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Pulsatility in CSF dynamics: pathophysiology of idiopathic normal pressure hydrocephalus

Sara Qvarlander, M.Sc.^{1,2} Bo Lundkvist, MD³ Lars-Owe D. Koskinen, MD, PhD³
Jan Malm, MD, PhD³ Anders Eklund, PhD^{1,2}

¹ Department of Radiation Sciences – Biomedical Engineering, Umeå University, Umeå, Sweden

² Centre of Biomedical Engineering and Physics, Umeå University, Umeå, Sweden

³ Department of Clinical Neuroscience, Umeå University, Umeå, Sweden

Corresponding author: Sara Qvarlander

Department of Radiation Sciences– Biomedical Engineering

Umeå University, 901 85 Umeå, Sweden

Telephone: +46907854067, Fax: +4690136717

Email: sara.qvarlander@radfys.umu.se

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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 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

Fifty-one 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 maximum increase of 24 mmHg above baseline. The pulsatility curve was thus determined in a wide range of ICP. Gait improvement was defined as 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 mmHg; -1.1 ± 1.5 mmHg, $p < 0.05$, $N=51$). Amplitude reduction was larger for gait improvers (-1.2 ± 1.6 mmHg, $N=42$) than non-improvers (-0.2 ± 0.5 mmHg, $N=9$) ($p < 0.05$), though mean ICP reduction did not differ.

Conclusion

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 can 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 the 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, though the scientific reports are conflicting.[8-14] Table 1 contains a list of definitions of 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, i.e. 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, that analysis of the curve and operating point can predict the potential reduction of 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 the ICP pulsations, and how these changes relate to gait improvement in patients with INPH.

Table 1. List of abbreviations

Abbreviation	Description
R_{out}	Resistance to CSF outflow
AMP	Pulse amplitude of cardiac related pulsations in ICP
ICP_r	ICP 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

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 standardized scheme including case history, clinical examination, MRI, CSF tap test, CSF dynamic investigation (i.e. 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 computerized 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 $\pm$ S.D), operated on with a Strata valve (Medtronic PS Medical, Goleta, CA, 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 shunts were included. An engineer (SQ), blinded to clinical data, performed an analysis of the recorded CSF dynamic data and created the pulsatility curves (as described below). The regional ethical board (IRB) at Umeå University approved the protocol of this study.

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} above 8.4 mmHg/(ml/min) or B) R_{out} between 4.2 - 8.4 mmHg/(ml/min) and more than 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 (1 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 standardized tests, and thus well documented in our database.

Inclusion criteria:

- Pre- and postoperative CSF dynamic investigation between November 18 2003 and April 7 2011
- Valid R_{out} determinations
- Functioning shunt at postoperative investigation

Figure 1. Selection process for the study population and population demographics.

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 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:

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

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, i.e. 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 vs. ICP relationship, i.e. the pulsatility curve.[15]

Figure 2. The pulsatility curve describes the relationship between AMP and 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 a linear regression (dashed line) where RPPC is the slope and P_0 is the intercept with the ICP-axis (grey cross). The baseline or resting values of ICP and AMP (ICP_r , AMP_r) defines the operating point (black circle) on the pulsatility curve.

CSF dynamic investigations

Investigations were performed with an 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 was sampled at 100 Hz, with hardware filtration at 20 Hz. For the measurement needle 100 Hz data sets [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 the ICP by pumping fluid to and from the CSF system to achieve a set of constant ICP levels up to 24 mmHg 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 ICP decrease, 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.

Post processing of data

Calculations were performed with MATLAB (MathWorks Inc., Natick, MA, USA). To avoid errors the data sets were manually investigated for disturbances and data with measurement difficulties was removed according to specific criteria (appendix, Web only). Ten investigations were excluded. 51 patients with sufficient valid data pre- and postoperatively were included in 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 five minutes of the baseline registration (Figure 3). These values defined the operating point on the pulsatility curve (Figure 4).

Figure 4. Median values of ICP and AMP measured during and just before infusion (when ICP is reduced after removal of a CSF sample) determined the pulsatility curve (circles). A linear regression (line) performed for the ICP dependent phase gave estimations of RPPC and P_0 . The distance between the operating point [ICP_r , AMP_r] (grey 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).

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 mmHg intervals. Intervals with fewer than three values were discarded to minimize 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 (i.e 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 $AMP + 4$ mmHg (or minimal $ICP + 4$ mmHg) and 33 mmHg were expected to fall within the ICP dependent zone of the pulsatility curve.[15] Median values within this range were used for the 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 data sets 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 (version 18.0.3, SPSS Inc., Chicago, IL, 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 samples t-tests (no assumption of equal variances). A p-value below 0.05 was considered statistically significant. Predictive power was evaluated with receiver operated characteristics (ROC) curves, where an area under the curve (AUC) 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 investigation for 24 of the patients. In this group we found no significant changes in AMP_{min} or ICP_{AMPmin} (Table 2, N=24).

The operating point shifted toward lower values after shunt surgery, with significant reduction of both ICP_r (-3.0 ± 2.9 mmHg) and AMP_r (-1.1 ± 1.5 mmHg) (Table 2, N=51).

Table 2. Pre- and postoperative parameters (mean $\pm$ SD) describing the operating point and pulsatility curve.

All patients (N=51)		
Parameter	Preoperative	Postoperative
ICP _r [mmHg]	12.5 $\pm$ 2.1**	9.5 $\pm$ 2.4
AMP _r [mmHg]	2.6 $\pm$ 1.6**	1.5 $\pm$ 0.6
RPPC	0.59 $\pm$ 0.14	0.58 $\pm$ 0.21
P ₀ [mmHg]	8.5 $\pm$ 3.5	8.3 $\pm$ 3.2
Subgroup with identifiable ICP independent zone (N=24)		
Parameter	Preoperative	Postoperative
Recommended ICP reduction [mmHg]	2.0 $\pm$ 1.7**	0.3 $\pm$ 2.4
Potential AMP reduction [mmHg]	0.8 $\pm$ 0.6	0.5 $\pm$ 0.7
ICP _{AMPmin} [mmHg]	10.8 $\pm$ 2.0	9.6 $\pm$ 2.7
AMP _{min} [mmHg]	1.4 $\pm$ 0.5	1.1 $\pm$ 0.6

** p<0.01 (paired t-test, compared to postoperative value)

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 AMP_{min} was significantly different when comparing improved 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 $\pm$ 1.6 mmHg versus -0.2 $\pm$ 0.5 mmHg, p<0.01), though 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 for gait improvement (figure 5).

Table 3. Pre- and postoperative parameters (mean $\pm$ SD) grouped by gait improvement**All patients (N=51)**

Preoperative parameter	Improved (N=42)	Non-improved (N=9)
ICP _r [mmHg]	12.6 $\pm$ 2.3	12.0 $\pm$ 1.1
AMP _r [mmHg]	2.8 $\pm$ 1.6**	1.4 $\pm$ 0.4
RPPC	0.59 $\pm$ 0.13	0.57 $\pm$ 0.20
P ₀ [mmHg]	8.1 $\pm$ 3.5*	10.6 $\pm$ 2.9
Postoperative parameter		
ICP _r [mmHg]	9.4 $\pm$ 2.3	10.0 $\pm$ 2.9
AMP _r □[mmHg]	1.6 $\pm$ 0.6	1.2 $\pm$ 0.4
RPPC	0.58 $\pm$ 0.21	0.57 $\pm$ 0.23
P ₀ [mmHg]	7.9 $\pm$ 3.1	10.2 $\pm$ 2.8

Subgroup with identifiable ICP independent zone (N=24)

Preoperative parameter	Improved (N=19)	Non-improved (N=5)
Recommended ICP reduction [mmHg]	2.4 $\pm$ 1.5	0.6 $\pm$ 1.7
Potential AMP reduction [mmHg]	1.0 $\pm$ 0.6**	0.3 $\pm$ 0.3
ICP _{AMPmin} [mmHg]	10.6 $\pm$ 1.8	11.6 $\pm$ 2.6
AMP _{min} [mmHg]	1.5 $\pm$ 0.5**	1.0 $\pm$ 0.2
Postoperative parameter		
Recommended ICP reduction [mmHg]	0.3 $\pm$ 2.6	-0.1 $\pm$ 1.4
Potential AMP reduction [mmHg]	0.5 $\pm$ 0.7	0.3 $\pm$ 0.6
ICP _{AMPmin} [mmHg]	9.1 $\pm$ 2.5	11.4 $\pm$ 3.2
AMP _{min} [mmHg]	1.2 $\pm$ 0.6*	0.8 $\pm$ 0.3

* p<0.05, ** p<0.01(independent samples t-test, compared to non-improved)

Figure 5. ROC-curves for the parameters with statistically significant predictive power: AMP_r (AUC 0.89, CI: 0.77-1.00), potential AMP reduction (AUC 0.81, CI: 0.65-0.96) and recommended ICP reduction (AUC 0.85, CI: 0.71-0.99).

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 of 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 of ICP_r , and not to alteration of the elastic properties of the craniospinal space.

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 were not lowered in spite of the ICP_r reduction from shunting. We hypothesize that future research will show both intra- and extra ventricular 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 ICP dependent zone of the pulsatility curve. Further reduction of 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 of 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, though 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 , e.g. due to increase in R_{out} , which would move the operating point to the right along the pulsatility curve. This harmonizes with the predictive test of increased R_{out} . During a tap test the ICP is reduced by CSF removal,[33] which means 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 , i.e. 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 weighs together 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 the necessary data is 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 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 the CSF dynamics similar to the pulsatility curve include RAP index[21] and elastance index (EI).[34] EI, 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. RAP index describes short term correlation between ICP and AMP , with values close to zero signifying

good compensatory reserve, i.e. a state of high compliance.[21] This harmonizes with the pulsatility curve analysis, since 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 (Appendix, Web only). 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.

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COMPETING INTERESTS

Sara Qvarlander and Bo Lundkvist declared no competing interests. Lars-Owe D. Koskinen has received honorary for lecturing from Johnson&Johnson (Codman company). Jan Malm is listed as an inventor on a patent re: CSF dynamic investigation apparatus, for which he has received royalties from Likvor AB. Anders Eklund 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.

CONTRIBUTORSHIP

Sara Qvarlander contributed to the study concept and design, analysis and interpretation of data, drafting and revision of the manuscript, as well as the statistical analysis. Bo Lundkvist contributed to the analysis and interpretation of data, and revision of the manuscript. Lars-Owe D. Koskinen contributed to the analysis and interpretation of data, and drafting and revision of the manuscript. Jan Malm contributed to the study concept and design, analysis and interpretation of data, and drafting and revision of the manuscript. Anders Eklund contributed to the study concept and design, analysis and interpretation of data, and drafting and revision of the manuscript.

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