Evaluating the Cerebrospinal Fluid Tap Test With the Hellström iNPH Scale for Patients With Idiopathic Normal Pressure Hydrocephalus – a Retrospective Cohort Study of 132 Patients

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Evaluating the cerebrospinal fluid tap test with the Hellström iNPH scale for patients with idiopathic normal pressure hydrocephalus – a retrospective cohort study of 132 patients

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Abstract

Background

The cerebrospinal fluid tap test (CSF TT) is used for selecting shunt surgery candidates in idiopathic normal pressure hydrocephalus (iNPH). Variations in performance, and different outcome measures and cut-off levels in previous research on the CSF TT make comparison of accuracy difficult between studies. We aimed to evaluate the CSF TT, by using the Hellström iNPH scale for shunted iNPH patients with a standardized method.

Methods

One hundred thirty-two shunt operated iNPH patients were retrospectively included in this study. The gait and balance domains in the iNPH scale were used as outcome measures for the CSF TT and the total iNPH scale score as postoperatively outcome. To identify responders a cut-off level ≥ 5 points was used. Differences between responders and non-responders to the CSF TT, as well as the sensitivity, specificity, positive and negative predictive values, accuracy and correlations between outcomes of the CSF TT and postoperatively were calculated.

Results

In the gait domain, there were 62.9% responders and correspondingly 42.7 % in the balance domain of the CSF TT. CSF TT responders had significantly better outcomes in both the gait and balance domains but not in the neuropsychology or continence domains postoperatively. The sensitivity and specificity of the CSF TT and the outcome of the total iNPH scale score postoperatively were 67.6% and 53.3% for gait and 47.5% and 73.3% for balance. For age ≥ 80 years, the sensitivity and specificity for gait were 52.2% and 60.0%, and for age ≤ 80 years

72.2% and 50.0%. Gait as an outcome measure for both the CSF TT and postoperatively had the highest sensitivity, (73.2%) and specificity (65.7%) for all ages.

Conclusions

The CSF TT, with Hellström's iNPH scale as the outcome measure, has clear limitations in predicting postoperative results. The gait domain may be used to detect changes of outcomes in gait, but the balance domain is too insensitive to use as an assessment for the CSF TT. The value of the CFS TT for patients over 80 years of age appears to be even lower. Differential diagnostic considerations together with radiological assessments remain cornerstones in selecting eligible shunt responders.

Keywords

Idiopathic normal pressure hydrocephalus, CSF TT, outcome, accuracy

Introduction

Idiopathic normal pressure hydrocephalus (iNPH) is a condition that usually has slowly progressive symptoms. In combination with a dilated cerebral ventricular system, the main symptoms are gait disturbance and poor balance, together with cognitive decline and urinary incontinence. The disease is caused by altered cerebrospinal fluid (CSF) dynamics, but the underlying pathophysiology is not fully understood (1). In a recent population-based study, the prevalence of iNPH among individuals 65 years and older, was 3.7%, and it increased with advancing age (2). The mean age at diagnosis is approximately 70 years (3). A shunt insertion, where CSF is drained from the ventricles, is effective and the result can be

71 compared with the effect of levodopa medication in Parkinson's disease (4). Approximately
72 three-quarter of the patients improve after surgery, and the most pronounced effect is on gait
73 performance (5,6).

74
75 There should be a focus on optimizing the postoperative shunt outcome. In order to achieve
76 this, a correct diagnosis is fundamental. However, diagnosing iNPH is challenging since the
77 symptoms mimic other neurodegenerative conditions and can also occur in combination with
78 other diseases (7). Therefore, there must be a clear distinction between a diagnosis of iNPH
79 and a positive response to a shunt operation. In recent years, new radiological methods have
80 been introduced for more accurate iNPH diagnosis, such as the disproportionately enlarged
81 subarachnoid space hydrocephalus (DESH) (8,9) and the Radscale (10), but the prediction of
82 shunt outcome in relation to these radiological parameters has not been clarified. CSF-
83 dynamic tests with various techniques can be used to evaluate patients with possible iNPH
84 (11). With the lumbar infusion test, the CSF outflow resistance and conductance are measured
85 (12). An elevated resistance has been suggested as a predictor of a positive outcome of shunt
86 surgery (13), but this test has been reported to have low sensitivity (12,14,15). External
87 lumbar drainage of CSF (ELD) for one to several days has a high positive predictive value but
88 requires hospital admission and has an inherent risk for complications (16–18). Less invasive
89 and commonly used is the cerebrospinal tap test (CSF TT), which involves a lumbar puncture
90 (LP) with removal of 30-50 ml CSF and clinical evaluation before and after the LP (19–22).
91 The CSF TT has mostly been associated with a high positive predictive value (PPV) and a
92 low negative predictive value (NPV), meaning that potential shunt responders would be
93 missed if the indication for surgery is based on a negative CSF TT (22,23). The current
94 international guidelines state that the CSF TT can be a tool with prognostic value (1,24,25).
95 However, the relevance of the CSF TT has though been questioned due to the low sensitivity

(22,23,26). There is no clear definition of what constitutes a positive CSF TT but an objective improvement in gait has been proposed as the most reliable outcome (27,28). The role attributed to the CSF TT in iNPH varies among clinicians, from being considered very valuable to being a test of limited significance. Standardized evaluation methods of the CSF TT would increase the validity and make comparison between different studies easier (29). In our center, we use the Hellström iNPH scale (30) to evaluate outcome in the four domains gait, balance, neuropsychology and continence, after surgery. The gait and balance domains are evaluated before and after the CFS TT. The Hellström iNPH scale is a standardized method that has rarely been used as an outcome measure in the evaluation of the CSF TT (23,31).

Methods

Aim and design

The aim of this study was to evaluate the CSF TT, using the Hellström iNPH scale (30) among shunted iNPH patients, in a large single center cohort. This is a retrospective study from Linköping University Hospital, Sweden. The participants were consecutively included between January 2016 and December 2019 and data was recorded from the patient's charts. The study was approved by the Swedish Ethical Review Authority, 2019-02260.

Participants

Patients with a possible iNPH diagnosis based on the American European guidelines of 2005 (1) and treated with shunt insertion of an adjustable valve, were included. Neuroimaging features for diagnosis were; enlarged ventricles on CT or MR with Evans index > 30 , no signs of obstruction to CSF flow and at least one of four supporting features (1). Patients were excluded if there was a lack of data from a CSF TT or the postoperative assessment. Of 173

120 iNPH patients, 132 were included in the statistical analysis. Of the 41 excluded patients, 22
121 did not undergo the CSF TT, five had been investigated with ELD and 15 patients had no
122 result from the follow-up assessment postoperatively. Of the 15 patients with no follow-up
123 data, eight had shunt complications, five had missing data due to unwillingness to participate
124 and two died. One of the deaths was caused by an acute subdural hematoma two months after
125 shunt surgery and the other by an intracerebral hematoma five days after surgery. A
126 flowchart of inclusion and exclusion is presented in figure 1 and the characteristics of the
127 included and non-included participants are shown in table 1.

Figure 1 Flow chart of inclusion and exclusion for 132 iNPH patients with results from CSF TT and follow-up evaluation

Clinical assessments

A specialized team including neurologists, neurosurgeons, neuro-radiologists, physiotherapists and occupational therapists assessed the patients preoperatively. The occupational therapist and physiotherapist assessments, accomplished within one week before the CSF TT, included all the measurements for gait, balance, neuropsychology and continence in the Hellström iNPH scale (30). All investigations were performed either in the outpatient or inpatient clinic. A neurologist performed the LP, with the patient in a recumbent position. To measure the intracranial pressure (ICP), a spinal fluid manometer was used and the pressure was measured for 30 seconds before removal of CSF. The exact amount of removed CSF was noted. Approximately three hours after the LP, a physiotherapist reassessed the patients, using the measurements within the gait and balance domains in the iNPH scale (30). In addition to the standardized assessments, the gait pattern was video-recorded. Neuropsychology and continence domains were not evaluated in the CSF TT. The patients were offered shunt surgery based on a consensus decision, considering all available clinical, radiological and laboratory data. CSF TT was used as an adjunctive test but a negative CSF TT did not exclude any patient. The scheduled time for follow-up was three months. At this time, the physiotherapist and occupational therapist used the same instruments as preoperatively, including all domains in the iNPH scale (30). We carefully checked that all necessary shunt valve adjustments or shunt revisions had been accomplished before the follow-up.

Outcome measures

The Hellström iNPH scale (30) is constructed to cover the symptoms of gait, balance, continence and neuropsychology using ordinal ratings and continuous measures. The gait domain score is calculated from a combination of an eight-grade ordinal gait scale, grading

the gait severity (figure 2) and the number of steps and time in seconds needed to walk 10 meters. Balance is measured with a seven-grade ordinal scale (figure 2) and continence with a six-grade ordinal scale. The neuropsychology domain uses four continuous measures. A limit of ≥ 5 points for the total iNPH scale is proposed as an improvement after surgery (30).

Gait scale	Balance scale
1 Normal	1 Able to stand independently for more than 30 s on either lower extremity alone
2 Slight disturbance of tandem walk and turning	2 Able to stand independently for <30 s on either lower extremity alone
3 Wide-based gait with sway, without foot corrections	3 Able to stand independently with the feet together (at the heels) for more than 30 s
4 Tendency to fall, with foot corrections	4 Able to stand independently with the feet together for < 30 s
5 Walking with cane	5 Able to stand independently with the feet apart (one foot length) for more than 30 s
6 Bi-manual support needed	6 Able to stand independently with the feet apart for < 30 s
7 Aided	7 Unable to stand without assistance
8 Wheelchair bound	

Figure 2 The ordinal grading steps for gait and balance in the Hellström iNPH scale (30).

The results in each domain are converted to a 0-100 score, where 100 represents the performance of an age-matched healthy population. In the total score, the gait domain is double weighted. If any domain has missing data, the total score is calculated with the available data (30), (figure 3).

$$\frac{2 \times \text{Gait} \pm \text{Neuropsychology} \pm \text{Balance} \pm \text{Continence}}{5 \text{ or number of available domain scores}} = 0-100$$

Figure 3 Calculation of the total iNPH scale score (30).

Statistical analysis

Normal distribution was tested with the Kolmogorov-Smirnov test. Normal distributed variables were presented with mean and Standard Deviations (SD), otherwise with median and interquartile range (IQR) or absolute and relative frequencies. A Mann-Whitney U test or Chi² test were used for comparisons between groups of included and non-included patients

and for comparison between responders and non-responders in the CSF TT. An improvement of ≥ 5 points for the gait and balance domain on the iNPH scale was considered to indicate a positive responder in the CSF TT. Sensitivity, specificity, positive and negative predictive values and accuracy were calculated. The Spearman rank-order test was used to calculate correlation between variables. The level of significance was set to ≤ 0.05 . Statistical analysis was carried out using IBM SPSS Statistics version 25.0, (IBM Corp. Armonk, NY).

Results

One hundred and thirty-two individuals, 70 male and 62 female with a mean age of 75.1 ± 6.2 years were included in the analysis. Among the 132 individuals, 83 (62.9%) were responders with a positive outcome (≥ 5 points) in the CSF TT in the gait domain on the iNPH scale. For the balance domain, 56 of 131 individuals, (42.7%), were responders in the CSF TT. Postoperatively, 102 individuals (77.3%) improved ≥ 5 points on the total iNPH scale, with a median improvement of 12 points (IQR: 5.3-18.0). Twenty-four patients (18.2%) had at least one shunt valve readjustment, 12 patients (9.1%) had a shunt revision and the median time to follow-up was 104.5 days (IQR: 45.5-142.8). Demographic variables and information about the opening ICP and drained volume of CSF in the CSF TT are presented in table 1.

Table 1 Characteristics of patients with iNPH diagnosis, included and excluded from data analysis

	Patients included (n=132)	Patients excluded (n=41)	P-value
Age, years	75.0 (72.0-79.8)	75.0 (70.0-78.5)	0.27 ^a
Sex, male/female (male %)	70/62(53.0%)	28/13(68.3%)	0.09 ^b
Hypertension, n (%)	79(59.8%)	20(48.8%)	0.21 ^b
Diabetes, n (%)	37(28.0%)	12(29.3%)	0.90 ^b
Ischemic heart disease, n (%)	29(22.0%)	8(19.5%)	0.74 ^b
Stroke, n (%)	14(10.6%)	4(9.8%)	0.88 ^b
MMSE-SR, n (0-30)	26.0(22.0-28.0) n=131	27.0 (23.0-28.0) n=34	0.36 ^a

Total iNPH scale score preoperatively, n	51.0(42.0-63.0)	56.0(40.5-66.0) n=37	0.57 ^a
Volume of CSF drained at CSF TT (ml)	48.0(44.5-50.0) n=117	47.0(41.8-50.0) n=20	0.37 ^a
Opening ICP at CSF TT (cmH ₂ O)	15.0(12.5-18.0) n=125	18.5(14.8-22.1) n=22	0.02^b
Positive responder CSF TT Gait ^c , n/total (%)	84/132(63.6%)	15/23(65.2%) n=23	0.24 ^b
Positive responder CSF TT Balance ^d n/total (%)	55/131(42.0%) n=131	7/24(29.2%) n=24	0.24 ^b
Duration baseline to surgery, days	125.5(102.0-157.0)	133.5(101.8-171.8) n=34	0.26 ^a
Duration surgery to follow-up, days	107.5(90.0-131.0)	106.0(92.5-158.5) n=25	0.61 ^a
Shunt readjustment before follow-up, n (%)	24/132(18.2%)	11/41(26.8%)	0.23 ^b
Shunt revision before follow-up, n (%)	12/132(9.1%)	13/41(30.8%)	0.01^b

a= Independent samples Mann-Whitney U test, b=Chi², c= Positive responder CSF TT Gait = ≥5 scores in the gait domain on the iNPH scale, d= Positive responder post CSF TT balance = ≥5 scores in the balance domain on the iNPH scale. Values are presented with median and interquartile range (IQR) or as proportions (%). Bold values are statistically significant. P≤0.05.

The CSF TT responders in the gait domain had significant larger improvements postoperatively. On the total iNPH scale, responders changed 14.0 (IQR: 7.0-21.0) points versus non-responders 9.0 (IQR:0-16.0) points compared to evaluation before surgery, P=0.008. In the gait domain postoperatively, CSF TT responders improved 25.0 (IQR: 11.0-35.0) points versus non-responders 6.0 (IQR:-4.0-19.5) points, P=0.001. The CSF TT responders in the balance domain showed significantly larger improvements on the total iNPH scale postoperatively, 15.5 (IQR: 7.3-22.8) points versus 9.0 (IQR: 2.0-16.0) points, P=0.003. Balance responders improved in the gait domain postoperatively, 20.0 (IQR: 7.5-35.8) points versus 16.0 (IQR: 3.0-26.0) points, P=0.046. CSF TT balance responders also showed significantly larger improvements in the balance domain postoperatively, 16.0 (IQR: 0-34.0) points versus 0 (IQR:0-0) points, P=0.001. No significant between group differences among CSF TT responders (gait or balance) compared to CSF TT non-responders were seen postoperatively in the neuropsychology or continence domains (table 2).

Table 2 Pre- and postoperative differences in iNPH scale scores for CSF TT responders and non-responders

	Responder CSF TT Gait (n=83) median, IQR	Non-responder CSF TT Gait (n=49) median, IQR	P- value	Responder CSF TT Balance (n=56) median, IQR	Non-responder CSF TT Balance (n=75) median, IQR	P - value
Δ iNPH scale Gait domain, scores	25.0(11.0-35.0)	6.0(-4.0-19.5)	0.01 ^a	20.0(7.5-35.8)	16.0(3.0-26.0)	0.05 ^a
Δ iNPH scale Balance domain, scores	0(0-17.0)	0(0-25.0)	0.92	16.5(0-34.0)	0(0-0)	0.01 ^a
Δ iNPH scale Neuropsychology domain, scores	5.0(-2.8-12.0) n=79	3.0(-5.0-10.0) n=43	0.31	5.0(-2.8-10.0) n=48	5.0(-5.0-12.0) n=70	0.89
Δ iNPH scale Continence domain, scores	0(0-20.0) n=78	0(0-30.0) n=45	0.32	0(0-20.0) n=50	0(0-20.0) n=72	0.65
Δ iNPH scale Total, scores	14.0(7.0-20.0)	9.0(0-16.0)	0.01 ^a	15.5(7.8-22.8)	9.0(2.0-16.0)	0.01 ^a

Independent samples Mann-Whitney U test. a=P≤0.05. Δ=differences between values pre- and postoperatively. Responder CSF TT Gait=improvement ≥ 5 points in the gait domain on the iNPH scale. Responder CSF TT balance=improvement ≥ 5 points in the balance domain on the iNPH scale.

The sensitivity using the gait domain as outcome in the CSF TT and the total iNPH scale as outcome postoperatively was 67.6% and the PPV 83.1%. The specificity was 53.3% and the NPV was 32.7% with an accuracy of 64.4%. For patients < 80 years, the sensitivity was 72.2% and for patients ≥ 80 years it was 52.2%. The PPV was 85.1% in the younger group and 75.0% among the elderly. The distributions of specificity in the same age groups were 50.0% versus 60.0% and the NPV was 31.3% versus 35.5%. The accuracy of the CSF TT for patients < 80 years was 67.7% and for patients ≥ 80 years old, 54.5%.

The balance domain as an outcome in the CSF TT had a lower sensitivity, 47.5% and a PPV of 85.7%. The specificity was 73.3% and the NPV was 29.3%. The most sensitive output was when using the gait domain as an outcome in the CSF TT and the same outcome postoperatively: sensitivity 73.2%, PPV 85.5%, specificity 65.7% and NPV 46.9% for all ages (table 3).

Table 3 Sensitivity, specificity, PPV, NPP and accuracy of the CSF Tap test with the outcomes Total iNPH Scale and Gait domain postoperatively

	Gait domain CSF TT/ Total iNPH scale postoperatively ^a N=132	Balance domain CSF TT/ Total iNPH scale postoperatively ^a N=131	Gait domain CSF TT/ Gait domain postoperatively ^b
Sensitivity	67.6	47.5	73.2
Specificity	53.3	73.3	65.7
Positive predictive value	83.1	85.7	85.5
Negative predictive value	32.7	29.3	46.9
Accuracy	64.4	53.4	71.2

Sensitivity, specificity, positive predictive value, negative predictive value and accuracy for CSF TT with cut off ≥ 5 points in the gait and balance domains on the iNPH scale. a= a positive outcome after surgery is ≥ 5 points on the total iNPH scale. b= a positive outcome after surgery is ≥ 5 points in the gait domain.

The change in the gait domain score at the CFS TT correlated significantly with change in outcome postoperatively in the total iNPH score, $r=0.32$, $p=0.01$ as well as with the change in the gait domain score separately, $r=0.51$, $p=0.01$. When using the gait domain score as an outcome in the CSF TT and the total iNPH scale score postoperatively, 69 of 132 (52%) individuals were true positive, 14 (11%) were false positive, 33 (25%) were false negative and 16 (12%) were true negative. With the outcome gait domain score at the CFS TT and the same outcome postoperatively, 71 of 132 (54%) were true positive, 12 (9%) were false positive, 26 (20%) were false negative and 23 (17%) were true negative (figure 4 and 5).

The correlation between changes in the balance domain in the CSF TT and change in the total iNPH scale score postoperatively was $r=0.59$, $p=0.01$. Seventy-one individuals had no change in the balance domain score in the CSF TT.

Figure 4 Correlation between changes in the CSF TT in the gait domain on the iNPH scale and changes in the total iNPH scale score postoperatively, Spearman's rho, $r=0.32$, $p=0.01$. Distribution of true and false, positive and negative outcomes in the CSF TT with bold lines at the five-point level of improvement. N=132.

Figure 5 Correlation between changes in the CSF TT in the gait domain on the iNPH scale and changes in the gait domain postoperatively, Spearman's rho, $r=0.51$, $p=0.01$. Distribution of true and false, positive and negative outcomes in the CSF TT with bold lines at the five-point level of improvement. N=132.

Discussion

The accuracy of predicting a favorable postoperative result from the CSF TT, using the Hellström iNPH scale as an outcome parameter, shows clear limitations. The cause of this limitation of the CSF TT may partly be a physiological phenomenon that is not possible to overcome.

In this single center study a structured CSF TT procedure is used, with control of drained volume, ICP and a careful process for follow-up and treating complications. Despite this, the negative predictive value remains low.

We used two different outcomes of the CSF TT, gait and balance. The iNPH scale is constructed to cover the most characteristic features in iNPH and to discriminate between patients with variations in symptoms and between patients and healthy individuals (30). The fact that 54% (71/131 individuals) had an unchanged balance score in the CSF TT indicates that the balance domain is too insensitive to discriminate small changes. Hellström et. al. (2012) were aware of the limitations in separating patients with different levels of symptom severity with the ordinal rating scale used in the balance domain (30).

The four domains of the iNPH scale are related but none of the domains could be excluded (30). It is evident that a positive response in the CSF TT in the gait and balance domains is not favorable for surgery outcome of neuropsychology, or for continence. This should not be surprising, but is still worth mentioning. In our results, as in previous research (23,32,33), gait is the most valid variable for detecting change in the CSF TT. When we used the gait domain, with a cut of level of > 5 points in the CSF TT and the same outcome postoperatively, the sensitivity was 73.2% and the specificity was 65.7%. These results are in line with a Japanese multicenter study (33) using the iNPH grading scale with a four-step ordinal scale grading gait, cognition, continence and a total score (34). Ishikawa and colleagues (2012) used the

modified Rankin scale as the outcome postoperatively. Eighty percent of the shunted participants were responders, and the sensitivity in the CSF TT, with the total iNPH grading scale score as the outcome, was 71.3% and the specificity was 65.0%. When using the gait scale score separately to the CSF TT (measured 1-2 days after the LP) the sensitivity decreased to 51.3% and the specificity increased to 85.0% (33). The difference in outcome measures and timing for assessment, limits the comparability between the studies. The choice of outcome measure and defining a cut-off value is essential in all evaluations. Precision, practical feasibility, clinical relevance and meaningfulness for the patients have to be considered. Gallagher et al. (2019) used the Global Rating of Change Scale to evaluate the patient's perceived improvement to detect minimal clinically important differences of the CSF TT. For example, the cut-off for the Timed up and Go test was a change of 13% and for the Timed up and Go test with an added cognitive task, it was a change of 11% (35). The cut-off >5 points in the total iNPH scale, is suggested by the authors to identify outcome postoperatively (30). The same cut-off level for the separate domains of gait and balance in the CSF TT has not been described, and this could be a limitation of our study.

In the European iNPH multicenter study, using the Hellström iNPH scale, a correlation between the CSF TT and outcome post-surgery was only found in the gait domain, with a low correlation ($r=0.22$) (23). In our study the correlation for the gait domain was higher ($r=0.51$). In the same study by Wikkelsø and colleagues (2013), the sensitivity (the total iNPH scale score both in the CSF TT and postoperatively), was 52.0% and the specificity was 59%. The authors mentioned the suboptimal methodology as a cause of the low predictive value (23). Even taking into account that our study is retrospective, the structured procedure and few dropouts probably increased the validity.

Seventy-seven percent of the operated participants improved on the total iNPH scale score after surgery, which is in line with the 75.0% improvement rate recently reported (5). The positive outcome rate for the gait domain of the CSF TT was 62.9% and 42.7% for the balance domain. The CSF TT was only an adjunctive test and the broad clinical assessments together with analysis of radiological characteristics and information on alternative explanations is probably the reason of the better postoperative outcome.

Even with the high PPV in our study, we had 14 of 132 individuals with a positive response in the CSF TT in the gait domain and a negative outcome at surgery in the total scale score. Deterioration in the other domains postoperatively could be an explanation, but when using the gait domain as the outcome from both the CSF TT and postoperatively the pattern remains (12 of 132). This is a retrospective study and thus a reflection of clinical routine, i.e. there was no blinding and both the patients and the assessors knew the conditions concerning the assessment routines. Thus, a placebo effect could be, at least partially, an explanation. The placebo effect is not evaluated in the CSF TT. Gupta and Lang (2011) described a case report of a sham procedure in the CSF TT. In their case, walking time decreased about 30% with both the sham procedure and the large-volume CSF TT (36). Another reason for the false positive results may be shunt dysfunctions at the follow-up. In our study, we had an accurate registration of shunt readjustments and complications. The follow-up results were registered with the shunt valves in the proper condition.

The diagnostic accuracy is strikingly low when evaluating patients over 80 years of age. The sensitivity of 52.2% for the gait domain means that the prediction of a postoperative positive outcome is slightly better than pure chance. Increased age has been reported as a negative factor for shunt surgery outcome (31,37) but it has also been reported that the age alone

should not exclude patients from surgery (38,39). A careful evaluation of patients over 80 years of age is important and the low accuracy of CSF TT for these patients has to be taken into consideration when deciding to offer a shunt operation.

Due to the high positive predictive value, there are those who support the use of the CSF TT as an additional test to detect ideal shunt candidates. The low negative predictive value emphasizes not excluding patients from surgery (24,25,29). Even with the standardized methodology in this present study, the diagnostic accuracy of the CSF TT is still limited. An accurate evaluation of other clinical symptoms together with a selective radiological assessment and meticulous consideration about other explanatory diagnosis are important aspects to take into account when selecting patients for shunt surgery.

Strengths and limitations

A limitation of this study is the retrospective design. We included patients over a period of four years and there were different examiners during that period. The fact that this is a single center study from a selected area in Sweden could even be a limitation. However, strengths of the study are that we used a standardized protocol and prospective inclusion. Using the robust iNPH scale, which tolerates missing values, is a strength and we had few missing data in the included material. The iNPH scale is valid when measuring outcome after surgery and we used a standardized cut-off level. The post CSF TT assessment was measured about three hours after the LP and we used no repetition. Virhammar and colleagues (2012) have reported that improvements in gait can occur with repeated measures, within 24 hours after the LP, if previous measurements were negative (40). Negative outcomes at the time point of three

hours, in the present study, could have been falsely negative. Another limitation is the lack of data from the patients who were not selected for surgery.

Conclusions

Using the gait domain in the Hellström iNPH scale for CSF TT can detect positive outcomes in gait after surgery but the negative predictive value is low. The balance domain is too insensitive to use as an assessment of the CSF TT. Clinical examinations, accurate radiological assessments and careful consideration of other explanations to cover all aspects of iNPH are important to find patients suitable for shunt surgery. The CSF TT is just a tool to predict positive outcome of the gait domain and can be used as a supplement. The CSF TT should be used even more carefully with patients over 80 years of age.

List of abbreviations

cmH ₂ O	centimeters of water
CSF	cerebrospinal fluid
CSF TT	cerebrospinal fluid tap test
ELD	external lumbar cerebrospinal fluid drainage
ICP	intracranial pressure
iNPH	idiopathic normal pressure hydrocephalus
IQR	Interquartile range
LP	Lumbar puncture
ml	milliliter

377 MMSE-SR Mini-Mental State Examination, Swedish revision

378

379 [Declarations](#)

380 [Ethical approval and consent to participate](#)

381 The study was approved by the Swedish Ethical Review Authority, 2019-02260.

382

383 [Consent for publication](#)

384 Not applicable.

385

386 [Availability of data and materials](#)

387 The materials and datasets are available from the corresponding author on reasonable request.

388

389 [Competing interests](#)

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395 [Authors' contributions](#)

396 Authors JR and FL designed the study. JR performed the data collection and analyzed the

397 results. JR, FL and AE interpreted the results, wrote the paper and approved the manuscript.

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Figures

Figure 1

Flow chart of inclusion and exclusion for 132 iNPH patients with results from CSF TT and follow-up evaluation

Gait scale	Balance scale
1 Normal	1 Able to stand independently for more than 30 s on either lower extremity alone
2 Slight disturbance of tandem walk and turning	2 Able to stand independently for <30 s on either lower extremity alone
3 Wide-based gait with sway, without foot corrections	3 Able to stand independently with the feet together (at the heels) for more than 30 s
4 Tendency to fall, with foot corrections	4 Able to stand independently with the feet together for < 30 s
5 Walking with cane	5 Able to stand independently with the feet apart (one foot length) for more than 30 s
6 Bi-manual support needed	6 Able to stand independently with the feet apart for < 30 s
7 Aided	7 Unable to stand without assistance
8 Wheelchair bound	

Figure 2

The ordinal grading steps for gait and balance in the Hellström iNPH scale (30).

$$\frac{2 \times \text{Gait} \pm \text{Neuropsychology} \pm \text{Balance} \pm \text{Continence}}{5 \text{ or number of available domain scores}} = 0-100$$

Figure 3

Calculation of the total iNPH scale score (30).

Figure 4

Correlation between changes in the CSF TT in the gait domain on the iNPH scale and changes in the total iNPH scale score postoperatively, Spearman's rho, $r=0.32$, $p=0.01$. Distribution of true and false, positive and negative outcomes in the CSF TT with bold lines at the five-point level of improvement. N=132.

Figure 5

Correlation between changes in the CSF TT in the gait domain on the iNPH scale and changes in the gait domain postoperatively, Spearman's rho, $r=0.51$, $p=0.01$. Distribution of true and false, positive and negative outcomes in the CSF TT with bold lines at the five-point level of improvement. N=132.