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Kahlon, Babar; Sundbärg, Göran; Rehncrona, Stig

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LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Lumbar infusion test in normal pressure hydrocephalus

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Objective – To compare potential clinical value of plateau pressure (P_{pl}), resistance to outflow (R_{out}), pulse-pressure amplitude (P_{plA}) and rate of pressure increase (v_P), taken from the constant rate lumbar infusion test (LIT), as predictors for the outcome of shunt surgery.

Methods – Recordings from preoperative LIT in 55 patients were scrutinized for the values of P_{pl} , P_{plA} , v_P and R_{out} . Gait, memory, spatial capacity and reaction ability were tested before and 6 months after shunt surgery. **Results** – Forty-three (78%) of the patients improved. There were no statistically significant differences in P_{pl} , R_{out} , P_{plA} or v_P between improved and not improved patients. Five patients with P_{pl} below 22 mmHg (the cut off level) improved after shunting, while 16 and eight patients with R_{out} below the cut off levels of 18 and 14 mmHg/ml/min improved. P_{plA} correlated with P_{pl} and R_{out} ($r = 0.74$ and 0.63 , respectively). In the group of patients with high P_{plA} (≥ 20 mmHg) as many as 93% improved but a high P_{plA} did not recruit more improved patients than P_{pl} or R_{out} alone. **Conclusion** – v_P or P_{plA} does not add useful information to P_{pl} for selecting patients with suspected NPH for surgery. R_{out} calculations from LIT does not provide advantage over using the steady-state plateau pressure for selecting patients for surgery and may increase the risk of missing patients who should benefit from surgery.

**B. Kahlon, G. Sundbärg,
S. Rehncrona**

Department of Neurosurgery, University Hospital, Lund, Sweden

Key words: lumbar infusion test; normal pressure hydrocephalus; patient selection; plateau pressure; resistance to outflow

B. Kahlon, Department of Neurosurgery, University Hospital, 221 85 Lund, Sweden

Tel.: +46 46 171581

Fax: +46 46 188150

e-mail: babar.kahlon@neurokir.lu.se

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As treatment of normal pressure hydrocephalus (NPH) by diversion of cerebrospinal fluid (CSF) with a shunt procedure was proved effective, it is assumed that resorption of CSF might be of central importance in the pathophysiology of this syndrome (1). After the description of NPH by Hakim and Adams (2) many authors have developed clinical tests for measuring the capacity for CSF resorption, aiming at selecting patients for shunt surgery (1, 3–6). Thus Hussey et al. found that a plateau pressure (P_{pl}) above 22 mmHg reached during a constant rate of infusion (0.76 ml/min) in the lumbar spinal CSF space could be used as selection criterion for shunt surgery (7). Ekstedt (5, 8) meticulously measured the CSF outflow conductance using a constant pressure infusion test (5) and Borgeesen (1) reported that conductance to outflow below 0.008 ml/min/mmHg could predict a good outcome of surgery. By analogy, in a recent study, Boon et al. (9) measuring the CSF outflow

resistance (R_{out}), i.e. the reciprocal of outflow conductance, reported that $R_{out} \geq 18$ mmHg resulted in the best likelihood ratio with improvement rates above 90% as measured with objective clinical evaluations. On the other hand, Malm et al. (10) had found that conductance to outflow measures were of little or no value as criterion of NPH.

In our department, we have a long experience (more than three decades) of using the constant rate lumbar infusion test (LIT) for selecting patients with clinical signs of NPH for surgery. In a recently published study we found that $P_{pl} \geq 22$ mmHg showed a positive predictive value of 80% and was complementary to the CSF taptest (11). In the present study, we scrutinized LIT curves in 55 consecutive patients to find if other measures than only the infusion pressure plateau level could be useful in predicting outcome after shunt surgery.

Materials and methods

Patients and surgery

Fifty-five patients who were referred to the Department of Neurosurgery, University Hospital in Lund, during years 1996–2001, with clinical symptoms of NPH and ventricular widening (Evans index > 30) on CT and/or MRI were included consecutively. Only the patients selected for surgery were studied. The patient material was a cohort of patients from an earlier study (11) with eight additional patients. Eighty-five percent (47/55) had no earlier CNS disease and were classified as idiopathic. Fifteen percent (8/55) were classified as secondary: four had an earlier history of spontaneous intracerebral haemorrhage, three had earlier history of head trauma and one had earlier CNS infection. The assumed provoking factors occurred more than 5 years before enrolment and the relationships to symptom development were unclear. All patients and relatives were informed and gave their consent to participation. The patients were selected for shunt surgery either because of a positive LIT with the only criterion of an infusion pressure plateau level above 22 mmHg ($n = 36$) or a positive CSF tap test ($n = 19$) (11). The patients were operated with either a ventriculo-peritoneal ($n = 54$), or ventriculo-venous ($n = 1$), adjustable shunt system (Codman-Hakim model 82-3100; Johnson & Johnson Co., Raynham, MA, USA). The opening pressure of the valve was set at 120–180 mmH₂O at surgery and adjusted (if needed) to the optimal individual level during the following months. If clinical suspicions of defective shunt function, the patients were re-examined with CT, X-ray and LIT. Three to 12 months (6 ± 4.6 ; mean \pm SD) after surgery the patients were re-evaluated using the same test battery as preoperatively (11, 12). This test battery included walk test, reaction time test, memory and identical forms test. Five percent (walk and reaction time) and 25% (memory and identical forms) improvement compared to the best of two baseline measurements was considered significant [for details see Ref. (11)]. Significant improvements in at least two of these four different tests as compared with preoperative results were required to classify the patient as objectively improved. The patients' and their relatives' subjective impressions of improvement were also recorded.

Lumbar infusion test

LIT was performed with the patient in the lateral recumbent position with two needles (diameter 0.9 mm) inserted in the lower lumbar region (L3-4 or L4-5). One of the needles was connected to a closed pressure recording device (DPT-6100, Smiths

Medical, Kirchseeon, Germany) and the other to an infusion pump (TOP syringe pump 5100; TOP Corporation, Tokyo, Japan). Pressure recording was calibrated stepwise between 0 and 50 mmHg immediately before and after each measurement. The initial steady-state CSF pressure was recorded (until a stable initial pressure curve for at least 10 min was obtained) before starting a constant rate (0.80 ml/min) infusion of Ringer solution (NaCl 6.6 g/l, KCl 0.3 g/l, CaCl 0.33 g/l; 290 mosm/kg) through one of the needles. The CSF pressure was continuously recorded through the other needle via the pressure-monitoring device connected to a printer. The CSF pressure was recorded continuously during a period of at least 45 min to establish a steady-state pressure plateau representing the pressure level at which absorption balanced infusion (Fig. 1). In one patient the infusion was stopped earlier than 45 min because pressure increased to above 50 mmHg. The steady-state plateau pressure (P_{pl}) exceeding 22 mmHg was used as a selection criterion for shunt surgery (7, 11).

Calculations and statistics

After the clinical follow up of the patients, P_{pl} was recalculated and the following additional measures were extracted from the recorded pressure curves (see Fig. 1): initial steady-state CSF pressure (P_{in} , mmHg), i.e. the pressure before starting the infusion; the rate of pressure increase during the first 5 min of infusion (v_p , mmHg/min); initial pulse-pressure amplitude (P_{inA} , mmHg), i.e. the pressure amplitude before the start of infusion; infusion plateau pulse-pressure amplitude (P_{plA} , mmHg),

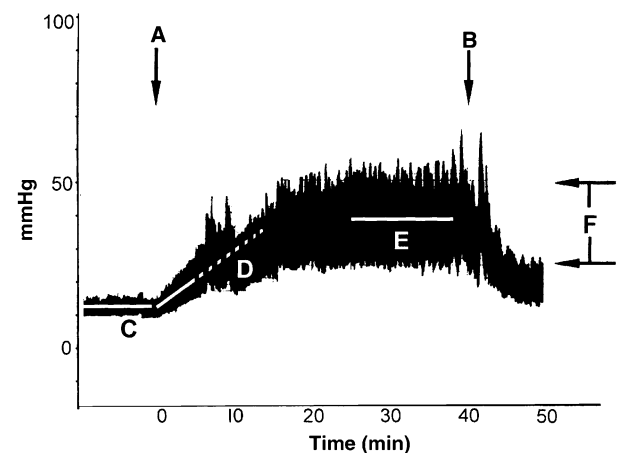


Figure 1. Lumbar infusion test recording (A) Start of the constant rate infusion (0.8 ml·min⁻¹). (B) End of the infusion. (C) Initial steady state cerebrospinal fluid pressure (P_{in}) (mmHg). (D) rate of pressure increase during the first 5 min (v_p) (mmHg·min⁻¹). (E) Steady state plateau pressure (P_{pl}) (mmHg). (F) Plateau pulse-pressure amplitude (P_{plA}) (mmHg).

i.e. the amplitude at the plateau; the time to reach the steady-state plateau pressure level (T_{pl} , min) as well as the total infusion time (T_{inf} , min). Resistance to outflow (R_{out}) was calculated as $(P_{pl} - P_{in})$ /infusion rate, mmHg/ml/min (1, 6, 8, 9).

Descriptive statistics are given as mean \pm SD. For comparisons between groups the non-parametric Mann–Whitney U -test was used. The Spearman rank correlation (r_s) was used for correlations. The statistical data was calculated with GraphPad InStat version 3.1 (GraphPad Software, San Diego, CA, USA).

Results

Demographic data and complications

In all 55 patients (22 males and 33 females) were included. Mean age was 73.5 ± 7.1 (range 43–85)

Table 1 Summary of preoperative LIT data in improved and not improved patients after shunt surgery

Category	Improved (n = 43)	Not improved (n = 12)	Mann–Whitney test (P-value)
P_{pl}	28.6 \pm 8.2	27.5 \pm 4.9	0.618
P_{in}	12.0 \pm 3.1	11.6 \pm 2.6	0.729
v_p	1.1 \pm 0.52	1.0 \pm 0.61	0.751
R_{out}	20.8 \pm 8.6	19.9 \pm 6.3	0.878
P_{inA}	4.9 \pm 2.5	4.0 \pm 1.8	0.294
P_{plA}	17.0 \pm 6.7	14.8 \pm 3.9	0.475
$P_{plA} - P_{inA}$	12.1 \pm 5.4	10.8 \pm 3.7	0.684
T_{pl}	33.7 \pm 12.4	31.7 \pm 8.7	0.691
T_{inf}	58.6 \pm 12.0 ¹	61.2 \pm 8.6	0.472

Values represent mean \pm SD. P_{pl} , steady-state plateau pressure (mmHg); P_{in} , steady-state initial pressure (mmHg); v_p , rate of pressure increase (mmHg/min); R_{out} , resistance to outflow (mmHg/ml/min); P_{inA} , initial pulse-pressure amplitude (mmHg); P_{plA} , plateau pulse-pressure amplitude (mmHg); T_{pl} , time to reach steady-state plateau pressure (min); T_{inf} , total infusion time (min).

¹ $n = 42$. One patient was excluded as the lumbar infusion was stopped after 20 min as the CSF pressure rose to above 50 mmHg with a short plateau.

Table 2 Summary of symptoms and improvement rates in relation to cut off levels

	Patients		Results after surgery, n (%)		Symptoms prior to surgery, n (%)		
	n	Age, Years (SD)	Objectively improved	Subjectively improved	Gait	Memory	Incontinence
All patients	55	74 (7)	43 (78)	52 (94)	52 (94)	42 (76)	39 (71)
Ppl \geq 22	49	74 (7)	38 (78)	47 (96)	46 (94)	38 (78)	36 (73)
Ppl <22	6	73 (7)	5 (83)	5 (83)	6 (100)	4 (67)	3 (50)
R out \geq 18	34	74 (6)	27 (79)	34 (100)	32 (94)	27 (79)	25 (74)
R out <18	21	72 (9)	16 (76)	18 (86)	20 (95)	15 (71)	14 (67)
R out \geq 14	45	74 (7)	35 (78)	45 (100)	43 (96)	36 (80)	33 (73)
R out <14	10	71 (7)	8 (80)	7 (70)	9 (90)	6 (60)	6 (60)
PplA \geq 20	14	77 (4)	13 (93)	14 (100)	13 (93)	13 (93)	9 (64)
PplA <20	41	72 (8)	30 (73)	38 (93)	39 (95)	29 (71)	30 (73)
PplA \geq 20 and Ppl \geq 22	14	78 (4)	13 (93)	14 (100)	13 (93)	13 (93)	9 (69)
PplA <20 and Ppl \geq 22	35	77 (8)	25 (71)	33 (94)	33 (94)	25 (71)	27 (77)
PplA \geq 20 and R out \geq 18	13	76 (4)	12 (92)	13 (100)	12 (92)	12 (92)	8 (62)
PplA <20 and R out \geq 18	21	73 (6)	15 (71)	21 (100)	20 (95)	15 (71)	17 (81)

years. Fifty-two (94%) of the patients had gait disturbance, 42 (76%) memory disturbance and 39 (71%) were incontinent, while 30 (54%) had all three symptoms.

The immediate post-surgical period was complicated with subdural haematomas/effusions in four patients. Two required surgical evacuation while two resolved after increasing the shunt opening pressure to 200 mmHg for a limited time period. One patient with pulmonary embolism was successfully treated with anticoagulants and one patient with a superficial wound infection healed with antibiotics. All complications resolved before the follow-up evaluation and we have no reasons to believe that they influenced the test results.

LIT data in improved and not improved patients

Basic LIT data as well as the numbers of improved and not improved patients are given in Table 1. For the total group of 55 patients the steady-state plateau pressure was 28.3 ± 7.5 mmHg (mean \pm SD) and R_{out} 20.5 ± 8.1 . Forty-three (78%) of the 55 patients (P_{pl} 28.6 ± 8.2 ; R_{out} 20.8 ± 8.6) improved while 12 (22%) patients (with P_{pl} 27.5 ± 4.9 ; R_{out} 19.9 ± 6.3) did not. There were no statistically significant differences between the levels of P_{pl} or of R_{out} values to denote whether the patients were objectively (i.e. in at least two of the tests) improved or not (Table 1). The initial CSF pressure, the rate of pressure increase during infusion, neither the initial nor the plateau amplitudes differed between the improved and not improved patients (Table 1).

Improvement rates in relation to cut off levels

There were no clear differences in preoperative symptoms in patients with P_{pl} , R_{out} or P_{plA} in the

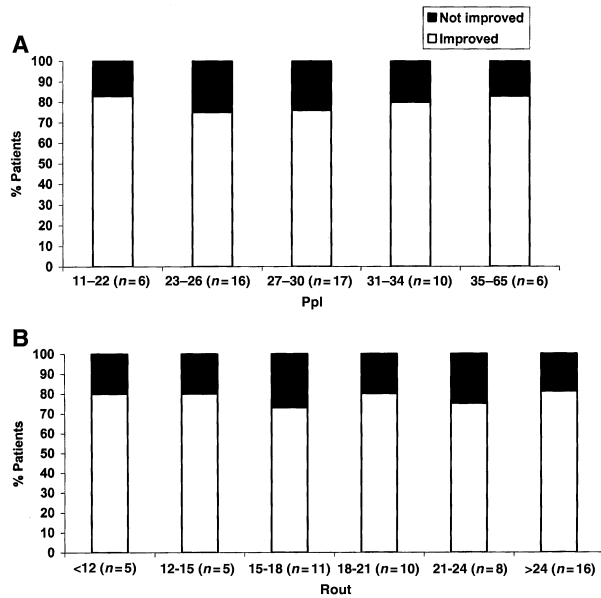


Figure 2. (A) Percent improved patients at different Ppl intervals. (B) Percent improved patients in different R out intervals. n, number of patients within each interval.

high or the low ranges (Table 2). The rate of subjective improvements (overall 94%) was higher than the test-verified improvements (overall 78%). This may be a result of the fact that improvement in more than one of the different tests was required to classify the patient as objectively improved. The highest proportion of improved patients was found in the group with high P_{plA} but these patients also had high P_{pl} and R_{out} values (Table 2).

P_{pl} and R_{out} – Figure 2A,B shows improvement rates in patient groups within different ranges of the plateau pressure and R_{out} . The proportion of improved (and not improved) patients was similar at all intervals. Out of the 49 patients with plateau pressures ≥ 22 (29.8 ± 6.4) mmHg, 38 (78%) improved. In six patients with $P_{pl} < 22$ (16.2 ± 3.3) mmHg, five patients (83%) also showed objectively verified improvements after surgery. The corresponding values for R_{out} in these groups were 21.8 ± 7.6 and 10.4 ± 4.4 mmHg/ml/min, respectively. Of the 34 patients with $R_{out} \geq 18$ (mean 25.2 ± 7.5) mmHg/ml/min, 27 (79%) improved after surgery as well as 16/21 (76%) patients with $R_{out} < 18$ (13.3 ± 4.1) mmHg/ml/min.

Pulse-pressure amplitude – There was a highly significant ($P < 0.001$) correlation between P_{plA} and P_{pl} ($r_s = 0.74$) as well as R_{out} ($r_s = 0.63$) (Fig. 3A,B). Fourteen patients had $P_{plA} \geq 20$ mmHg and all had a plateau pressure ≥ 22 (34.8 ± 9.3) mmHg and a high R_{out} (26.3 ± 9.9 mmHg/ml/min). Thirteen

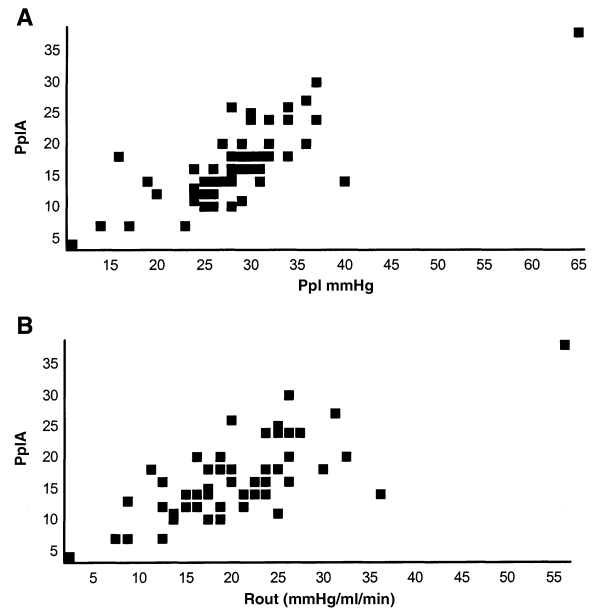


Figure 3. The plateau pressure amplitude (P_{plA} , mmHg) as correlated to: (A) the steady state plateau pressure (Ppl); and (B) the cerebrospinal fluid outflow resistance (R_{out}).

(93%) of them ($P_{plA} 25.2 \pm 4.8$ mmHg) improved after shunting while the improvement rate in 41 patients with $P_{plA} < 20$ mmHg (13.4 ± 3.5) was lower (73%). If $R_{out} \geq 18$ mmHg/ml/min was combined with a $P_{plA} \geq 20$ mmHg, 12 of 13 (92%) of the patients improved. One patient had $P_{plA} \geq 20$ mmHg but $R_{out} < 18$ mmHg/ml/min and this patient improved after surgery.

These results indicate that a high P_{plA} combined with the usually used cut off levels for infusion plateau pressure and R_{out} may further increase the chance for a beneficial effect of shunting.

Discussion

The present data support that LIT can predict improvement after shunt surgery in suspected NPH and close to 80% of the patients improved whether the steady-state plateau pressure level (P_{pl}) or resistance to outflow (R_{out}) was calculated and used as criterion for surgery. Calculations of R_{out} deselected more patients with improvement from surgery than the P_{pl} measurement. Unexpectedly, there were no statistically significant differences in P_{pl} or in R_{out} between improved and not improved groups after shunting. This observation may tend to reduce the clinical value of using LIT alone for patient selection and emphasize the importance of clinical judgement of symptoms (10). In an earlier study we found that the CSF tap test, which measures another aspect, is a useful complement (11). The main objective of the present study was to

find if additional information extracted from the LIT recordings could be of importance for predicting the result of shunt surgery. We will first discuss the value of R_{out} before discussing indices of compliance.

R_{out}

From a theoretical point of view R_{out} could be assumed to be of great importance as it is a direct measure of the capacity for CSF resorption. In the present material we find no results that support the view that calculations of R_{out} offer any advantages as compared with recording P_{pl} for predicting the outcome of surgery. On the contrary R_{out} calculations may increase the risk of deselecting patients who would benefit from a shunting procedure. Thus at an R_{out} cut off level of 18 mmHg/ml/min, as suggested by Boon et al. (9), 16 of the 43 patients with post-surgical improvement and, at 14 mmHg/ml/min eight patients had not been selected for shunt surgery. Using a P_{pl} cut off level of 22 mmHg only five patients of the 43 improved patients had been missed. This discrepancy may be related to the fact that the original method by Katzman and Hussey defines pathologic CSF dynamics based upon the patients' ordinary ICP challenged by the extra infusion of mock CSF (at approximately double the normal CSF production rate). Calculations of R_{out} instead deduct the initial pressure in the equation and, therefore, will exclude the influence of the patients' ordinary ICP level and may underestimate patients with ordinary resting ICP in the higher normal range or patients with a slightly increased ICP (13).

Admittedly, R_{out} as well as CSF conductance measurements using the more elegant (but more complicated) methods give more information about the CSF resorption capacity (1, 5, 8, 10). They have, however, in clinical practice never been shown to be better predictors of outcome from shunt surgery than a simple measurement of the P_{pl} . Our data indicate that the original cut off level based on P_{pl} at a constant rate infusion may have clinical advantages.

Measures of compliance

A decreased compliance with restriction of the compensatory reserves is assumed to be involved in the development of NPH symptoms (6, 14). Therefore, we calculated the rate of pressure increase before reaching the steady-state plateau and measured the pulse-pressure amplitude at the plateau level as estimates of the compensatory

reserves in these patients. Thus a rapid increase in pressure during a constant infusion would indicate lower compensatory reserves and vice versa. By the same token high pulse-pressure amplitude would indicate low compensatory reserves. There were no differences in v_p or P_{plA} between the improved and not improved patients and neither v_p nor P_{plA} could select additional patients for improvement after shunting, who were not already selected by a $P_{pl} \geq 22$ mmHg or $R_{out} \geq 18$ mmHg/ml/min. However, if P_{plA} was above 20 mmHg the proportion of improved patients with $P_{pl} \geq 22$ increased from 79 to 93%. Our results do not indicate that measurements of the pulse-pressure amplitude or the rate of pressure increase in LIT give additional help to P_{pl} and R_{out} for selecting patients for shunting, but they indicate that high plateau pulse-pressure amplitude will increase the possibility for improvement in patients already selected.

Conclusion

Measurements of the rate of pressure increase during infusion or the pulse-pressure amplitude with the LIT do not give additional useful information to the P_{pl} measurement for selecting patients with suspected NPH for shunt surgery.

Calculation of R_{out} from LIT using a constant rate infusion, does not provide any advantage over using a simple measurement of the P_{pl} . Using R_{out} measurements instead may result in an increased number of missed patients, who should have improved from surgery.

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