith Bigot-Corbel, Vincent Roualdes, Julie Leroy, Philippe Damier, and Hélène Pouclet-Courtemanche. “Idiopathic Normal Pressure Hydrocephalus and Frontotemporal Dementia: An Unexpected Association.” *Brain Communications* 4, no. 6 (2022): fcac319. https://doi.org/10.1093/braincomms/fcac319.

Hallqvist, Caroline, Helena Grönstedt, and Lisa Arvidsson. “Gait, Falls, Cognitive Function, and Health-Related Quality of Life after Shunt-Treated Idiopathic Normal Pressure Hydrocephalus-a Single-Center Study.” *Acta Neurochirurgica* 164, no. 9 (September 2022): 2367–73. https://doi.org/10.1007/s00701-022-05309-4.

He, Mengmeng, Zhenyu Qi, Yunxiang Shao, Hui Yao, Xuewen Zhang, Yang Zhang, Yu Shi, et al. “Quantitative Evaluation of Gait Changes Using APDM Inertial Sensors After the External Lumbar Drain in Patients With Idiopathic Normal Pressure Hydrocephalus.” *Frontiers in Neurology* 12

(2021): 635044. https://doi.org/10.3389/fneur.2021.635044.
Hnin, Htet Htet, Sunee Bovonsunthonchai, Theerapol Witthiwej, Roongtiwa Vachalathiti, and Rattapha Ariyaudomkit. “Feasibility of Action Observation Effect on Gait and Mobility in Idiopathic Normal Pressure Hydrocephalus Patients.” *Dementia & Neuropsychologia* 15, no. 1 (March 2021): 79–87. https://doi.org/10.1590/1980-57642021dn15-010008.
Ishikawa, Masatsune, and Etsuro Mori. “Association of Gait and Cognition after Surgery in Patients with Idiopathic Normal Pressure Hydrocephalus.” *Scientific Reports* 13, no. 1 (October 27, 2023): 18460. https://doi.org/10.1038/s41598-023-45629-8.
Ishikawa, Masatsune, Shigeki Yamada, and Kazuo Yamamoto. “Agreement Study on Gait Assessment Using a Video-Assisted Rating Method in Patients with Idiopathic Normal-Pressure Hydrocephalus.” *PloS One* 14, no. 10 (2019): e0224202. https://doi.org/10.1371/journal.pone.0224202.
Isik, Ahmet Turan, Derya Kaya, Esra Ates Bulut, Ozge Dokuzlar, and Pinar Soysal. “The Outcomes Of Serial Cerebrospinal Fluid Removal In Elderly Patients With Idiopathic Normal Pressure Hydrocephalus.” *Clinical Interventions in Aging* 14 (2019): 2063–69. https://doi.org/10.2147/CIA.S228257.
Jóhannsdóttir, Anika Maí, Christian Bonde Pedersen, Sune Munthe, Frantz Rom Poulsen, and Bjarni Jóhannsson. “Idiopathic Normal Pressure Hydrocephalus: Validation of the DESH Score as a Prognostic Tool for Shunt Surgery Response.” *Clinical Neurology and Neurosurgery* 241 (June 2024): 108295. https://doi.org/10.1016/j.clineuro.2024.108295.
Junkkari, A., H. Sintonen, N. Danner, H. K. Jyrkkänen, T. Rauramaa, A. J. Luikku, A. M. Koivisto, et al. “5-Year Health-Related Quality of Life Outcome in Patients with Idiopathic Normal Pressure Hydrocephalus.” *Journal of Neurology* 268, no. 9 (September 2021): 3283–93. https://doi.org/10.1007/s00415-021-10477-x.
Kawahara, Takashi, Kazunori Arita, Shingo Fujio, Nayuta Higa, Hiroki Hata, F. M. Moinuddin, and Ryosuke Hanaya. “Patients of Idiopathic Normal-Pressure Hydrocephalus Have Small Dural Sac in Cervical and Upper Thoracic Levels: A Supposed Causal Association.” *Surgical Neurology International* 14 (2023): 391. https://doi.org/10.25259/SNI_474_2023.
Kawahara, Takashi, Masamichi Atsuchi, Kazunori Arita, Shingo Fujio, Nayuta Higa, F. M. Moinuddin, Koji Yoshimoto, and Ryosuke Hanaya. “Dural Sac Shrinkage Signs on Spinal Magnetic Resonance Imaging Indicate Overdrainage after Lumboperitoneal Shunt for Idiopathic Normal Pressure Hydrocephalus.” *Surgical Neurology International* 13 (2022): 269. https://doi.org/10.25259/SNI_291_2022.
Kihlstedt, Carl-Johan, Jan Malm, Alfonso Fasano, and David Bäckström. “Freezing of Gait in Idiopathic Normal Pressure Hydrocephalus.” *Fluids and Barriers of the CNS* 21, no. 1 (March 8, 2024): 22. https://doi.org/10.1186/s12987-024-00522-y.
Kockum, Karin, Johan Virhammar, Katrine Riklund, Lars Söderström, Elna-Marie Larsson, and Katarina Laurell. “Diagnostic Accuracy of the iNPH Radscale in Idiopathic Normal Pressure Hydrocephalus.” *PloS One* 15, no. 4 (2020): e0232275. https://doi.org/10.1371/journal.pone.0232275.
Laticevschi, Tiberiu, Alma Lingenberg, Stéphane Armand, Alessandra Griffa, Frédéric Assal, and Gilles Allali. “Can the Radiological Scale ‘iNPH Radscale’ Predict Tap Test Response in Idiopathic Normal Pressure Hydrocephalus?” *Journal of the Neurological Sciences* 420 (January 15, 2021): 117239. https://doi.org/10.1016/j.jns.2020.117239.
Lilja-Lund, Otto, Lars Nyberg, Martin Maripuu, and Katarina Laurell. “Dual-Task Performance in Older Adults With and Without Idiopathic Normal Pressure Hydrocephalus.” *Frontiers in Aging Neuroscience* 14 (2022): 904194. https://doi.org/10.3389/fnagi.2022.904194.
Mazzeo, Salvatore, Filippo Emiliani, Silvia Bagnoli, Sonia Padiglioni, Lorenzo Maria Del Re, Giulia Giacomucci, Juri Balestrini, et al. “Alzheimer’s Disease CSF Biomarker Profiles in Idiopathic Normal Pressure Hydrocephalus.” *Journal of Personalized Medicine* 12, no. 6 (June 6, 2022).

https://doi.org/10.3390/jpm12060935.
Möhwald, Ken, Max Wuehr, Julian Decker, Eric-Manuel Asch, Fabian Schenkel, Ben Illigens, and Roman Schniepp. “Quantification of Pathological Gait Parameter Thresholds of Idiopathic Normal Pressure Hydrocephalus Patients in Clinical Gait Analysis.” *Scientific Reports* 12, no. 1 (October 31, 2022): 18295. https://doi.org/10.1038/s41598-022-22692-1.
Morel, Eric, Alma Lingenberg, Stéphane Armand, Frédéric Assal, and Gilles Allali. “Normal Pressure Hydrocephalus and Cognitive Impairment: The Gait Phenotype Matters Too.” *European Journal of Neurology* 31, no. 8 (August 2024): e16328. https://doi.org/10.1111/ene.16328.
Mori, Laura, Federica Collino, Annalisa Marzi, Lucia Pellegrino, Marta Ponzano, Davide Del Chiaro, Sara Maestrini, et al. “Useful Outcome Measures in INPH Patients Evaluation.” *Frontiers in Neurology* 14 (2023): 1201932. https://doi.org/10.3389/fneur.2023.1201932.
Mostile, Giovanni, Federico Contrafatto, Roberta Terranova, Claudio Terravecchia, Antonina Luca, Martina Sinitò, Giulia Donzuso, et al. “Turning and Sitting in Early Parkinsonism: Differences Between Idiopathic Normal Pressure Hydrocephalus Associated with Parkinsonism and Parkinson’s Disease.” *Movement Disorders Clinical Practice* 10, no. 3 (March 2023): 466–71. https://doi.org/10.1002/mdc3.13638.
“Normal Pressure Hydrocephalus - an Overview | ScienceDirect Topics.” Accessed November 24, 2024. https://www.sciencedirect.com/topics/neuroscience/normal-pressure-hydrocephalus.
Oike, Ryo, Yasuaki Inoue, Kazuhito Matsuzawa, and Takatoshi Sorimachi. “Screening for Idiopathic Normal Pressure Hydrocephalus in the Elderly after Falls.” *Clinical Neurology and Neurosurgery* 205 (April 24, 2021): 106635. https://doi.org/10.1016/j.clineuro.2021.106635.
Popal, Abdul Malik, Zhoule Zhu, Xinxia Guo, Zhe Zheng, Chengwei Cai, Hongjie Jiang, Jianmin Zhang, Anwen Shao, and Junming Zhu. “Outcomes of Ventriculoperitoneal Shunt in Patients With Idiopathic Normal-Pressure Hydrocephalus 2 Years After Surgery.” *Frontiers in Surgery* 8 (2021): 641561. https://doi.org/10.3389/fsurg.2021.641561.
Pyrgelis, Efstratios-Stylianos, George P. Paraskevas, Vasilios C. Constantinides, Fotini Boufidou, Georgios Velonakis, Leonidas Stefanis, and Elisabeth Kapaki. “Callosal Angle Sub-Score of the Radscale in Patients with Idiopathic Normal Pressure Hydrocephalus Is Associated with Positive Tap Test Response.” *Journal of Clinical Medicine* 11, no. 10 (May 20, 2022). https://doi.org/10.3390/jcm11102898.
Razay, George, Melissa Wimmer, and Iain Robertson. “Incidence, Diagnostic Criteria and Outcome Following Ventriculoperitoneal Shunting of Idiopathic Normal Pressure Hydrocephalus in a Memory Clinic Population: A Prospective Observational Cross-Sectional and Cohort Study.” *BMJ Open* 9, no. 12 (December 3, 2019): e028103. https://doi.org/10.1136/bmjopen-2018-028103.
Reis, Rodolfo Casimiro, Renata Harumi Gobbato Yamashita, Davi Jorge Fontoura Solla, Laís Fajardo Ramin, Manoel Jacobsen Teixeira, and Fernando Campos Gomes Pinto. “Treatment of Idiopathic Normal Pressure Hydrocephalus with a Novel Programmable Valve: Prospective Evaluation of Costs, Efficacy, and Safety.” *Asian Journal of Neurosurgery* 18, no. 3 (September 2023): 548–56. https://doi.org/10.1055/s-0043-1771370.
Rocha, Samanta Fabrício Blattes da, Pedro André Kowacs, Ricardo Krause Martinez de Souza, Matheus Kahakura Franco Pedro, Ricardo Ramina, and Hélio A. Ghizoni Teive. “Serial Tap Test of Patients with Idiopathic Normal Pressure Hydrocephalus: Impact on Cognitive Function and Its Meaning.” *Fluids and Barriers of the CNS* 18, no. 1 (May 6, 2021): 22. https://doi.org/10.1186/s12987-021-00254-3.
Rohatgi, Saurabh, Amol Dua, Arman Avesta, Rehab Naeem Khalid, Andrea Diociasi, Karen Buch, Jeremy N. Ford, and Rajiv Gupta. “Predicting Gait Speed Improvement in Idiopathic Normal Pressure Hydrocephalus Patients: The Role of Evans Index and Ventricular Volume.” *Cureus* 16, no. 6 (June 2024): e61799. https://doi.org/10.7759/cureus.61799.
Shimizu, Yoko, Motoki Tanikawa, Mitsuya Horiba, Kento Sahashi, Shoji Kawashima, Akihiko Kandori, Tomoyasu Yamanaka, et al. “Clinical Utility of Paced Finger Tapping Assessment in Idiopathic

Normal Pressure Hydrocephalus." *Frontiers in Human Neuroscience* 17 (2023): 1109670. https://doi.org/10.3389/fnhum.2023.1109670.

Sinha, Mallika, Jitin Bajaj, Ambuj Kumar, Ketan Hedaoo, Sandeep Sharma, Kamesh Konchada, Shailendra Ratre, Vijay S. Parihar, Narayan M. Swamy, and Yad R. Yadav. "Lumboperitoneal Shunts - Patient Selection, Technique, and Complication Avoidance: An Experience of 426 Cases." *Neurology India* 69, no. Supplement (December 2021): S481–87. https://doi.org/10.4103/0028-3886.332265.

Sotoudeh, Houman, Zahra Sadaatpour, Ali Rezaei, Omid Shafaat, Ehsan Sotoudeh, Mohsen Tabatabaie, Aparna Singhal, and Manoj Tanwar. "The Role of Machine Learning and Radiomics for Treatment Response Prediction in Idiopathic Normal Pressure Hydrocephalus." *Cureus* 13, no. 10 (October 2021): e18497. https://doi.org/10.7759/cureus.18497.

Sundström, Nina, Johanna Rydja, Johan Virhammar, Lena Kollén, Fredrik Lundin, and Mats Tullberg. "The Timed up and Go Test in Idiopathic Normal Pressure Hydrocephalus: A Nationwide Study of 1300 Patients." *Fluids and Barriers of the CNS* 19, no. 1 (January 10, 2022): 4. https://doi.org/10.1186/s12987-021-00298-5.

Takeuchi, Totaro, and Eishi Kasahara. "Surgical Indications and Operative Results of Lumbosubarachnoid-Lumboepidural Shunting in 29 Patients with Idiopathic Normal Pressure Hydrocephalus under Local Anesthesia." *Neurologia Medico-Chirurgica* 59, no. 12 (December 15, 2019): 498–503. https://doi.org/10.2176/nmc.oa.2019-0151.

Takeuchi, Totaro, and Kozo Yajima. "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." *Neurologia Medico-Chirurgica* 59, no. 7 (July 15, 2019): 281–86. https://doi.org/10.2176/nmc.oa.2018-0318.

Tominaga, Hiroyuki, Hiroto Tokumoto, Shingo Maeda, Ichiro Kawamura, Masato Sanada, Kazumasa Kawazoe, Eiji Taketomi, and Noboru Taniguchi. "High Prevalence of Lumbar Spinal Stenosis in Cases of Idiopathic Normal-Pressure Hydrocephalus Affects Improvements in Gait Disturbance after Shunt Operation." *World Neurosurgery: X* 20 (October 2023): 100236. https://doi.org/10.1016/j.wnsx.2023.100236.

Wu, Dan, Abhay Moghekar, Wen Shi, Ari M. Blitz, and Susumu Mori. "Systematic Volumetric Analysis Predicts Response to CSF Drainage and Outcome to Shunt Surgery in Idiopathic Normal Pressure Hydrocephalus." *European Radiology* 31, no. 7 (July 2021): 4972–80. https://doi.org/10.1007/s00330-020-07531-z.

Yamada, Shigeki, Yukihiko Aoyagi, Masatsune Ishikawa, Makoto Yamaguchi, Kazuo Yamamoto, and Kazuhiko Nozaki. "Gait Assessment Using Three-Dimensional Acceleration of the Trunk in Idiopathic Normal Pressure Hydrocephalus." *Frontiers in Aging Neuroscience* 13 (2021): 653964. https://doi.org/10.3389/fnagi.2021.653964.

Yang, Yifeng, Meijing Yan, Xiao Liu, Shihong Li, and Guangwu Lin. "Improve the Diagnosis of Idiopathic Normal Pressure Hydrocephalus by Combining Abnormal Cortical Thickness and Ventricular Morphometry." *Frontiers in Aging Neuroscience* 16 (2024): 1338755. https://doi.org/10.3389/fnagi.2024.1338755.