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Clinical study

The benefit of delayed reassessment post high-volume CSF removal in the diagnosis of shunt-responsive idiopathic normal-pressure hydrocephalus

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ABSTRACT

The principle aim of the study was to demonstrate the value of performing delayed reassessment in the diagnosis of idiopathic normal-pressure hydrocephalus (iNPH) and selection of suitable candidates for ventriculoperitoneal shunting (VPS).

Thirty-one consecutive patients underwent the NPH protocol at the Flinders Medical Centre between March 2017 and November 2018. The protocol involved mobility and cognitive testing with reassessment post high-volume cerebrospinal fluid (CSF) removal at 24 h and 48 h. The Assessment of Quality of Life 6D (AQoL-6D) questionnaire and International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF) were completed and repeated again at 6 weeks and 6 months post shunting. Results were analysed to determine the significance of delayed reassessment.

Twenty patients (64.5%) underwent insertion of a VPS on the basis of objective improvements and specific criteria. Of these, 6 patients (30%) were shunted based on delayed reassessment at 48 h post CSF removal. Continued improvements were seen for all mobility and cognitive tests from baseline to 48 h post CSF removal. At 6 weeks and 6 months post shunting, there was an overall mean improvement in AQoL-6D and ICIQ-UI SF for the cohort and the improvement was also observed in the subgroup of patients who met shunt criteria at 48 h post CSF removal.

In the diagnosis of shunt-responsive idiopathic normal-pressure hydrocephalus, delayed reassessment post CSF removal improves sensitivity and is therefore important.

1. Introduction

Idiopathic normal-pressure hydrocephalus (iNPH), first noted by Hakim in 1957 [1], is now a well-recognised entity yet the diagnosis and management of the condition remains controversial. The precise incidence and prevalence of iNPH is not known, but it is likely underdiagnosed. A set of guidelines encompassing the value of clinical presentation, supplementary diagnostic tests, surgical management, and outcome assessment were developed by Marmarou et al. in 2005 [2]. However, due to a lack of randomised trials in the field, questions remain. With an ever-ageing population, it is anticipated that more patients will be given a diagnosis of iNPH and thus further advancements in understanding are important.

Here, we address one particular dilemma regarding the diagnosis of patients suspected to have iNPH. Specifically, we look at the importance of timing of reassessment following removal of cerebrospinal fluid (CSF) via a high-volume CSF tap test (CSFTT) or prolonged external lumbar drainage (ELD). A delayed improvement in objective measures following removal of CSF has been demonstrated by several groups [3,4]. Our study emphasises the need for delayed reassessment in order to improve sensitivity and not dismiss patients who may have potentially otherwise benefited from ventriculoperitoneal shunt (VPS) insertion.

2. Methods

We collected data from 31 consecutive patients who underwent the NPH assessment protocol at Flinders Medical Centre (FMC) between March 2017 and November 2018. Recruitment was based on a reasonable clinical suspicion of iNPH with supportive radio-

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logical findings. Referrals came from other healthcare professionals including neurologists, geriatricians and general practitioners.

The study protocol was approved by the Southern Adelaide Clinical Human Research Ethics Committee (reference number HREC/17/SAC/273) and was conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007). All participants gave their informed consent in writing for data collection and analysis.

2.1. NPH assessment protocol

Recruited patients first underwent a battery of mobility and cognitive tests either as an outpatient or inpatient, serving as a baseline for later comparison following CSF removal. The mobility tests were: 10 m walk test (10 mwt), de Morton Mobility Index (DEMMI) and Berg Balance Scale (BBS). Patients were videoed allowing for a subjective assessment and comparison of the quality of their mobility before and after CSF removal. The cognitive tests were: Addenbrooke's Cognitive Examination – III (ACE-III) and Trail Making Test A and B (TMT A and TMT B). These results were recorded as time-point 1 (TP 1).

The process of CSF removal and subsequent repeat testing was conducted as an inpatient. A high-volume CSFTT was performed with an aim to remove 30–50 ml. Patients were positioned in the lateral decubitus position and a measurement of the opening and closing pressure of CSF was recorded. Once the 30 ml mark was reached, CSF removal continued unless the patient complained of a significant headache, indicating low intracranial pressure. Patients remained resting flat in bed for 4 h following the lumbar puncture (LP).

The mobility and cognitive tests were repeated at 24 h and 48 h post CSF removal and results were recorded as time-point 2 (TP 2) and time-point 3 (TP 3), respectively.

A record was also obtained of the patient's and observer's subjective opinion of performance at TP 2 and TP 3. Observers were typically a family member or friend, present during the testing process.

The results of the objective mobility and cognitive tests were compared to baseline and used to decide if a patient was a suitable candidate for insertion of a VPS. This was on the basis of significant improvements in the individual tests and a set of predefined rules. For the mobility tests, the result was deemed a significant improvement if: 10 mwt $\geq$ 0.05 m/s; DEMMI $\geq$ 10 points; BBS $\geq$ 5 points. Furthermore, the result was deemed to be a marked significant improvement if: 10 mwt $\geq$ 0.10 m/s; DEMMI $\geq$ 20 points; BBS $\geq$ 10 points. For the cognitive tests, the result was deemed a significant improvement if: TMT A $\geq$ 7 s; TMT B $\geq$ 7 s; ACE-III $\geq$ 5 points. In order to qualify for a VPS, the patient had to have at least one significant result in mobility tests plus at least one significant result in cognitive tests at either TP 2 or TP 3. Alternatively, they had to have at least one marked significant result in mobility tests alone at either TP 2 or TP 3 despite no significant improvement in cognitive tests. Thus, more weight was given to improvement in the objective mobility testing.

The patient was electively readmitted for shunting within weeks of testing. All patients had a VPS with a programmable valve. This was either a Medtronic Strata II™ or Codman Certas™ with baseline settings of 1.5 or 4, respectively. Patients had routine post-operative imaging including a plain CT brain and shunt series X-ray to confirm appropriate shunt positioning. Patients were reviewed 6 weeks and 6 months post shunting, with repeat CT brain at 6 weeks or sooner if there was a clinical concern. If there were symptoms or imaging findings consistent with over-drainage, the shunt setting was increased by a factor of 1 setting. If the patient indicated that they had minimal improvement, and there were no concerns of over-drainage, the shunt setting was decreased by a factor of 1 setting. Patients who had a shunt setting adjustment were followed up sooner with or without a repeat CT brain.

For patients who did not qualify for VPS on the basis of the CSFTT, yet there was still a reasonable clinical suspicion of having iNPH, such as having a classic magnetic gait and/or the subjective feeling was favouring improvement at TP 2 or TP 3, repeat testing was conducted through an ELD protocol. This involved readmission and insertion of a lumbar drain with drainage of 10 ml/h for 24 h (total 240 ml). Assessments were again carried out after 24 h and 48 h post cessation of CSF drainage. If significant objective improvements were recorded on repeat testing, then the patient was offered a VPS.

Patients who did not ultimately qualify for a VPS through the NPH protocol, were referred back to neurology or geriatrics for a further opinion on the potential underlying aetiology of their clinical issue.

2.2. Questionnaires

Patients were asked two specific questionnaires namely the Assessment of Quality of Life 6D (AQoL-6D) and the International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF). The baseline questionnaires were done prior to CSF removal, usually on the day of admission. In patients who underwent insertion of a VPS, the questionnaires were repeated again at 6 weeks and 6 months post shunting and compared to baseline.

2.3. Statistical analysis

Statistical analysis was performed on patients who underwent insertion of a VPS. Summary statistics (mean and standard deviation) were calculated for mobility and cognitive assessments as well as results from the questionnaires. Results on TMT B were excluded as a high proportion of patients (n = 10/20, 50%) were unable to complete the task in the required time-frame. Fixed effects regression analysis using robust variance estimation with clustering by patients was performed to estimate the linear contrasts of the mobility and cognitive testing results between different time points (TP 2 vs TP 1, TP 3 vs TP 1, TP 3 vs TP 2). Tests for the linear contrasts were 2-sided with a significance level of 0.05. All statistical analyses were performed using Stata/IC 14 [5].

3. Results

3.1. Study participants and patient demographics

A total number of 31 patients underwent the NPH protocol, and of these, 20 patients (64.5%) subsequently underwent insertion of a VPS (Table 1). Nineteen patients (95%), qualified on the basis of results from a high-volume CSFTT alone whereas one patient (5%) was shunted following repeat testing through the lumbar drain protocol. The remaining patients (n = 11, 35.5%) were not shunted as they did not show benefit on objective testing and did not qualify for further reassessment via the lumbar drain protocol. Two of these patients were not able to participate completely due to significant mobility impairment (wheelchair bound) at baseline. Three other individuals had above average baseline results and minimal gains post CSFTT. The remaining 6 patients, likewise did not show any benefit.

For the shunted patients, the median age was 72 years (range 56–87 years), 15 (75%) of which were male and 5 (25%) female. None of these patients were in a wheelchair at baseline but 10 required either a single point stick (n = 3, 15%) or four-wheel

Table 1
Patient demographics.

Variables	All patients (n = 31)		Shunted patients (n = 20)	
Age (years):				
Median	73		72	
Range	56–87		56–87	
Gender:	**n**	**(%)**	**n**	**(%)**
Male	21	(67.7)	15	(75)
Female	10	(32.3)	5	(25)
Mobility aids:	**n**	**(%)**	**n**	**(%)**
Unaided	16	(51.6)	10	(50)
Single point stick	4	(12.9)	3	(15)
Four-wheel walker	9	(29.0)	7	(35)
Wheelchair	2	(6.5)	0	(0)

walker (n = 7, 35%). The remaining patients (n = 10, 50%), were mobilising without the use of an aid at baseline.

Of the shunted patients, 14 (70%) qualified on the basis of the results at TP 2 (24 h post CSF removal), whereas 6 patients (30%), qualified after repeat testing at TP 3 (48 h post CSF removal).

The results from the shunted patients were further statistically analysed.

3.2. Lumbar puncture results

The mean opening pressure was 17.5 cmCSF (range 7–29 cmCSF). The median volume drained was 40 ml (range 25–240 ml). The outlier of 240 ml was the patient who underwent the lumbar drain protocol. One patient only had 25 ml drained due to a significant low-pressure headache experienced during the LP.

3.3. Mobility and cognitive assessments

The mean performances in mobility and cognitive testing at baseline, 24 h, and 48 h are shown in Table 2. At 24 h there were improvements of 0.125 m/s ($P = 0.0032$) in 10 mwt, 4.05 ($P = 0.053$) in DEMMI, 3.35 ($P = 0.013$) in BBS, 14.7 s ($P = 0.092$) in TMT A, and 3.50 ($P = 0.0013$) in ACE-III (Table 3). By 48 h robust improvements in all performance measures were observed, compared to baseline (Table 3).

Table 2
Performance in mobility and cognitive testing.

Variable	Mean (SD)		
	TP 1 (n = 20)	TP 2 (n = 20)	TP 3 (n = 20)
Mobility tests			
10 mwt (m/s)	0.748 (0.327)	0.873 (0.254)	0.913 (0.293)
DEMMI	61.3 (20.2)	65.4 (20.2)	68.7 (21.7)
BBS	41.0 (9.7)	44.4 (8.6)	45.6 (9.7)
Cognitive tests			
TMT A (s)	82.2 (47.3)	67.5 (32.2)	61 (31.3)
ACE-III	73.3 (14.7)	76.8 (14.4)	79.9 (14.1)

10 mwt, 10 m walk test; ACE-III, Addenbrooke's Cognitive Examination – III; BBS, Berg Balance Scale; DEMMI, de Morton Mobility Index; SD, standard deviation; TMT A, Trail Making Test A; TP 1, time-point 1 (baseline); TP 2, time-point 2 (24 h post CSF removal); TP 3, time-point 3 (48 h post CSF removal).

The improvements in individual mobility and cognitive tests are demonstrated graphically in Figs. 1 and 2, respectively. Fig. 1A, 1C and 1E demonstrate the mean results of mobility tests for all shunted patients and show the trend of continued improvement from baseline to 48 h post CSF removal. Fig. 1B, 1D and 1F show a comparison of mean results between patients shunted on the basis of the 24-h results ($Mean_1$) to those shunted on the basis of the 48-h results ($Mean_2$). Improvements are seen in both groups. Similar trends and comparisons in cognitive assessments are shown in Fig. 2.

3.4. Questionnaires

At 6 weeks and 6 months post shunting, 19 patients (95%) and 18 patients (90%) completed the questionnaires, respectively. One patient (5%) did not complete either of the questionnaires as they were unwell from a concurrent medical condition and also had a permanent indwelling catheter. One patient (5%) was lost to follow-up at 6 months. The mean results for the questionnaires at baseline, 6 weeks and 6 months are shown in Table 4.

With regards to the AQoL-6D questionnaire, there was a mean increase in score of 0.158 ($P = 0.0013$) and 0.234 ($P < 0.001$) at 6 weeks and 6 months, respectively, compared to baseline. Furthermore, there was a mean increase of 0.0755 ($P = 0.0112$) at 6 months compared to 6 weeks (Table 5). That is, there was strong evidence of improvement in AQoL-6D at 6 weeks and patients continued to improve at 6 months post shunting (Fig. 3A).

With regards to the ICIQ-UI SF questionnaire, there was a mean decrease in score of 4.21 ($P < 0.001$) and 3.69 ($P = 0.0040$) at 6 weeks and 6 months, respectively, compared to baseline. There was a mean increase of 0.522 ($P = 0.45$) at 6 months compared to 6 weeks (Table 5). That is, there was strong evidence of improvement in ICIQ-UI SF at 6 weeks but no further improvement beyond this at 6 months (Fig. 3C).

Taken together, these results show an improvement in the questionnaires from baseline at 6 weeks, which are sustained at 6 months post shunting. Similar results are seen when comparing patients shunted on the basis of the 24-h post CSF removal results ($Mean_1$) to those shunted based on 48-h post CSF removal results ($Mean_2$) (Fig. 3B,D).

3.5. Complications

Of the 20 patients who were shunted, 2 (10%) developed asymptomatic bilateral subdural hygromas noted on the routine CT brain at 6 weeks post shunting. These patients had their shunt valve increased by a factor of 1 setting with resultant resolution of

Table 3
Performance in mobility and cognitive testing (linear contrasts).

Variable	Contrast (95% CI; *P* value)		
	TP 2 v TP 1	TP 3 v TP 1	TP 3 v TP 2
Mobility tests			
10 mwt (m/s)	0.125 (0.048–0.202; 0.0032)	0.165 (0.098–0.231; <0.001)	0.0395 (−0.0092–0.0882; 0.11)
DEMMI	4.05 (−0.59–8.16; 0.053)	7.35 (2.05–12.65; 0.0092)	3.30 (0.68–5.92; 0.016)
BBS	3.35 (0.80–5.90; 0.013)	4.60 (1.97–7.22; 0.0016)	1.25 (−0.43–2.93; 0.14)
Cognitive tests			
TMT A (s)	−14.7 (−32.0–2.6; 0.092)	−21.2 (−37.6 to −4.7; 0.015)	−6.45 (−13.0–0.78; 0.053)
ACE-III	3.50 (1.55–5.45; 0.0013)	6.60 (3.75–9.45; <0.001)	3.10 (1.25–4.95; 0.0023)

10 mwt, 10 m walk test; ACE-III, Addenbrooke's Cognitive Examination – III; BBS, Berg Balance Scale; DEMMI, de Morton Mobility Index; SD, standard deviation; TMT A, Trail Making Test A; TP 1, time-point 1 (baseline); TP 2, time-point 2 (24 h post CSF removal); TP 3, time-point 3 (48 h post CSF removal).

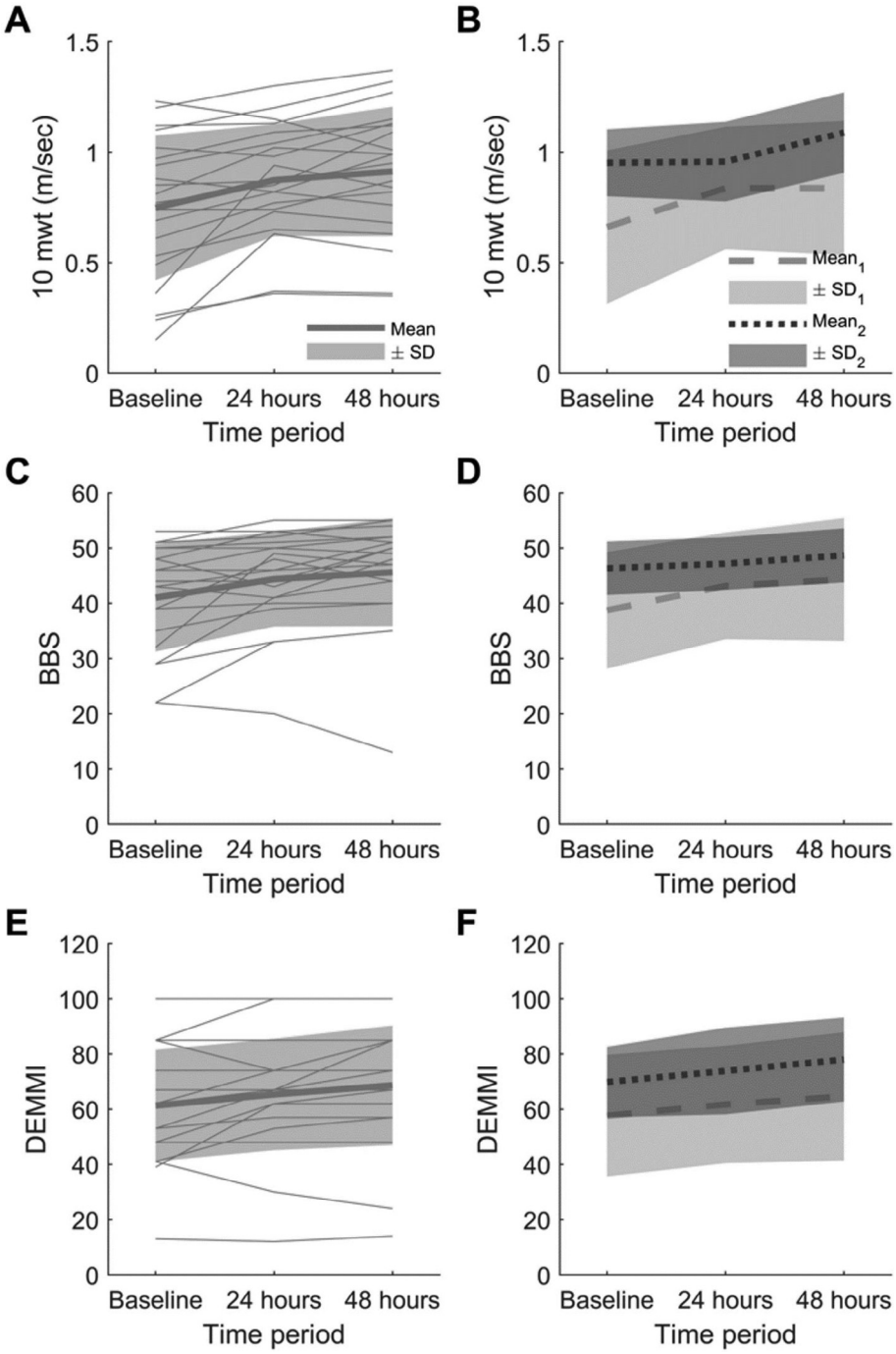

Fig. 1. Changes in mobility testing at 24 h and 48 h post CSF removal. *Left column*, individual and overall mean responses; *right column*, mean responses of subgroups meeting shunt criteria after 24 h ($Mean_1$) and 48 h ($Mean_2$). The shaded areas lie within one standard deviation of the mean. *(A) and (B)*, 10 m walk test; *(C) and (D)*, Berg Balance Scale; *(E) and (F)*, de Morton Mobility Index. SD, standard deviation.

the hygromas. One of these patients also required subsequent revision of the distal catheter due abdominal adhesions causing formation of an abdominal wall CSF collection. Despite this, both patients had objective improvements based on the questionnaires at 6 weeks and 6 months post shunting. One patient (5%) developed an asymptomatic small subdural haematoma on routine delayed imaging. Again, their shunt valve was increased by a factor of 1 setting with resultant resolution of the subdural haematoma. This patient had a significant improvement based on the AQoL-6D questionnaire but not the ICIQ-UI SF questionnaire at 6 weeks. Two patients (10%) suffered low-pressure headaches early post shunting necessitating an increase in the valve setting. Although both of these patients had resultant improvement in headaches following adjustment, one of them did not benefit from their shunt at 6 weeks nor 6 months based on the questionnaires. There were no mortalities related to the VPS insertion during the study period.

4. Discussion

Insertion of a VPS in patients with a suspected diagnosis of iNPH is not without potential morbidity and thus the decision should be

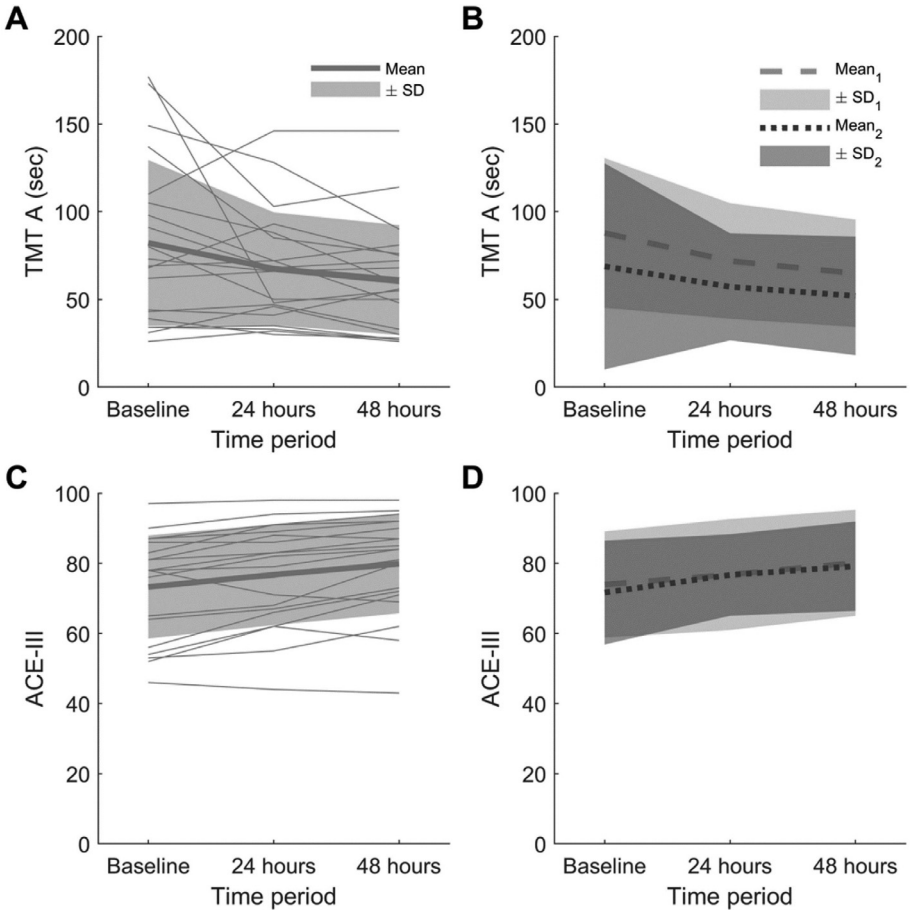

Fig. 2. Changes in cognitive testing at 24 h and 48 h post CSF removal. *Left column*, individual and overall mean responses; *right column*, mean responses of subgroups meeting shunt criteria after 24 h ($Mean_1$) and 48 h ($Mean_2$). The shaded areas lie within one standard deviation of the mean. *(A) and (B)*, Trail Making Test A; *(C) and (D)*, Addenbrooke's Cognitive Examination – III. SD, standard deviation.

Table 4
Outcomes at 6 weeks and 6 months.

Variable	Mean (SD)		
	Baseline (n = 19)	6 weeks (n = 19)	6 months (n = 18)
AQoL-6D	0.569 (0.213)	0.727 (0.197)	0.825 (0.123)
ICIQ-UI SF	7.37 (5.88)	3.16 (4.49)	3.17 (4.03)

AQoL-6D, Assessment of Quality of Life 6D; ICIQ-UI SF, International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form; SD, standard deviation.

given due consideration. The generally adopted approach is to shunt only on the basis of objective improvements in assessments after some form of CSF removal. Options include high-volume CSF tap test in the order of 30–50 ml, determination of CSF outflow resistance via an infusion test or prolonged ELD. A single standard for the prognostic evaluation of iNPH patients is lacking, but supplemental tests can increase predictive accuracy for prognosis to greater than 90% [6]. Prolonged ELD in excess of 300 ml is associated with high sensitivity (50–100%) and high positive predictive value (80–100%) in the diagnosis of shunt-responsive iNPH [6]. However, compared with a simple LP there is higher morbidity with increased risk of over-drainage particularly in patients with cognitive impairment and lowered compliance with remaining still in bed [2].

In addition to assessment post CSF removal, there is ongoing work in identifying less invasive approaches, including neuropsychological testing, urodynamic studies, video- and computer-assisted gait assessment and functional brain imaging [7]. Although these supplemental tests, in addition to tests involving CSF removal, may assist in the diagnostic process, one of the major dilemmas is the overlap that exists between iNPH and other diagnoses such as neurodegenerative disorders, cerebrovascular disease, urological conditions and spinal stenosis [7]. Ultimately the goal is to identify patients who will benefit from CSF diversion or the so-called "shunt responders", and avoid unnecessary, and

Table 5
Outcomes at 6 weeks and 6 months (linear contrasts).

Variable	Contrast (95% CI; *P* value)		
	6 weeks v baseline	6 months v baseline	6 months v 6 weeks
AQoL-6D	0.158 (0.0706–0.246; 0.0013)	0.234 (0.144–0.323; <0.001)	0.0755 (0.0194–0.132; 0.0112)
ICIQ-UI SF	−4.21 (−6.44 to −1.98; <0.001)	−3.69 (−6.04–−1.34; 0.0040)	0.522 (−0.900–1.94; 0.45)

AQoL-6D, Assessment of Quality of Life 6D; CI, confidence interval; ICIQ-UI, International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form.

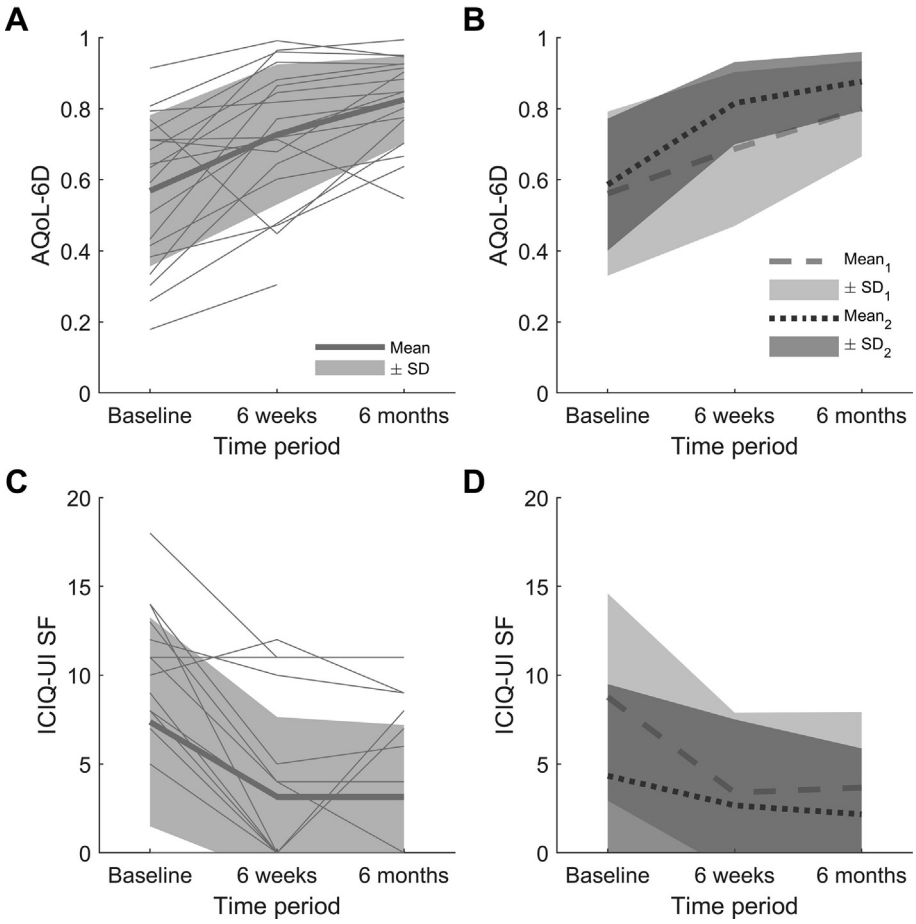

Fig. 3. Changes in questionnaire results at 6 weeks and 6 months post shunting. *Left column*, individual and overall mean responses; *right column*, mean responses of subgroups meeting shunt criteria after 24 h ($Mean_1$) and 48 h ($Mean_2$). The shaded areas lie within one standard deviation of the mean. *(A) and (B)*, Assessment of Quality of Life 6D; *(C) and (D)*, International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form. SD, standard deviation.

potentially risky, shunt insertion in individuals not felt likely to benefit.

The pathophysiology of iNPH is not entirely understood but several theories exist. It is felt that there are three main components: disturbed CSF circulation, poor pressure-volume compensation and abnormal cerebral blood flow (CBF) [8]. Some studies have shown that there is a correlation between normal CBF before shunting with a positive outcome, yet other studies have not been able to demonstrate this [8]. Likewise, there is weak evidence to suggest patient outcome after shunting is correlated with preserved autoregulation before shunting [8]. One group suggested that patients with ventriculomegaly commonly have a perinatal event followed by one of four main presentations: 1) incidental ventriculomegaly with or without headache; 2) highly symptomatic presentation (including reduced consciousness) and raised ICP; 3) early presenting with symptoms of headache and nausea (with abnormal pulsatility); and 4) late presenting with features common to normal-pressure hydrocephalus [9].

In our study we aimed to demonstrate the importance of delayed reassessment following high- volume CSF removal in order to capture all potential shunt responders. Of the 20 patients who were offered a shunt, 6 (30%) of them were shunted on the basis of the repeat testing at 48 h. Had we stopped at 24 h, these patients would not have been shunted and the potential therapeutic benefit would have been missed. In the study by Schniepp et al. [3], nearly half of the objective responders would have been missed within the first 24 h after LP. Kang et al. [4] reported on a patient who underwent a repeat CSFTT 3 months following initial testing with a negative result at 24 h. The patient underwent repeat testing given clinical deterioration, but on the subsequent occasion had multiple reassessments over 7 days following the LP. Peak benefit in mobility tests were seen at 72 h and by 7 days the benefit declined. The patients subsequently benefited from shunting. In another study [10], gait assessments were performed following removal of 30 ml of CSF on day 1 and repeated at day 4. This group found that the results at day 4 were not superior to those on day 1. However, there were no assessments during the interval period and thus the peak in improvement post LP may not have been captured.

One theory for the delayed improvement after repeat testing is simply due to learning effect. This, however, is disputed by the findings of several studies. Schniepp et al. [3] performed repeat mobility assessments post LP at 1–8 h, 24 h, 48 h and 72 h. The maximal increase in gait velocity was seen at 48 h after the LP. Following this however, the results trended back towards baseline. Solana et al. [11] analysed changes documented on 5 neuropsychological tests and several motor ability scales in a series of 32 patients with NPH who underwent the same battery on 4 consecutive days. Results were compared to 30 healthy volunteers. Interestingly, patients in the NPH cohort did not demonstrate statistically significant differences in any of the neuropsychological, apart from one test at day 3, or motor tests over 4 days. The healthy group did however demonstrate statistically significant improvement in several of the neuropsychological tests and in the motor performance test. The authors concluded therefore, that clinical improvement after retesting in patients with NPH reflects real changes rather than learning effect.

It is unclear why some patients may only show a delayed effect post CSF removal. Momjian et al. demonstrated that patients with iNPH have disturbed autoregulation of cerebral arteries, especially near the lateral ventricles, leading to oedema and local ischaemia and ultimately contributing to gait disturbance [12]. Removal of CSF results in improvement in periventricular vascular autoregulation. Additionally, by removing CSF, periventricular oedema can be improved as a result of changes in the interstitial fluid pressure with a downstream effect of enhanced clearance of vasoactive and neurotoxic metabolites [13]. Given that these processes may not be immediate phenomena, this can help to explain the delayed improvements seen in some individuals.

The natural history of iNPH is yet to be clarified. A clear understanding could potentially aid in the decision to treat versus manage conservatively and also influence timing of treatment. Presently, a standard approach is to proceed to shunting early after objective benefit is identified with supplementary testing. The rationale is to limit further progression and ideally reverse symptoms. Andrén et al. [14] compared the outcomes of iNPH patients who were treated after a delay of 6 months (n = 33) to patients who waited less than 3 months (n = 69). They used the iNPH scale and modified Rankin Scale (mRS) to measure outcomes at 3 months post-surgery. Although the magnitude of improvement post shunting was similar for both groups, the final outcome was significantly worse in the "delayed" group. Thus, they concluded that in order to maximise benefit of shunt treatment, surgery should be performed soon after diagnosis.

The clinical course post shunting of an iNPH patient can vary and although there are several grading scales for iNPH, there is no accepted standard for outcome assessment and long-term follow-up [15]. Studies have reported that prolonged positive response occurs in as few as 29% of iNPH cases [7]. There is also a group who suffer a clinical deterioration following shunting possibly related to over-drainage and associated low-pressure symptoms or from complications including infection or subdural haematoma. If a patient has an adjustable valve, it is possible to alter the setting to manage low-pressure symptoms or in the extreme case, depending on the valve used, effectively stop CSF diversion. The difficulty arises when a patient has not had an obvious complication and the benefit they've had from shunting has only been transient. An assessment needs to be made to decide if this is reflective of shunt malfunction or if it is the natural history of the disease taking over. One group routinely investigates this cohort of patients by performing a high-volume (40 ml) tap of the shunt reservoir and assessing mobility and cognitive function pre- and post-tap [16]. In their reported cohort of 29 patients, 18 subsequently underwent shunt revision after demonstrating positive results post tapping of the reservoir, and all of these patients saw an improvement in symptoms post revision.

In our cohort of iNPH patients who underwent insertion of a VPS, we demonstrated continued improvements in both mobility and cognitive assessments from baseline to 48 h post high-volume CSF removal. Patient mean results of the AQoL-6D and ICIQ-UI SF questionnaires indicated an overall benefit of VPS insertion out to 6 months post shunting, and this held when comparing patients who met shunt criteria based on results at 24 h versus 48 h post CSF removal.

5. Conclusion

A clinical management standard for diagnosing iNPH and identifying potential shunt responders remains to be determined. Here we have evaluated the importance of timing of testing post high-volume CSF removal and have demonstrated that delayed reassessment improves the sensitivity of detecting shunt responders.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jocn.2019.11.011.

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