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RESEARCH PAPER

# Pulsatility in CSF dynamics: pathophysiology of idiopathic normal pressure hydrocephalus

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## ABSTRACT

**Background** It is suggested that disturbed CSF dynamics are involved in the pathophysiology of idiopathic normal pressure hydrocephalus (INPH). The pulsatility curve describes the relationship between intracranial pressure (ICP) and the amplitude of cardiac related ICP pulsations. The position of baseline ICP on the curve provides information about the physiological state of the CSF dynamic system. The objective of the study was to investigate if shunt surgery modifies the pulsatility curve and the baseline position on the curve, and how this relates to gait improvement in INPH.

**Methods** 51 INPH patients were investigated with lumbar CSF dynamic investigations preoperatively and 5 months after shunt surgery. During the investigation, ICP was measured at baseline, and then a CSF sample was removed, resulting in pressure reduction. After this, ICP was regulated with an automated infusion protocol, with a maximum increase of 24 mm Hg above baseline. The pulsatility curve was thus determined in a wide range of ICP values. Gait improvement was defined as a gait speed increase ≥0.1 m/s.

**Results** The pulsatility curve was unaltered by shunting. Baseline ICP and amplitude were reduced (−3.0 ±2.9 mm Hg; −1.1±1.5 mm Hg; $p<0.05$, n=51). Amplitude reduction was larger for gait improvers (−1.2±1.6 mm Hg, n=42) than non-improvers (−0.2±0.5 mm Hg, n=9) ($p<0.05$) although mean ICP reduction did not differ.

**Conclusions** The pulsatility curve was not modified by shunt surgery, while the baseline position was shifted along the curve. Observed differences between gait improvers and non-improvers support cardiac related ICP pulsations as a component of INPH pathophysiology.

## INTRODUCTION

Idiopathic normal pressure hydrocephalus (INPH) is a condition of unknown cause distinguished by enlarged cerebral ventricles and a gait disturbance, often accompanied by cognitive decline and urinary incontinence.[1] The combination of enlarged ventricles and gait/balance disturbances may be more common than previously believed.[2] It is postulated that disturbed CSF dynamics are involved in the pathophysiology. The conventional view posits increased resistance to CSF outflow ($R_{out}$)[3–5] while other hypotheses suggest increased pulsations in intracranial pressure (ICP).[6 7] Both $R_{out}$ and baseline amplitude of cardiac related pulsations have been suggested as predictive tests for selecting patients for shunt surgery although the scientific reports are conflicting.[8–14] Table 1 contains a list of definitions of the abbreviations used.

We previously described the pulsatility curve,[15] the relationship between mean ICP and pulse amplitude of the cardiac related pulsations in ICP (AMP). The curve includes a linear ICP dependent phase, consistent with the previously established mathematical model according to Marmarou and Avezaat,[16 17] and an essentially constant ICP independent phase at lower ICP.[15] Results suggested that the predictive power of baseline pulse amplitude ($AMP_r$) could be affected by its position on the pulsatility curve—that is, its proximity to the ICP independent phase. We refer to this position, which describes the baseline or resting characteristics of the CSF system, as the operating point. Our hypothesis is that the pulsatility curve is unchanged by a CSF shunt while the operating point moves along the curve. Furthermore, we postulated that analysis of the curve and operating point can predict the potential reduction in $AMP_r$ from shunt surgery and, in accordance with theories on the role of pulsations in INPH, also the clinical response to surgery. The aim of this study was to investigate the effect of shunt surgery on the pulsatility curve and ICP pulsations, and how these changes relate to gait improvement in patients with INPH.

## METHODS

### Study design

Umeå University Hospital is a tertiary hospital serving the northern parts of Sweden. Patients admitted because of clinical suspicion of normal pressure hydrocephalus are prospectively investigated according to a standardised scheme, including case history, clinical examination, MRI, CSF tap test, CSF dynamic investigation (ie, ICP and $R_{out}$) and gait evaluation, including video recording and velocity measurement. The battery is repeated at follow-up, 3–6 months after surgery. Data are recorded in a computerised database. Analysis of ICP pulse amplitudes has never been used in the preoperative selection of shunt candidates.

Using the data from this prospective database, but blinded for preoperative CSF dynamic results, two neurologists (JM, BL) retrospectively identified cases that fulfilled the international criteria of INPH.[1] The inclusion procedure is described in detail in figure 1. Fifty-one INPH patients (21 women; mean age 73±6 years), operated on with a Strata valve (Medtronic PS Medical, Goleta, California, USA), were enrolled. All had valid determinations of ICP and $R_{out}$ before and after surgery and were older than 60 years. Only patients with functioning CSF

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**Table 1** List of abbreviations

| Abbreviation | Description |
|---|---|
| $R_{out}$ | Resistance to CSF outflow |
| AMP | Pulse amplitude of cardiac related pulsations in intracranial pressure |
| $ICP_r$ | Intracranial pressure at baseline/rest |
| $AMP_r$ | AMP at baseline/rest |
| PVI | Pressure volume index |
| RPPC | Relative pulse pressure coefficient, slope of linear relationship between ICP and AMP |
| $P_0$ | Pressure constant of the mathematical model of CSF dynamics |
| $AMP_{min}$ | Minimal level of AMP |
| $ICP_{AMPmin}$ | ICP at minimal AMP |

shunts were included. An engineer (SQ), blinded to the clinical data, performed an analysis of the recorded CSF dynamic data and created the pulsatility curves (as described below). The regional ethics board (institutional review board) at Umeå University approved the protocol of this study.

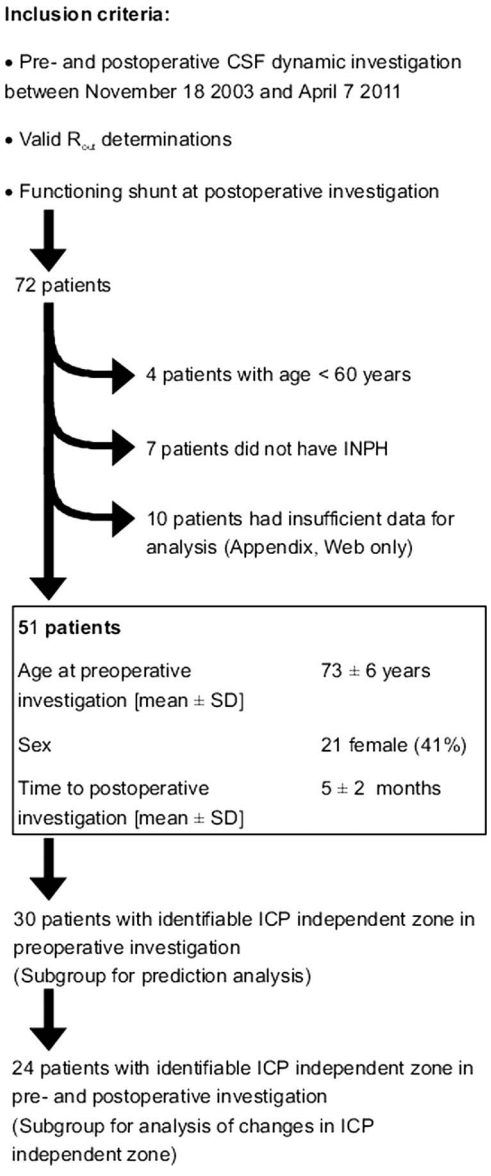


**Figure 1** Selection process for the study population and population demographics. ICP, intracranial pressure; INPH, idiopathic normal pressure hydrocephalus; $R_{out}$, resistance to CSF outflow.

## Definitions

All patients shunted at Umeå University Hospital undergo CSF dynamic investigation at surgical follow-up, and $R_{out}$ was used for the definition of CSF shunt dysfunction: (A) $R_{out}$ >8.4 mm Hg/(ml/min) or (B) $R_{out}$ 4.2–8.4 mm Hg/(ml/min) and >50% of the preoperative value.[18] These limits are selected to fit the Strata shunt. Shunt revision, irrespective of the indication, was also defined as shunt dysfunction (one case).

Gait improvement was defined as increase in gait speed ≥0.1 m/s.[19] For nine patients where gait speed was not available, outcome was estimated by a physician (JM), having no information about the results of the CSF dynamic investigation, based on the video recording of gait/balance tests. Mean time from surgery to postoperative investigation was 5 months. Gait speed was chosen as an indicator of improvement from shunt surgery as it is an objective measure, which was mandatorily investigated with standardised tests, and thus well documented in our database.

## The pulsatility curve

The pulsatility curve has two zones: one low ICP zone where AMP is essentially ICP independent and one ICP dependent zone where AMP increases linearly with ICP[15] (figure 2). The ICP dependent zone is consistent with the well known exponential pressure/volume relationship of the CSF system,[16 17] which is often illustrated as linear in a semi-logarithmic plot where the slope is referred to as the pressure volume index (PVI).[16] As

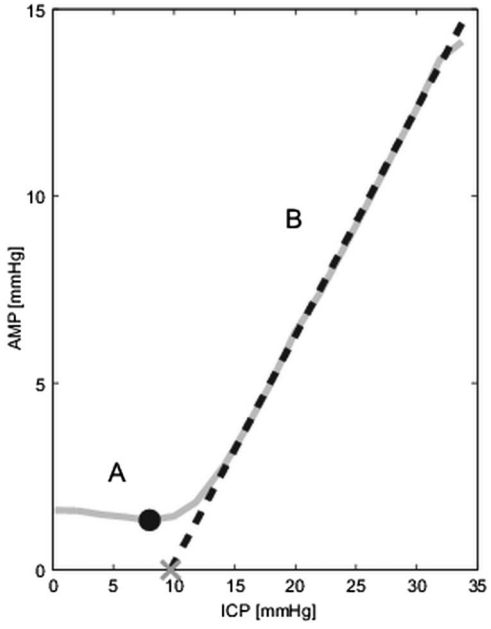


**Figure 2** The pulsatility curve describes the relationship between pulse amplitude of cardiac related pulsations in intracranial pressure (AMP) and intracranial pressure (ICP). The curve includes an ICP independent zone at low ICP (A), where AMP is essentially constant, and an ICP dependent zone (B), where AMP increases linearly with ICP. The ICP dependent zone can be defined with linear regression (broken line), where relative pulse pressure coefficient is the slope and $P_0$ (pressure constant of the mathematical model of CSF dynamics) is the intercept with the ICP axis (cross). The baseline or resting values of ICP and AMP ($ICP_r$, $AMP_r$) define the operating point (black circle) on the pulsatility curve.

shown by Avezaat and van Eijndhoven, the linear relationship between AMP and ICP can be derived from the above described established mathematical model of the system[16 17] as:

$$AMP = RPPC \times (ICP - P_0)$$

where AMP is the ICP pulse amplitude and $P_0$ a reference pressure.[17] RPPC (relative pulse pressure coefficient)[20] is thus the slope of the linear relationship between AMP and ICP in this zone. RPPC is dependent on the pulsatile intracranial arterial volume change of each cardiac cycle, as well as the PVI of the CSF system.[20] In the low ICP zone of the pulsatility curve, generally below normal baseline pressure, the exponential pressure/volume relationship postulated by Marmarou does not apply[21] and the system can in this ICP interval be described as having a close to constant compliance—that is, a linear pressure/volume relationship.[15 22] The combination of a linear pressure/volume curve for a low ICP interval and an exponential pressure/volume curve from normal to elevated ICP generates the two phased pulse amplitude versus ICP relationship (ie, the pulsatility curve).[15]

## CSF dynamic investigations

Investigations were performed with a Umeå developed infusion apparatus[23] (CELDA, Likvor AB, Umeå, Sweden). CSF pressure was measured through two needles inserted into the CSF space at the L3–L4 interspace. One needle was used to infuse and withdraw artificial CSF; the other was the main measurement needle. Data were sampled at 100 Hz, with hardware filtration at 20 Hz. For the measurement needle, 100 Hz datasets[15] were stored.

The CSF dynamic investigations started with a baseline registration followed by manual removal of a 10–16 ml CSF sample, which results in ICP reduction (figure 3). This reduction provided the data below baseline ICP which was essential for mapping the lower parts of the pulsatility curve (figure 4). CSF removal was followed by infusion. The standard protocol was constant pressure infusion,[23] which entails regulating ICP by pumping fluid to and from the CSF system to achieve a set of constant ICP levels up to 24 mm Hg above baseline (figure 3). Constant flow infusion at 1.5 ml/min was used in case of difficulty withdrawing fluid from the CSF space (13 investigations).

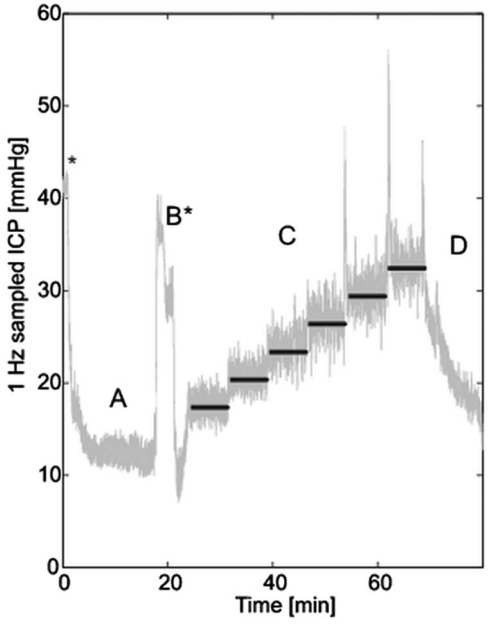


**Figure 3** A standard CSF dynamic investigation included a baseline registration (A), followed by removal of a CSF sample (B) which leads to a decrease in intracranial pressure (ICP), a constant pressure infusion protocol (C) and a relaxation phase (D). Black lines show the regulated pressure levels of the constant pressure infusion. *Patient in the seated position.

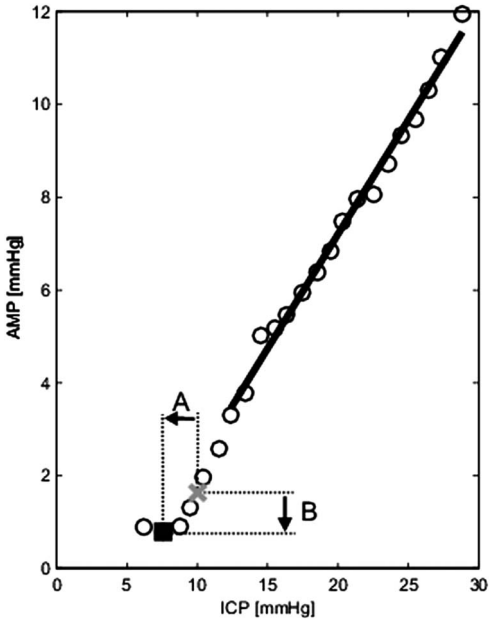


**Figure 4** Median values for intracranial pressure (ICP) and pulse amplitude of cardiac related pulsations in intracranial pressure (AMP) measured during and just before infusion (when ICP is reduced after removal of a CSF sample) determined the pulsatility curve (open circles). A linear regression (line) performed for the ICP dependent phase gave estimations of relative pulse pressure coefficient and $P_0$ (pressure constant of the mathematical model of CSF dynamics). The distance between the operating point ($ICP_r$, $AMP_r$) (cross) and the point of minimal AMP ($ICP_{AMPmin}$, $AMP_{min}$) (black square) provided the estimates of recommended ICP reduction (A) and potential AMP reduction (B).

## Postprocessing of data

Calculations were performed with MATLAB (MathWorks Inc, Natick, Massachusetts, USA). To avoid errors, the datasets were manually investigated for disturbances, and data with measurement difficulties were removed according to specific criteria (see online supplementary appendix). Ten investigations were excluded. Fifty-one patients with sufficient valid data pre- and postoperatively were included in the analysis of the effect of shunt surgery on CSF dynamics (figure 1).

For each 1.5 s period, ICP was calculated as the mean of unfiltered pressure, and AMP as the difference between the maximum and minimum of filtered pressure. Filtration (10th order Butterworth zero phase filters) was used to remove slow and respiratory waves (high pass cut-off frequency 0.5 Hz), and periodic noise from the infusion pump (low pass cut-off frequency 10 Hz).

Resting (baseline) values of ICP ($ICP_r$) and AMP ($AMP_r$) were determined as the mean values of ICP and AMP of the last 5 min of the baseline registration (figure 3). These values defined the operating point on the pulsatility curve (figure 4).

The pulsatility curve was mapped using data measured during infusion, and just prior to it when ICP was reduced due to the removed CSF sample (figure 3). To achieve a reliable and stable

depiction of the pulsatility curve, ICP values were divided into 1 mm Hg intervals. Intervals with fewer than three values were discarded to minimise the influence of noise. For each interval, median ICP and the corresponding median AMP value were calculated. These results defined the pulsatility curve (figure 4). The choice of median value over mean was made to reduce the influence of single outlier values.

### The two zones of the pulsatility curve

In addition to baseline values $ICP_r$ and $AMP_r$, the infusion part of the investigation ensured that the ICP dependent zone was identified for all 51 patients. Thus all patients were included in analysis of the linear relationship of AMP and ICP (ie, RPPC and $P_0$), and the operating point ($ICP_r$ and $AMP_r$). RPPC was determined as the slope of a linear regression of the ICP dependent zone, and $P_0$ as the intercept with the ICP axis. ICP values between ICP at minimal AMP+4 mm Hg (or minimal ICP+4 mm Hg) and 33 mm Hg were expected to fall within the ICP dependent zone of the pulsatility curve.[15] Median values within this range were used for linear regression, with AMP as the dependent parameter (figure 4).

Although AMP is essentially constant in the low ICP zone of the pulsatility curve, careful analysis reveals a trend of slightly negative slope on the group level[15] which would mean that there is a minimum AMP point in the transition between the two zones. The minimal median value of AMP was used to estimate the lowest level of AMP achievable ($AMP_{min}$). Potential AMP reduction was calculated as $AMP_r - AMP_{min}$ (figure 4). The ICP that corresponded to $AMP_{min}$ ($ICP_{AMPmin}$) was used to estimate the ideal ICP level for attaining maximal AMP reduction. Recommended ICP reduction was then defined as $ICP_r - ICP_{AMPmin}$ (figure 4). To correctly determine $AMP_{min}$ and parameters relating to it, the ICP independent zone of the pulsatility curve needed to be included in the measured data. The datasets were therefore manually investigated to determine if the ICP independent zone was identifiable. For the predictive analysis there was a reduction from 51 to 30 patients due to the demand of identifying the ICP independent zone in the preoperative investigation, which required sufficient sampled data below baseline ICP. For 24 patients, both pre- and postoperative investigations included the ICP independent zone (figure 1). This subgroup was used for analysis of $AMP_{min}$, $ICP_{AMPmin}$, potential AMP reduction and recommended ICP reduction.

### Statistics

Statistics were calculated with PASW Statistics (V.18.0.3; SPSS Inc, Chicago, Illinois, USA). Pre- and postoperative values were compared using two tailed paired Student's t tests. Values for improved and non-improved patients were compared using two tailed independent sample t tests (no assumption of equal variances). A p value $<0.05$ was considered statistically significant. Predictive power was evaluated with receiver operated characteristic (ROC) curves, where an area under the curve significantly different from 0.5 was considered significantly predictive.

## RESULTS

### Effect of shunt surgery

The ICP dependent zone of the pulsatility curve (figure 3) is described by RPPC and $P_0$, which showed no significant changes following shunt surgery (table 2, n=51). The ICP independent zone of the curve could be identified in both the pre- and postoperative investigations for 24 of the patients. In this group, we found no significant changes in $AMP_{min}$ or $ICP_{AMPmin}$ (table 2, n=24).

**Table 2** Preoperative and postoperative parameters (mean±SD) describing the operating point and pulsatility curve

| Parameter | Preoperative | Postoperative |
|---|---|---|
| All patients (n=51) | | |
| $ICP_r$ (mm Hg) | 12.5±2.1** | 9.5±2.4 |
| $AMP_r$ (mm Hg) | 2.6±1.6** | 1.5±0.6 |
| RPPC | 0.59±0.14 | 0.58±0.21 |
| $P_0$ (mm Hg) | 8.5±3.5 | 8.3±3.2 |
| Subgroup with identifiable ICP independent zone (n=24) | | |
| Recommended ICP reduction (mm Hg) | 2.0±1.7** | 0.3±2.4 |
| Potential AMP reduction (mm Hg) | 0.8±0.6 | 0.5±0.7 |
| $ICP_{AMPmin}$ (mm Hg) | 10.8±2.0 | 9.6±2.7 |
| $AMP_{min}$ (mm Hg) | 1.4±0.5 | 1.1±0.6 |

**p<0.01 (paired t test, compared with postoperative value).
AMP, pulse amplitude of cardiac related pulsations in ICP; $AMP_{min}$, minimal level of AMP; $AMP_r$, AMP at baseline/rest; ICP, intracranial pressure; $ICP_r$, ICP at baseline/rest; $ICP_{AMPmin}$, ICP at minimal AMP; $P_0$, pressure constant of the mathematical model of CSF dynamics; RPPC, relative pulse pressure coefficient.

The operating point shifted towards lower values after shunt surgery, with a significant reduction in both $ICP_r$ (−3.0 ±2.9 mm Hg) and $AMP_r$ (−1.1±1.5 mm Hg) (table 2, n=51).

Comparisons according to gait improvement (table 3) showed that preoperative $AMP_r$ was significantly larger in the improved patients, while $ICP_r$ was similar. Both pre- and postoperative AMPmin was significantly different when comparing improved

**Table 3** Preoperative and postoperative parameters (mean±SD) grouped by gait improvement

| | Improved (n=42) | Not improved (n=9) |
|---|---|---|
| *All patients (n=51)* | | |
| Preoperative parameter | | |
| $ICP_r$ (mm Hg) | 12.6±2.3 | 12.0±1.1 |
| $AMP_r$ (mm Hg) | 2.8±1.6** | 1.4±0.4 |
| RPPC | 0.59±0.13 | 0.57±0.20 |
| $P_0$ (mm Hg) | 8.1±3.5* | 10.6±2.9 |
| Postoperative parameter | | |
| $ICP_r$ (mm Hg) | 9.4±2.3 | 10.0±2.9 |
| $AMP_r$ (mm Hg) | 1.6±0.6 | 1.2±0.4 |
| RPPC | 0.58±0.21 | 0.57±0.23 |
| $P_0$ (mm Hg) | 7.9±3.1 | 10.2±2.8 |
| *Subgroup with identifiable ICP independent zone (n=24)* | | |
| Preoperative parameter | **Improved (n=19)** | **Not improved (n=5)** |
| Recommended ICP reduction (mm Hg) | 2.4±1.5 | 0.6±1.7 |
| Potential AMP reduction (mm Hg) | 1.0±0.6** | 0.3±0.3 |
| $ICP_{AMPmin}$ (mm Hg) | 10.6±1.8 | 11.6±2.6 |
| $AMP_{min}$ (mm Hg) | 1.5±0.5** | 1.0±0.2 |
| Postoperative parameter | | |
| Recommended ICP reduction (mm Hg) | 0.3±2.6 | -0.1±1.4 |
| Potential AMP reduction (mm Hg) | 0.5±0.7 | 0.3±0.6 |
| $ICP_{AMPmin}$ (mm Hg) | 9.1±2.5 | 11.4±3.2 |
| $AMP_{min}$ (mm Hg) | 1.2±0.6* | 0.8±0.3 |

*p<0.05, **p<0.01 (independent sample t test, compared with not improved).
AMP, pulse amplitude of cardiac related pulsations in ICP; $AMP_{min}$, minimal level of AMP; $AMP_r$, AMP at baseline/rest; ICP, intracranial pressure; $ICP_r$, ICP at baseline/rest; $ICP_{AMPmin}$, ICP at minimal AMP; $P_0$, pressure constant of the mathematical model of CSF dynamics; RPPC, relative pulse pressure coefficient.

and non-improved patients; no other postoperative parameter was significantly different.

The change in $AMP_r$ after shunting was significantly larger for improved than non-improved patients (−1.2±1.6 mm Hg vs −0.2±0.5 mm Hg; $p<0.01$) although there was some overlap. The change in $ICP_r$ was not significantly different ($p=0.30$).

Predictive analysis was based on the 30 patients (24 gait improvers) where the ICP independent zone of the pulsatility curve was identifiable in the preoperative data (figure 1). ROC curve analysis showed that $AMP_r$, potential AMP reduction and recommended ICP reduction were all significantly predictive of gait improvement (figure 5).

## DISCUSSION

This study supported the hypothesis of a pulsatility curve that is unaltered by shunt surgery, and an operating point that shifts towards lower values after shunting (table 2). The identified differences between patients with and without gait improvement (table 3) are in agreement with theories of ICP pulsations being a component of the pathophysiology of INPH. $AMP_r$ depends on several patient specific factors, and the unaltered pulsatility curve suggested that most of them were unaffected by shunting. We therefore believe that determining the position of the baseline values (the operating point) on the pulsatility curve provides a valuable complement to the absolute value of $AMP_r$ in identifying the patients who will, and maybe even more importantly who will not, respond to shunt surgery.

### Effect of shunt surgery

Several effects of shunt surgery have been previously established, including alterations in CSF dynamics,[24 25] which can lead to secondary changes in cerebral blood flow and metabolism,[26–28] and CSF content,[29] but it is not confirmed which effects lead to the reverse of the clinical symptoms. This study confirmed that shunting reduced $ICP_r$ and $AMP_r$,[24 25] but also showed that the pulsatility curve was not altered by shunting. That RPPC, which is dependent on PVI and the pulsatile intracranial volume change in arterial blood,[30] did not change after surgery suggests that these parameters are unaffected by shunting. This implies that any improvement in compliance was primarily due to the reduction in $ICP_r$, and not to alteration of the elastic properties of the craniospinal space.

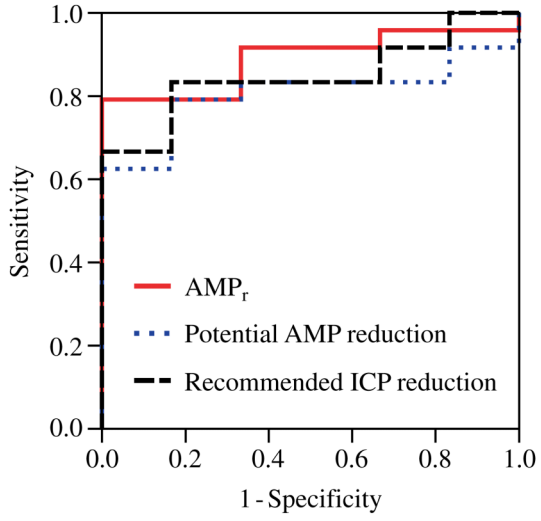


**Figure 5** Receiver operated characteristic curves for the parameters with statistically significant predictive power: $AMP_r$ (area under the curve (AUC) 0.89, CI 0.77 to 1.00), potential AMP reduction (AUC 0.81, CI 0.65 to 0.96) and recommended intracranial pressure (ICP) reduction (AUC 0.85, CI 0.71 to 0.99). AMP, pulse amplitude of cardiac related pulsations in ICP; $AMP_r$, AMP at baseline/rest.

In this study, reduction of $AMP_r$ from shunt surgery was caused by reduction of $ICP_r$, as the operating point shifted along the pulsatility curve from a position in the ICP dependent zone towards lower values (table 2). That $AMP_r$ reduction after shunting was significantly larger for patients with improved gait speed, despite a lack of difference in $ICP_r$ reduction (table 3), implies that this effect may be a key factor in clinical outcome. This was further supported by larger preoperative potential AMP reduction in improved patients. The low value for the non-improved patients suggests that the smaller achieved $AMP_r$ reduction in this group was due to preoperative operating points that were already in, or close to, the ICP independent zone of the pulsatility curve. Thus their $AMP_r$ values were not lowered in spite of the $ICP_r$ reduction from shunting. We hypothesise that future research will show both intra- and extraventricular enlargement in this category of patients, a sign of an atrophic process rather than redistribution of CSF.[2]

### Shunt adjustment

As reduced $AMP_r$ seemed to influence gait improvement in this study, it is reasonable to suggest that shunt adjustment leading to further reduction would be beneficial. Examination of the postoperative potential AMP reduction should be suggestive of how much more $AMP_r$ could be reduced by lowering the shunt setting. Our results suggest that non-improved patients should be eligible for lowering of shunt setting only if they are operating in the ICP dependent zone of the pulsatility curve. Further reduction in $ICP_r$ in those patients who already have an operating point in the ICP independent zone would not achieve further $AMP_r$ reduction, and may in some cases lead to increased $AMP_r$.[31] This analysis requires a postoperative CSF dynamic investigation, which we believe is of benefit for all patients, both in confirming that shunts are properly functioning and to help determine whether to adjust shunt settings. Avoiding lowering of the shunt setting in those patients where further $AMP_r$ reduction is not likely may reduce problems relating to over drainage from setting the operating pressure of the shunt too low.

The achieved reduction in $ICP_r$ in non-improved patients in this study (similar to that of improved patients) implies that the lack of $AMP_r$ reduction was not due to too high shunt settings. In fact the slightly negative postoperative recommended ICP reduction (table 3) implies some of them may have benefitted somewhat from higher shunt setting, although none showed signs of over drainage.

### Predictive tests

$AMP_r$ has previously been shown to have good positive predictive power but lower negative predictive power for shunt response in INPH.[13 14 32] $AMP_r$ could be increased either by augmented pulsatile arterial volume change or by decreased compliance.[30] This study supports compliance reduction through increased $ICP_r$, for example, due to increase in $R_{out}$, which would move the operating point to the right along the pulsatility curve. This harmonises with the predictive test of increased $R_{out}$. During a tap test, ICP is reduced by CSF removal,[33] which means the clinical response is tested with the patient's operating point moved into the ICP independent zone of the pulsatility curve.[15] With support from currently used tests, we hypothesised that studying the position of $ICP_r$ and

$AMP_r$ (ie, the operating point) on the pulsatility curve would be beneficial in the difficult task of identifying the non-responders among those with low $AMP_r$. Tap tests and infusion tests, including pulsatility curve analysis, offer complementary information as an infusion test describes the potential for altering CSF dynamics by reducing ICP while a tap test or extended lumbar drainage test determines the functional response to such a decrease. We therefore suggest that tap tests and infusion tests should be used together, which can be done using the same lumbar puncture. Ultimately, we believe the best approach to selecting INPH patients for shunt surgery is that a skilled physician takes into account the clinical examination, history and radiological findings, along with the results of predictive tests.

The predictive analysis of the current study is limited, as the group of patients with all of the necessary data was small, with an unbalance between the number of improved and non-improved patients, and preselected based on $R_{out}$ and response to tap test. Potential AMP reduction and recommended ICP reduction showed similar predictive power to $AMP_r$ (figure 5), and we believe that combining $AMP_r$ with pulsatility curve analysis may lead to improved accuracy in prediction of shunt response. Before introducing pulsatility curve analysis as a clinical predictive test for INPH, a prospective study is needed to determine the sensitivity and specificity of pulsatility curve analysis for selection of patients for shunt surgery. That study should use an improved infusion protocol specifically designed to determine the pulsatility curve. Such an infusion protocol requires lowering of ICP beneath baseline to ensure data in the ICP independent zone, but is less dependent on ICP increase.

Previously investigated parameters which describe aspects of CSF dynamics similar to the pulsatility curve include the RAP Index[21] (an index of cerebrospinal compensatory reserve) and the Elastance Index.[34] The Elastance Index, which is similar to RPPC but uses diastolic pressure rather than mean ICP, has shown good predictive results for INPH in a previous study[34] but RPPC did not predict gait improvement in this study. A high RPPC could however contribute to increased potential AMP reduction, which did predict gait improvement for patients with operating points in the ICP dependent zone. The RAP Index describes the short term correlation between ICP and AMP, with values close to zero signifying good compensatory reserve (ie, a state of high compliance).[21] This harmonises with the pulsatility curve analysis, as a very low RAP at baseline is suggestive of an operating point in the ICP independent phase.

Measuring AMP with lumbar fluid catheters requires free passage at the needles to avoid attenuation from obstructive tissue. In this study, five of 112 investigations had to be excluded for that reason (see online supplementary appendix). Comparison of the waveform from the two needles can be used to develop an algorithm for quality assurance.

## CONCLUSION

In this study, the pulsatility curve was unaltered by shunt surgery, and the operating point was shifted along the curve towards lower values after shunting. Preoperative $AMP_r$ and potential AMP reduction, as well as achieved $AMP_r$ reduction, were significantly larger for patients with improved gait speed than those without, which supports theories that link ICP pulsations to the pathophysiology of INPH. In general, the pulsatility curve provides a new way of thinking for selecting INPH patients for surgery, it offers possibilities for 'intelligent' shunt adjustments and opens up for the development of new devices for management of the disease. The findings and theories put forward in this paper should be verified and further investigated in a large prospective study.

**Contributors** SQ contributed to the study concept and design, analysis and interpretation of the data, drafting and revision of the manuscript, as well as the statistical analysis. BL contributed to the analysis and interpretation of the data, and revision of the manuscript. L-ODK contributed to the analysis and interpretation of the data, and drafting and revision of the manuscript. JM contributed to the study concept and design, analysis and interpretation of the data, and drafting and revision of the manuscript. AE contributed to the study concept and design, analysis and interpretation of the data, and drafting and revision of the manuscript.

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**Competing interests** L-ODK has received honorary for lecturing from Johnson and Johnson (Codman Company). JM is listed as an inventor on a patent (re: CSF dynamic investigation apparatus), for which he has received royalties from Likvor AB. AE has received honorary for lecturing from DePuy Inc and is listed as an inventor on a patent (re: CSF dynamic investigation apparatus), for which he has received royalties from Likvor AB.

**Ethics approval** The study was approved by the regional ethics review board in Umeå.

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