Fluids and Barriers of the CNS

RESEARCH

Open Access

Ventriculosagittal sinus shunt for treating hydrocephalus with elevated cerebrospinal fluid protein

Yikang Wang[1], Di Wang[1], Yu Tian[1], Yilong Yao[1] and Qi Yu[1*]

Abstract

This study aimed to investigate the feasibility, acceptability, and preliminary efficacy of a ventriculosagittal sinus (VSS) shunt in the treatment of hydrocephalus with elevated cerebrospinal fluid (CSF) protein content. In this single-center retrospective analysis, we enrolled 80 patients with hydrocephalus and elevated CSF protein levels. Based on these procedures, primary cohort was divided into two groups using CSF protein (CSFP) for subsequent analysis to determine the relationship between the clinical effect and CSFP. Preoperative and postoperative computer tomography (CT) scans, clinical symptoms, and CSF laboratory test were compared. Clinical records of 80 patients were analyzed; 44 patients received VSS shunt, 30 patients received ventriculoperitoneal (VP) shunt, and 6 patients received ventriculobladder (VB) shunt. The most significant changes in ventricular size in the VSS shunt group were detected on the 7th day postoperatively from the collected imaging data. Six months after shunt surgery, the overall success rate for VSS shunt (35 of 44, 79.5%) was markedly higher than that for VP shunt (12 of 30, 40%) and VB shunt (1 of 6, 16.7%). The VSS shunt has a positive clinical effect in hydrocephalus with abnormal CSF laboratory results (elevated protein levels), which is more significant than the clinical success rate of VP shunt in terms of both symptoms and imaging results. The degree of relief and improvement of imaging and symptoms were unrelated to the CSFP content. There was no significant difference in the efficacy of VSS shunt between the CSFP < 1.0 g/L group and the CSFP > 1.0 g/L group. No intracranial or extracranial complications related to the surgery were noted during follow-up. The VSS shunt should be considered the first-line treatment option in cases of hydrocephalus with elevated CSFP levels. Moreover, VSS shunt can immediately improve symptoms and alleviate hydrocephalus even though the CSFP was elevated.

Keywords Hydrocephalus , Sagittal sinus , Cerebrospinal fluid , Ventriculosagittal sinus shunt , Ventriculoperitoneal shunt

Background

Hydrocephalus is a complex disease in the field of neurosurgery, resulting from a variety of causes, regardless of the patient's age. Headache, cognitive impairment, and gait abnormalities are common symptoms of hydrocephalus [1]. The established treatment strategy for communicating hydrocephalus (CH) due to dysfunction of CSF absorption is to drain CSF into the extracranial space, primarily the peritoneum. Endoscopic third ventriculostomy is a common treatment for obstructive hydrocephalus (OH). However, patients who undergo shunt treatment face a high likelihood of shunt revision and various shunt complications. Recent studies have shown that the average shunt survival rate at 5 years after shunt

*Correspondence:
Qi Yu
qi.yu@cmu.edu.cn
[1] Department of Neurosurgery, Shengjing Hospital of China Medical University, Room 1701, Sanhao Street 36, Shenyang 110004, China

surgery is 34% or less [2]. Poor shunt durability can lead to increased patients' financial costs, reduced quality of life, and psychological trauma for patients. It is imperative to develop more stable and reliable shunt systems.

The most common cause of shunt malfunction is mechanical failure. Moreover, early complications of VP shunt include rapid decompression and subdural hematoma [3]. Several reviews have concluded that the complications and failure rates of shunt surgery are determined by the pressure differences between ventricles and shunt targets, these differences fluctuate based on posture and daily physical activities. This means that maintaining the function of these shunting systems against the physiologic circulation of CSF is a challenge [4–7]. Programmable shunt valves and antisiphon devices can partially address the problem of the CSF siphoning effects. However, mechanical failure, such as tube obstruction, seems unsolvable. Proximal peritoneal catheter occlusion in VP shunt is caused by abnormal CSF composition or unpredictable factors, such as spontaneous knotting [8, 9]. Notably, elevated CSFP is the most common factor. As a result of the drainage of CSF to extracranial outlet sites in the manner of non-physiological CSF flow, in some of those spaces, the absorption function weakens. Moreover, proteins that cannot be absorbed may obstruct catheters, and shunt surgery ultimately fails.

Several published series have suggested that the option of shunt procedures close to CSF physiologic flow would reduce the risk of shunt failure in theory [4, 5, 10, 11]. The VSS shunt delivers excess CSF to the superior sagittal sinus (SSS), which is adjacent to thephysiologic circulation of CSF, where CSF is secreted into the cranial venous sinus. This concept was first proposed in 1896 by Gartner, and in 1908, Payr implanted tubes from the ventricle to the longitudinal sinus and the jugular vein [4]. One major advantage of the VSS shunt is its ability to normalize intraventricular pressure (IVP) without complications in extracranial sites of the body, unlike other shunt operations. The clinical effect and safety of ventriculosinus shunts have been demonstrated in several reported case series. The VSS shunt has been applied as a surgical treatment for hydrocephalus with postoperative infection after VP shunt failure, and no repeat infection has occurred [12, 13]. Consequently, VSS shunt should be considered an option for hydrocephalus patients with elevated CSFP, particularly when CSF laboratory results contraindicate the placement of VP shunt.

Compared to the lower level of CSFP in healthy individuals, elevated CSFP can occur in postinfectious hydrocephalus and postoperative infections following shunt surgery, particularly in patients with hydrocephalus secondary to intracranial neoplasia. In cases of neoplasia or infection, elevated CSFP levels should be restored to normal or near normal for preliminary shunt surgery. In general, continued drainage of CSF until shunt surgery can be performed is often a prolonged process; however, in addition to surgery, the progression of hydrocephalus and many inevitable problems associated with CSF external drainage must also be considered. Traditional strategies for normal CSF drainage are unsuitable for CSF with elevated protein content, as longer catheters are known to increase the possibility of large protein floc deposition [14]. Pressing the reservoir continuously can partially promote the flow rate of CSF, reducing the risk of smaller protein floc accumulation. Additionally, drainage of fluid with elevated protein underlies the adhesions or wrappings of the catheter end and tissue [15, 16]. We expect to establish an ideal shunt system for hydrocephalus with elevated protein content in CSF, featuring a shorter catheter length and a site capable of steadily absorbing CSF. Considering the physiological circulation of CSF and its role in the process of intracranial infection, the VSS shunt might become a promising approach for hydrocephalus patients with elevated CSF protein levels.

Herein, we analyzed the outcomes and preliminary efficacy of VSS shunt, VP shunt, and VB shunt to identify the most effective surgical approach for future hydrocephalus treatment.

Methods

Patient population and study endpoints

Eighty patients with hydrocephalus accompanied by elevated CSFP underwent shunt surgery from May 2010 to May 2023 at Shengjing Hospital of China Medical University. The mean age was 48.0 years, and 53.7% (43 of 80) were male (Table 1). An elevated CSFP was defined as a value greater than 0.45 g/L. In addition to the three groups of shunts, namely, VSS, VB, and VP shunts, the cohort was divided into two groups based on intraoperative CSFP levels: the CSFP < 1.0 g/L group (48 of 80, 60%; mean CSFP = 0.704 g/L) and the CSFP > 1.0 g/L group (32 of 80, 40%; mean CSFP = 1.637 g/L), according to laboratory examination. Ultimately, the entire cohort was divided into six groups: the VSS shunt-CSFP < 1.0 g/L group (29 of 80), VSS shunt-CSFP > 1.0 g/L group (15 of 80), VB shunt-CSFP < 1.0 g/L group (2 of 80), VB shunt-CSFP > 1.0 g/L group (4 of 80), VP shunt-CSFP < 1.0 g/L group (18 of 80) and VP shunt-CSFP > 1.0 g/L group (12 of 80). The rates of clinical success and clinical failure in each group were analyzed and compared. Moreover, postoperative imaging and symptom changes were

Table 1 Patient demographics

Patient characteristics

	CSFP>1.0g/L (n=32)	CSFP<1.0g/L (n=48)	Total Cohort (n=80)
Baseline Data*			
EI	0.49	0.457	0.47
FH/ID	0.565	0.526	0.541
MMSE	13	13.542	13.325
BI	41.719	44.792	43.563
CSFP(g/L)	1.637	0.704	1.077
*: $\bar{x}$			
Demographics			
Age	47.3	48.4	48
Sex			
Male	16 (50%)	27 (56.25%)	43 (53.75%)
Female	16 (50%)	21 (43.75%)	37 (46.25%)
Causes of hydrocephlus			
Post-infectious	2 (6.25%)	14 (29.17%)	16 (20%)
Post-traumatic	5 (15.63%)	4 (8.33%)	9 (11.25%)
Post-hemorrhagic	18 (56.25%)	16 (33.33%)	34 (42.5%)
iNPH	6 (18.75%)	6 (12.5%)	12 (15%)
CH	0	2 (4.17%)	2 (2.5%)
OH	1 (3.13%)	6 (12.5%)	7 (8.75%)
Comorbidities			
Hypertension	28 (87.5%)	38 (79.17%)	66 (82.5%)
Diabetes	12 (37.5%)	23 (47.92%)	35 (43.75%)
Smoking history	17 (53.13%)	24 (50%)	41 (51.25%)
Dyslipidemia	17 (53.13%)	12 (25%)	29 (36.25%)
Venous Thromboembolism	5 (15.63%)	5 (10.42%)	10 (12.5%)
Previous treatment			
No shunt history	7 (21.88%)	9 (18.75%)	16 (20%)
After a shunt failure	30 (93.75%)	34 (70.83%)	64 (80%)
Presenting symptoms			
Headache	28 (87.5%)	36 (75%)	62 (77.5%)
Cognitive impairment	23 (71.88%)	32 (66.67%)	55 (68.75%)
Gait abnormalities	25 (78.13%)	45(93.75%)	70 (87.5%)
Incontinence	19 (59.38%)	16 (33.33%)	35 (43.75%)
Nausea and vomiting	17 (53.13%)	11 (22.92%)	28 (35%)
Epilepsy	10 (31.25%)	7 (14.58%)	17 (21.25%)

recorded to compare clinical outcomes. Before shunt surgery, all patients underwent various CSF bedside drainage procedures to maintain the CSFP as normal as possible, and consist CSFP levels for at least 3 days prior to surgery were required. Key surgical techniques and procedure-related complications were recorded during hospitalization. All participants provided informed consent.

We used the Mini-Mental State Examination (MMSE, more details in Figure S1) and Barthel Index (BI, more details in Figure S2) to estimate the level of cognitive impairment. The MMSE and BI are widely used in clinical practice for the assessment and treatment of hydrocephalus [17, 18]. Hydrocephalus was diagnosed by magnetic resonance imaging (MRI). The frontal horn/internal diameter (FH/ID) ratio is defined as the ratio between the frontal horn and internal frontal diameter, coupled with the Evans' index (EI) (the ratio between the frontal horn and the inner skull diameter), which are two popular tools for diagnosing hydrocephalus [19, 20]. We also collected medical history, CSF data, and data from physical examinations of the nervous system.

Clinical success was defined as continued effectiveness of the shunt system for more than 3 months as well as the identification of improvement both on imaging and according to symptoms of hydrocephalus at 3 months. The use of the 3-month outcome for efficacy assessment was the result of our thorough consideration. From 2010 to 2023, for patients who experienced shunt revision or removal due to elevated CSFP, the average duration of symptom recurrence was 2.8 months. Figure S3 shows the details of the follow-up information. In addition, this strategy is based on the theory that the failure rates of various diversion surgeries are very high at three months. Figure S4 showed full follow-up information for the cohort participants. Clinical failure was defined as no improvements in symptoms or imaging findings of hydrocephalus. The shunt system was found to be ineffective at 3 months, ultimately leading to revision or removal of the shunt system. Specifically, improvement was defined as a decrease in EI or FH/ID by more than 0.1 and an increase in MMSE score by more than 2 or an increase in BI score by more than 5 in terms of symptoms. Moreover, revision or surgical exploration can lead to clinical failure. Recovery of shunt system function through adjustment of the opening pressure of the programmable valve did not.

The inclusion criteria were as follows: (a) CSFP > 0.45 g/L, (b) MRI showing dilated ventricles, (c) cognitive impairment, incontinence, gait abnormalities, increased intracranial pressure, and (d) normal blood coagulation function. The first inclusion criterion was based on a series of studies on CSF and hydrocephalus [21–23]. The exclusion criteria included pregnancy, any infection, lack of follow-up records since surgery, missing or extreme data during the follow-up period, serious chronic diseases, and failure to meet the inclusion criteria. The flowchart of the participants' selection process in this study is detailed in Figure S5. The primary endpoint was deployment of the shunt system for at least 1 month, and the second endpoint was evaluated based on MRI features (Evans' Index, FH/ID ratio) and symptoms (MMSE score, BI score). The safety outcome was defined as the occurrence of serious complications resulting from VSS shunt. Patients were not affected by subjective factors or personal tendencies when the doctors explained their conditions to the patients and before patients underwent surgery.

Surgical procedure

The VSS shunt system comprises a valve (consisting of an adjustable differential pressure unit and a gravitational unit), a reservoir, and catheters. Preoperative magnetic resonance venography (MRV) was used to acquire the anatomic landmarks of the SSS. Under the conditions allowed, the surgical procedures could be assisted by a computer-assisted stereotactic neurosurgery navigation system if necessary. Whole hair removal and general anesthesia was performed with patients in the supine position. The frontal puncture point was placed 2–3 cm lateral to the midline and 1.5–2.5 cm frontal to the coronal suture. Making a straight scalp skin incision and drilling a skull hole, the ventricular catheter was then introduced into the ventricle between 4 and 6 cm through the skull hole and dural hole. After verifying the normal outflow of CSF, the IVP was calculated, and the catheter was clamped. The opening pressure of the valve was adjusted to 5 cm Hg lower than that of IVP. Enough space was left to position the valve and reservoir backward from the frontal puncture point, approximately 6–8 cm in adults (Fig. 1a–c).

The second puncture was made at the top of the SSS and alongside the sagittal suture. A 4-cm long skin incision was made in the forward and backward direction, and a skull hole was drilled as before to expose the SSS. Deep blue vascular shadows could be faintly observed below the dura. A wide subcutaneous tunnel was made between two punctures to pass the catheter. A 1 mL syringe was used to prick the dura and draw backward carefully, to define the location of the SSS, and a small incision was made on the SSS. The catheter was quickly inserted into the SSS and advanced 15 cm. Injection of 10 mL of normal saline was performed to determine whether the catheter was placed in the SSS. The valve and reservoir were positioned in the substratum of galea aponeurotic between two punctures. Around two skull

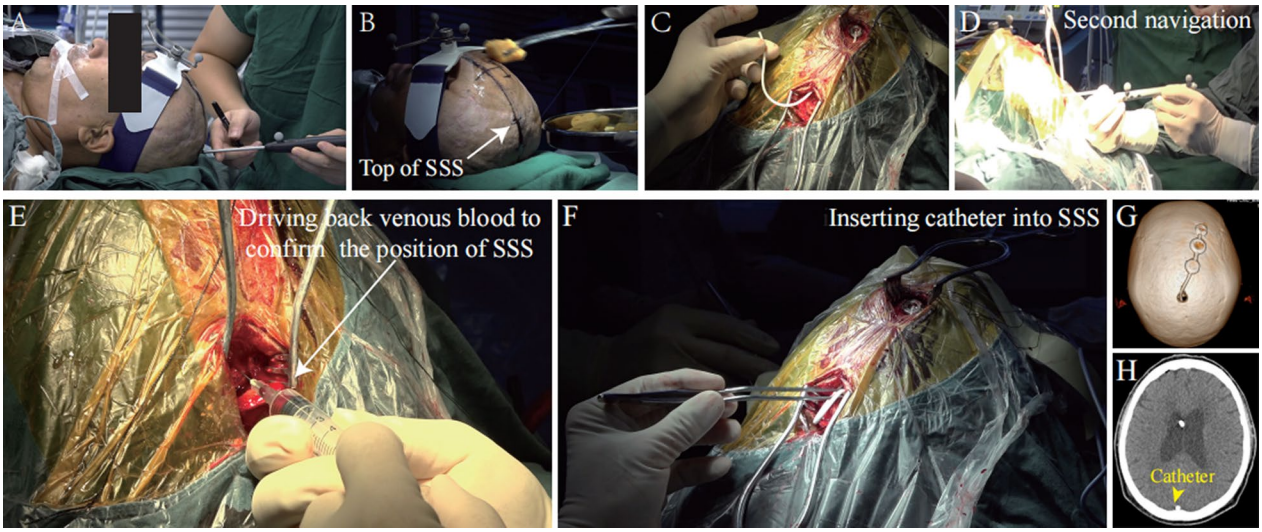

Fig. 1 Procedures for VSS shunt. Surgical design: With the application of a computer-assisted stereotactic neurosurgery system (**a**), two incisions were made at the routine frontal puncture point and the top of the SSS (**b**). The ventricular puncture was completed, and the catheter was introduced forward through the subcutaneous tunnel (**c**). The position of the SSS was confirmed with the navigation system before the SSS was cut (**d**). A syringe was used to carefully draw back venous blood. The precise location of the SSS was confirmed by the blood in a syringe (**e**). The prepared catheter was slowly inserted into the SSS (**f**). The exact implantation of a fixed VSS shunt system was checked postoperatively via 3D reconstructed CT scans (**g, h**)

holes, the gelatin sponge was filled with hemostasis to avoid CSF leakage. The function of the shunt system was confirmed by pressing the reservoir and the shunt system seated. A three-dimensional (3D) reconstructed CT scan was performed on day 1 Postoperatively to check the accuracy of shunt system implantation (Fig. 1d–g). The brief surgical process of the VP shunt (Figure S6) and VB shunt (Figure S7) could be found in the supplementary materials.

Statistical analysis

Continuous variables are expressed as $\bar{x} \pm$ standard error of the mean (SEM). Fisher's exact test was used to determine categorical variables. Repeated-measures ANOVA was used to analyze continuous variables between baseline and the results, as well as in between-group comparisons. Paired *t* test was used for analysis of 6-month follow-up data. The between-group effect was tested using Bonferroni correction. A p value < 0.05 represented statistical significance. Statistical Product and Service Solutions (SPSS) 27.0, developed by IBM, was used for statistical analysis (Figs. 2, 3).

Results

Baseline population

In total, 44 patients accepted the VSS shunt, 30 patients accepted the VP shunt, and 6 patients accepted the VB shunt. In our study, the mean CSFP was 1.077 g/L, and 38.6% (32 of 80) had a CSFP > 1 g/L. Elevated CSFP originated from postoperative infection of shunt surgery (64 of 80, 80%) and postinfectious hydrocephalus (16 of 80, 20%), which is identical to the result that 20% (16 of 80) of patients accepted shunt surgery for the first time and that 80% (64 of 80) of patients had previously undergone one or more failed shunt surgeries. The causes of hydrocephalus in this study were diverse, with post-traumatic hydrocephalus (9 of 80, 11.3%), postinfectious hydrocephalus (16 of 80, 20%), posthemorrhagic hydrocephalus (34 of 80, 20%), idiopathic Normal Pressure Hydrocephalus (iNPH) (12 of 80,15%), congenital hydrocephalus (CH) (2 of 80,3%) and OH (7 of 80,9%). Moreover, the causes of post-infectious hydrocephalus included encephalitis (8 of 16, 50%), meningitis (6 of 16, 37.5%), and tuberculous meningitis (8 of 16, 12.5%). The following results are expressed as the means: EI, 0.47; FH/ID, 0.541; MMSE, 13.325; and BI, 43.563 (Table 1).

Clinical outcomes

All eligible patients underwent surgery with successful implantation of the shunt system. No clinical failures of shunt surgery in our study occurred due to surgery-related infections, and no serious complications of shunt surgery were recorded. The average procedure time was 85 min. The time points of clinical failure for the VSS shunt, VP shunt, and VB shunt ranged from 9 to 70 days and were not at the same time within 3 months. All patients with clinical failure experienced shunt system

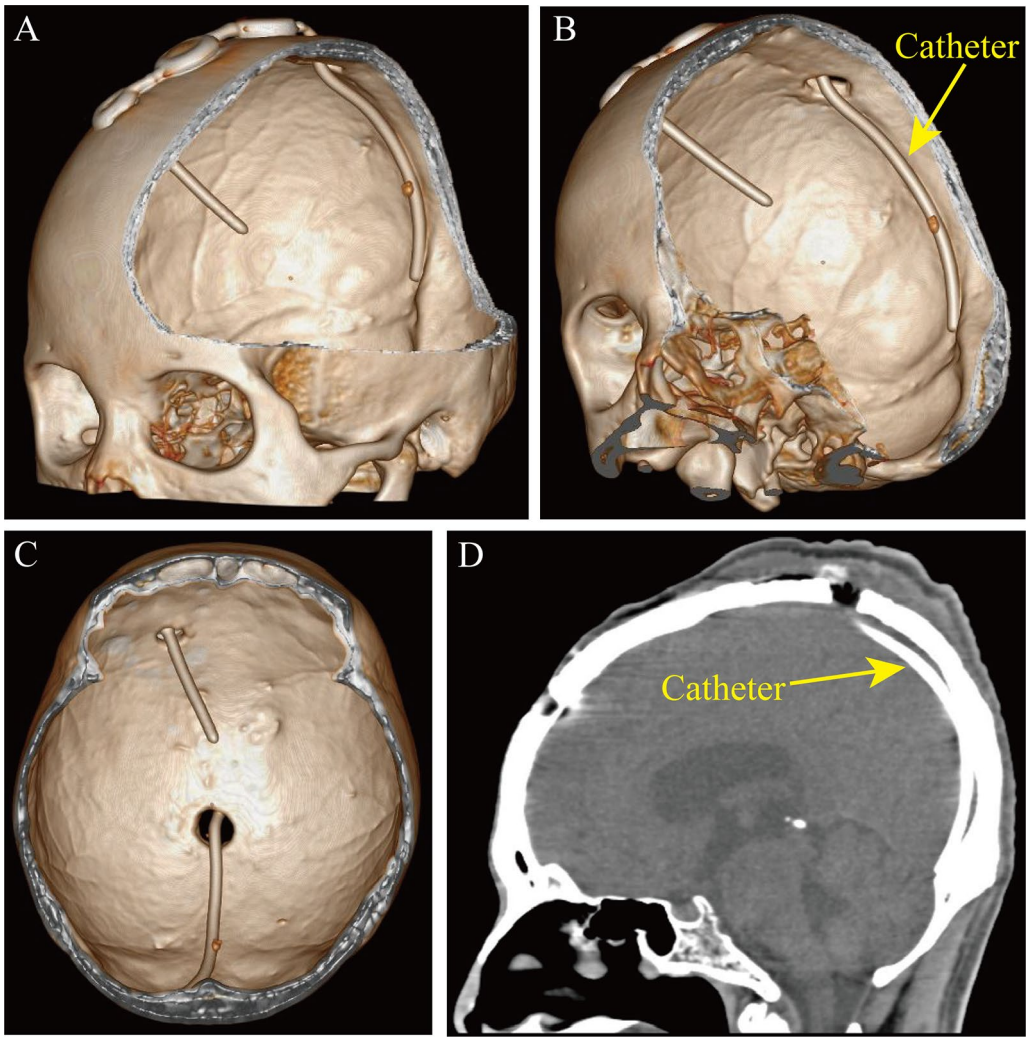

Fig. 2 The implantation of the VSS shunt system in the cranial venous sinus was scanned using 3D CT with a 1.0 mm-slice thickness. The volume rendering technique was utilized to generate dimensional images in three orientations. The data obtained were treated in an image workstation for 3D reconstruction to show the position of the VSS shunt system (**a–c**). The entire length of the catheter was measured in the sagittal plane, and the end of the distal catheter had not reached the confluence of sinuses and was concurrently below the ventricular end of the catheter on the horizontal plane (**d**)

revision under local anesthesia, and only 3% (3 of 29) regained function.

In terms of outcomes at 3 months, clinical success was achieved in 79.5% (35 of 44) of VSS shunts, 40% (12 of 30) of VP shunts, and 16.7% (1 of 6) of VB shunts (Table 2, $p < 0.01$). The percentage of clinical success with the VSS shunt was significantly greater than that with the VP shunt and the VB shunt. Moreover, the clinical success rates were 79.3% (23 of 29) in the VSS shunt-CSFP < 1.0 g/L group, 80% (12 of 15) in the VSS shunt-CSFP > 1.0 g/L group, 50% (1 of 2) in the VB shunt-CSFP < 1.0 g/L group, 0 (0 of 4) in the VB shunt-CSFP > 1.0 g/L group, 35.3% (6 of 17) in the VP shunt-CSFP < 1.0 g/L group and 46.2% (6 of 13) in the VP shunt-CSFP > 1.0 g/L group (Fig. 4). To evaluate the short-term postoperative changes in imaging data after surgery, we analyzed imaging data collected on the 7th day. The results revealed that differences in EI (F: 9.237, Table 3a, $p < 0.05$) and FH/ID (F: 9.309, Table 3b, $p < 0.05$) were statistically significant among the three types of shunt surgery (Fig. 5). Finally, with respect to symptoms and imaging, no differences in clinical effects were observed when comparing the VSS shunt-CSFP < 1.0 g/L group with the VSS shunt-CSFP > 1.0 g/L group (Table 4a, $p = 0.711$; Table 4b, $p = 0.841$; Table 4c, $p = 0.642$; Table 4d, $p = 0.558$). The average amount of

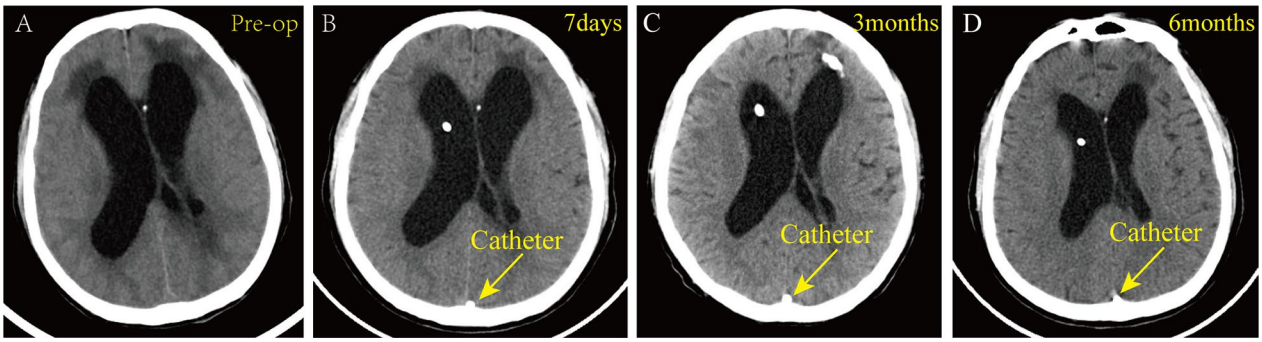

Fig. 3 A 50-year-old man was diagnosed with hydrocephalus, and the cause was a brain abscess with intracranial infection (**a**). The patient had undergone 21 days of lumbar drainage, and an antibiotic was administered to prevent infection. Afterward, the CSFP was continuously maintained above normal, with a content exceeding 0.75 g/L. Moreover, symptoms of infection, such as fever and neck stiffness, had completely disappeared, and four consecutive CSF cultures were negative. We implanted a VSS shunt for the patient. After the operation, considerable improvement in his symptoms was observed, such as hydrocephalus during gait and level of cognitive ability. After VSS shunt system implantation, CT scans at 7 days, 3 months, and 6 months post-procedure revealed diminished dilatation of the lateral ventricles (**b–d**)

Table 2 Comparisions of the clinical success ratio between three operations

Groups	Clinical success	Clinical failure	Total	Radio of clinical success
VSS shunt	35	9	44	80% (35 of 44)
VP shunt	12	18	30	40% (12 of 30)a
VB shunt	1	5	6	17% (1 of 6)a

a: p<0.01(comparing with VSS shunt)， Fisher's exact test

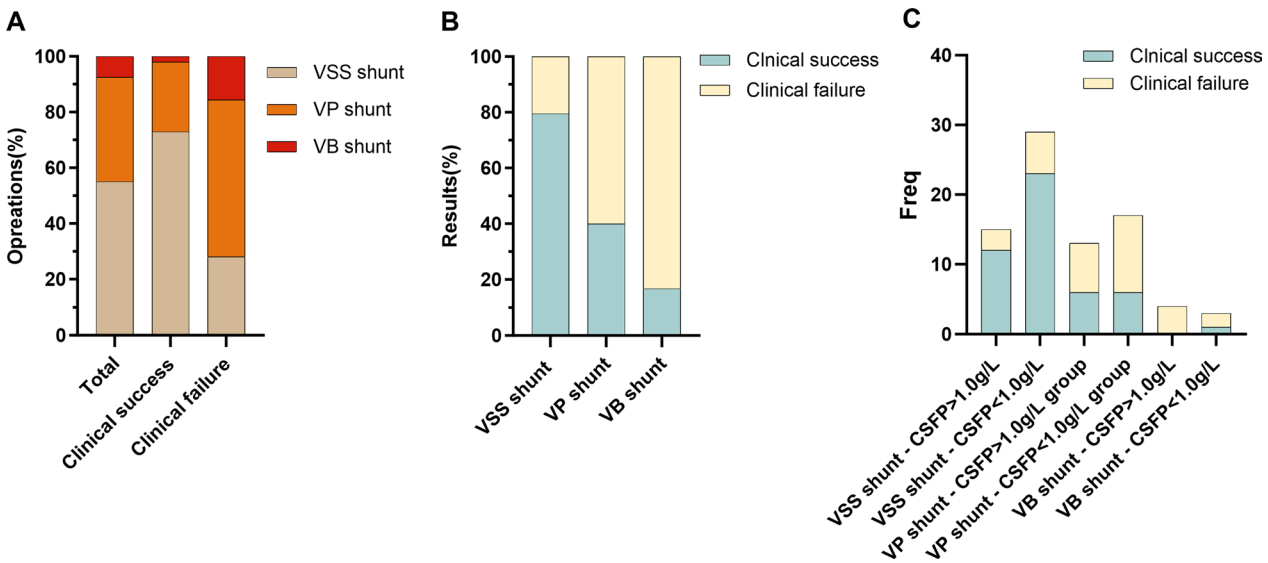

Fig. 4 Comparisons of 3 operative methods for hydrocephalus patients with elevated CSFP. **a, b** Outcomes of shunt surgeries in each group. **c** Proportion of 3 types of shunt surgeries in the total, clinical success and clinical failure groups

Table 3 Postoperative changes on the 7th day in ventricle size (x ± SEM) on CT (a) (EI) and (b) FH/1D

a: Postoperative changes on the 7th day in ventricle size (x ± SEM) on CT (EI)

	VSS shunt(n=44)	VP shunt(n=30)	VB shunt(n=6)	F value	P value
Baseline EI*	0.44±0.10	0.50±0.09	0.53±0.08	3.9	0.024
7Days EI*	0.37±0.1	0.49±0.09A	0.53±0.08A	16.553	<0.01
F value	137.72	19.33	2.14		
P value	p<0.01	p<0.01	p<0.01		
Time Effect(F,P)			33.908, <0.01		
Time*Groups Effect(F,P)			41.958, <0.01		
Groups Effect(F,P)			9.237, <0.05		
*:x ± SEM					
A: p<0.05(comparing with VSS shunt)					

b: Postoperative changes on the 7th day in ventricle size (x ± SEM) on CT (FH/ID)

	VSS shunt(n=44)	VP shunt(n=30)	VB shunt(n=6)	F value	P value
Baseline FH/ID*	0.51±0.12	0.57±0.10	0.61±0.11	3.987	0.023
7Days FH/ID*	0.43±0.11	0.56±0.10A	0.60±0.11A	16.74	<0.01
F value	119.59	17.54	1.82		
P value	p<0.01	p<0.01	p<0.01		
Time Effect(F,P)			30.551, <0.01		
Time*Groups Effect(F,P)			34.679, <0.01		
Groups Effect(F,P)			9.309, <0.05		
*:x ± SEM					
A: p<0.05(comparing with VSS shunt)					

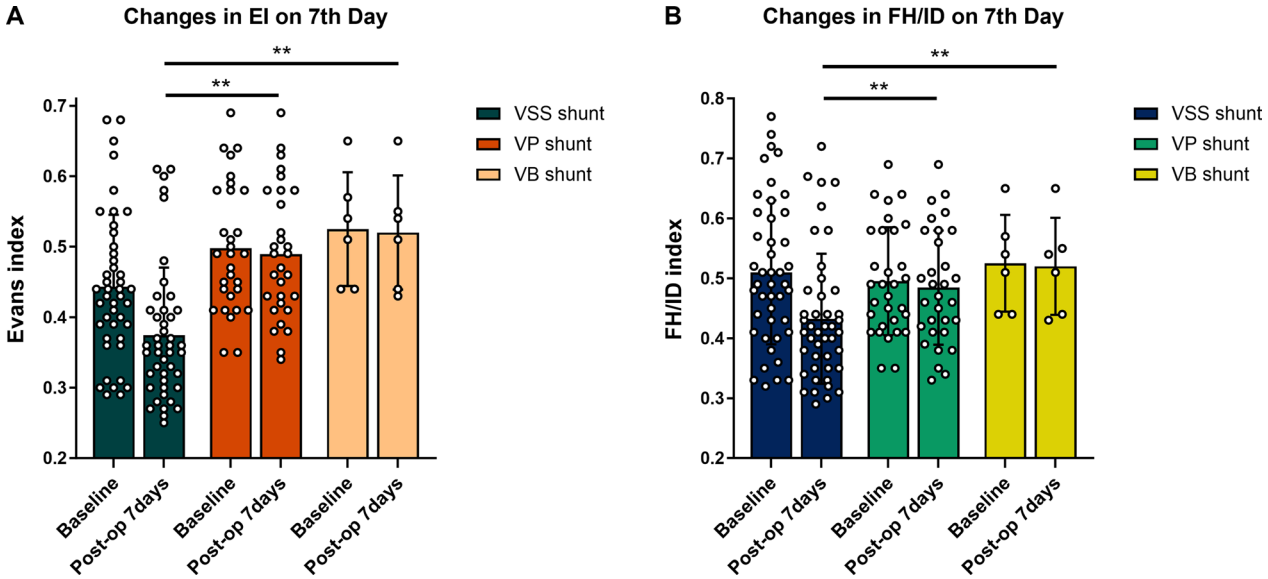

Fig. 5 Short-term imaging follow-up revealed hydrocephalus with elevated CSFP treated by three categories of operative methods. **a** Changes in the Evans index on the 7th day; **b** changes in FH/ID on the 7th day

change between the two groups, as well as the overall trend of change between the two groups, was essentially the same (Figure S8).

Based on clinical success, we also evaluated the differences in treatment efficacy. Compared with the VP shunt (n = 12), the VSS shunt (n = 35) resulted in

Table 4 Comparing post-op changes in imaging and symptoms between VSS shunt—CSFP > 1.0 g/L group and VSS shunt—CSFP < 1.0 g/L group

a: Comparisons in imaging (EI)

	CSFP>1 (n=12)	CSFP<1 (n=23)	F value	P value
BaselineEI*	0.45±0.09	0.45±0.10	0.075	0.786
7Days EI*	0.38±0.08	0.36±0.09	0.2	0.657
90Days EI*	0.37±0.09	0.36±0.09	0.152	0.699
F value	27.341	86.781		
P value	p<0.01	p<0.01		
Time Effect (F, P)		99.267, <0.01		
Time*Groups Effect (F, P)		0.258, 0.774		
Groups Effect (F, P)		0.139, 0.711		
*: x ± SEM				

b: Comparisons in imaging (FH/ID)

	CSFP>1 (n=12)	CSFP<1 (n=23)	F value	P value
BaselineFH/ID*	0.52±0.11	0.52±0.11	0.059	0.809
7Days FH/ID*	0.43±0.1	0.43±0.1	0.037	0.848
90Days FH/ID*	0.43±0.1	0.42±0.1	0.024	0.877
F value	24.327	68.767		
P value	p<0.01	p<0.01		
Time Effect (F, P)		81.815, <0.01		
Time*Groups Effect (F, P)		0.113, 0.894		
Groups Effect (F, P)		0.041, 0.841		
*: x ± SEM				

c: Comparisons in symptoms (MMSE)

	CSFP>1 (n=12)	CSFP<1 (n=23)	F value	P value
Baseline MMSE*	12.5±7.09	13.26±6.08	0.11	0.742
7Days MMSE*	20.33±7.63	21.65±7.51	0.241	0.627
90Days MMSE*	21.08±7.03	22.48±6.98	0.314	0.579
F value	126.653	225.098		
P value	p<0.01	p<0.01		
Time Effect (F, P)		312, <0.01		
Time*Groups Effect (F, P)		0.412, 0.666		
Groups Effect (F, P)		0.22, 0.642		
*: x ± SEM				

d: Comparisons in symptoms (BI)

	CSFP>1 (n=12)	CSFP<1 (n=23)	F value	P value
Baseline BI*	38.33±19.58	44.57±18.4	0.867	0.359
7Days BI*	68.75±23.27	71.74±22.24	0.138	0.713
90Days BI*	71.67±20.26	75.22±19.74	0.251	0.62
F value	134.579	296.729		
P value	p<0.01	p<0.01		
Time Effect (F, P)		405.975, <0.01		
Time*Groups Effect (F, P)		0.815, 0.452		
Groups Effect (F, P)		0.35, 0.558		
*: x ± SEM				

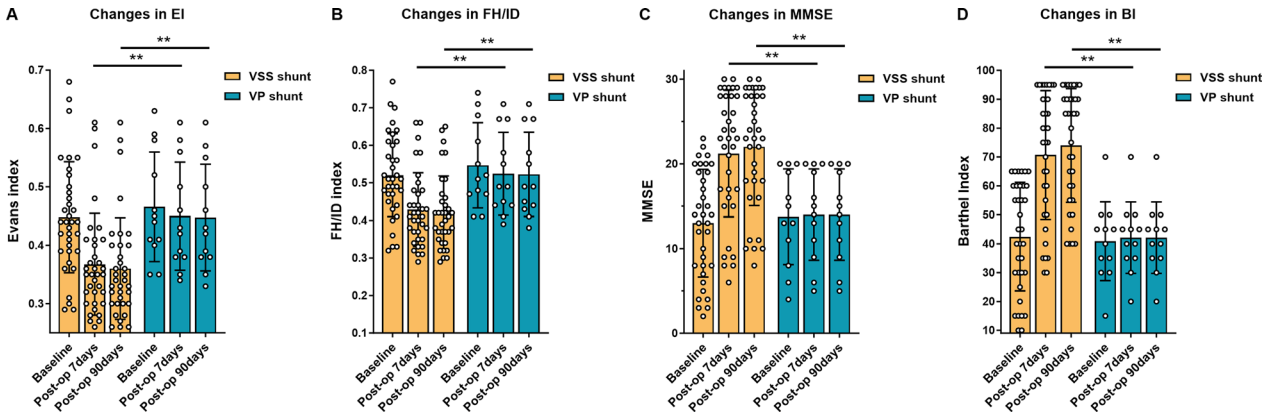

Fig. 6 Comparisons of postoperative changes between the VSS shunt and the VP shunt on the 7th day and 90th day. **a** Changes in EI; **b** Changes in FH/ID; **c** Changes in MMSE; **d** Changes in BI

prominent improvement in the EI, FH/ID, MMSE, and BI at the three-month follow-up (Fig. 6). The EI of patients before VSS shunt placement was 0.45 ± 0.09, and that after surgery was 0.36 ± 0.09 (F value: 119.59). The EI of patients before the VP shunt was 0.47 ± 0.09, and that after surgery was 0.45 ± 0.09, with an F value of 17.29. Time*Groups Effect: F value: 23.716; Between-Groups Effect: F value: 4.376 (Table 5a). The preoperative FH/ID was 0.52 ± 0.11, the postoperative FH/ID was 0.42 ± 0.10, and the F value was 92.06. For the VP shunt, the preoperative FH/ID was 0.55 ± 0.11, the postoperative FH/ID was 0.52 ± 0.11, and the F value was 15.45. Time * Groups Effect: F value: 17.252; Between-Groups Effect: F value: 4.649 (Table 5b). The MMSE score was 13 ± 6.35 before the VSS shunt and 22 ± 6.92 after the surgery, with an F value of 356.08. The MMSE score was 13.75 ± 5.63 before the VP shunt and 14 ± 5.38 after the surgery, with an F value of 3.67. Time*Groups Effect: F value: 113.147; Between-Groups Effect: F value: 4.847 (Table 5c). The BI was 42.43 ± 18.76 preoperatively and 74 ± 19.70 postoperatively, with an F value of 435.35. For the VP shunt, the preoperative BI was 40.83 ± 13.62, the

Table 5 Comparing post-op changes in imaging with baseline (a) (EI), (b) FII/ID, (c) MMSE and (d) BI

a: Comparing post-op changes in imaging with Baseline (EI)

	VSS shunt(n=35)	VP shunt(n=12)	F value	P value
Baseline EI*	0.45±0.09	0.47±0.09	0.317	0.576
7Days EI*	0.37±0.09	0.45±0.09(A)	7.783	0.008
90Days EI*	0.36±0.09	0.45±0.09(A)	8.756	0.005
F value	114.51	17.29		
P value	<0.01	<0.01		
Time Effect (F, P)		55.442, <0.01		
Time*Groups Effect (F, P)		23.716, <0.01		
Groups Effect (F, P)		4.376, <0.05		
*:x ± SEM A: p<0.05 (comparing with VSS shunt)				

b: Comparing post-op changes in imaging with Baseline (FH/ID)

	VSS shunt(n=35)	VP shunt(n=12)	F value	P value
Baseline FH/ID*	0.52±0.11	0.55±0.11	0.503	0.482
7Days FH/ID*	0.43±0.10	0.52±0.11(A)	7.965	0.007
90Days FH/ID*	0.42±0.10	0.52±0.11(A)	8.996	0.004
F value	92.06	15.45		
P value	<0.01	<0.01		
Time Effect (F, P)		46.763, <0.01		
Time*Groups Effect (F, P)		17.252, <0.01		
Groups Effect (F, P)		4.649, <0.05		
*:x ± SEM A: p<0.05 (comparing with VSS shunt)				

c: Comparing post-op changes in symptoms with Baseline (MMSE)

	VSS shunt(n=35)	VP shunt(n=12)	F value	P value
Baseline MMSE*	13±6.35	13.75±5.63	0.131	0.719
7Days MMSE*	21.2±7.47	14±5.38(A)	9.417	0.004
90Days MMSE*	22±6.92	14±5.38(A)	13.212	0.001
F value	356.08	3.67		
P value	<0.01	<0.01		
Time Effect (F, P)		125.762, <0.01		
Time*Groups Effect (F, P)		113.147, <0.01		
Groups Effect (F, P)		4.847, <0.05		
*:x ± SEM A: p<0.05 (comparing with VSS shunt)				

d: Comparing post-op changes in symptoms with Baseline (BI)

	VSS shunt(n=35)	VP shunt(n=12)	F value	P value
Baseline BI*	42.43±18.76	40.83±13.62	0.073	0.788
7Days BI*	70.71±22.3	42.08±12.33(A)	17.741	<0.001
90Days BI*	74±19.70	42.08±12.33(A)	27.561	<0.001
F value	435.35	3.67		
P value	<0.01	<0.01		
Time Effect (F, P)		153.648, <0.01		
Time*Groups Effect (F, P)		131.529, <0.01		
Groups Effect (F, P)		11.207, <0.05		
*:x ± SEM A: p<0.05 (comparing with VSS shunt)				

postoperative BI was 42.08 ± 12.33, and the F value was 3.67. Time*Groups Effect: F value: 131.529; Between-Groups Effect: F value: 11.207 (Table 5d). Given that there was only one case of clinical success in the VB shunt group, its treatment efficacy was not representative or typical; therefore, the use of a VB shunt was not included in the comparisons ($p < 0.05$ for all comparisons). A total of 37 eligible participants had markedly improved symptoms at the time of 6-month follow-up compared to baseline (Table S1 and S2).

Discussion

An imbalance between CSF secretion and absorption is the cause of hydrocephalus, and in most cases, the clinical symptoms are attributed to dilated ventricles. Identifying the most appropriate extracranial or intracranial outlet site of the CSF is highly important for the treatment of hydrocephalus. Over the past few decades, other safe and effective outlet sites or innovative methods for hydrocephalus have not received widespread acceptance except for the VP shunt; lack of durability and safety are drawbacks of the ventriculoatrial (VA) shunt and the lumbo-peritoneal (LP) shunt [24]. The use of a VSS shunt, an alternative treatment to a VP shunt for hydrocephalus, has been increasingly attempted by neurosurgeons since the early 2000s [4, 5, 7]. Despite recent case reports suggest the VSS shunt is a safe and feasible option, no relevant comprehensive research has been published in this field. In our study, we recommend the VSS shunt for hydrocephalus with elevated protein content in the CSF.

Ventriculoperitoneal shunts are widely considered as the preferred treatment for hydrocephalus because of the large space in the peritoneum and the simplicity of the operation procedure. However, the VP shunt inevitably produces harmful complications, and the rates of VP shunt obstructions and infections are approximately 15% and 12.9%, respectively [25, 26]. As shown in the latest figure, the average rate of VP shunt revision and removal is 53% [5]. Shunt infection is a common and serious complication possibly leading to the removal of a catheter, with 3 months being the time point for occurrence of all types of shunt failures. The 3–4 month period for VP shunt failure is due to various factors, including malfunction due to elevated CSFP. Many patients experience shunt failure develop symptoms by the third postoperative month. This finding is supported by previous research and follow-up data from our institute, where patients experienced shunt failure due to elevated CSFP [27–30]. Overdrainage and underdrainage are related to physics of body position, with ventricular pressure being positive in the horizontal position and negative in the upright position. Distal catheter obstruction often occurs in conjunction with adhesions and wrapping of the greater omentum [9, 29, 31]. Shunt availability and safety are major concerns because of obstruction and infection. We used laparoscopic exploration to shorten

the catheter and maintain the patency of the distal end. Multiple rapid presses on the reservoir can contribute to the drainage of the shunt system. For patients with intracranial infection, continuous lumbar drainage (LD) or percutaneous reservoir puncture drainage is typically the preferred initial treatment. However, the failure of repeated revision and positive bacterial cultures of the catheter represents the removal of shunt systems. In some cases, peritoneal adhesions and fibrosis cause the peritoneum to lose the ability to absorb CSF [29]. Ascites, peritoneal irritation, pseudocyst, and perforation are also abdominal complications of VP shunts [15]. Normal abdominal absorption of CSF is likely to interfere with and be disupted by elevated CSF. Similar to cirrhosis with ascites, the complications of high protein content ascites include greater omentum thickening and spontaneous bacterial peritonitis. Under normal conditions, the flow of fluid in the abdomen is 50 mL per day, and the protein content is less than 25 g/L [32]. The slow thickening of part of the greater omentum tissue and encapsulated abdominal fluid is the result of the decline in the reabsorption of high protein content fluid, increasing the risk of peritonitis. In the case of elevated protein content in the CSF flowing towards the greater omentum, the terminal lymphatics on the greater omentum first lose the function of reabsorption. The thickened greater omentum tissue wraps around the distal end of the catheter, causing adhesions between the wall of the catheter and greater omentum tissue; thereafter, catheter obstruction occurs [9, 15]. Although the position of the catheter in the peritoneal cavity varies with body posture in theory, the distal end of the catheter still has a strong possibility of localization and wrapping.

The greater omentum is a layer of the serous membrane, and the normal function of absorption is immune to the viscosity of the liquid due to the smooth surface. Under physiological conditions, the greater omentum is not susceptible to the protein content of the liquid in the peritoneum, and the delicate balance between normal secretion and absorption of the greater omentum is disrupted by the VP shunt [14, 16]. The elevated protein content in the peritoneum induces hyperplasia of greater omentum tissue; however, when this occurs, the volume or size of the greater omentum increases by only approximately 5%, and this situation does not appear until the CSFP is generally greater than 1 g/L [33]. Notably, no published research has indicated the reversibility of this mechanism. Therefore, the ample absorption ability of the peritoneum must be preserved to ensure the clinical effect of the VP shunt. In other words, the protein in CSF should be lowered to a certain level, usually 0.4 g/L.

The volume of CSF drainage depends on the pressure gradient between the ventricles and the extracranial recipient site. For programmable valve implantation, the determinant is the open pressure of the valve. When the volume of drainage is less, the flow velocity of the CSF decreases, sometimes creating intermittent drainage. This results in the deposition of protein flocs, and finally, the large amount of suspended sediment obstructs the shunt system. Such mechanical failures mostly occur before and after the valve, followed by the catheter connections [26, 34]. Small amount of suspended sediment can be flushed away by continuously pressing on the reservoir. First, this approach works, but more time and frequency are needed after several trials. The worst-case scenario is that no resilient reservoir appears after repeated pressing attempts. If overdrainage of CSF is excluded, patients and doctors would consider performing shunt system revision. Recent clinical research on hydrocephalus reported that the general rate of revision within a 6-month follow-up was 25%–30% [6].

The safety and efficacy of devices draining CSF into cavities other than the peritoneum have been tested in recent years, and VSS shunts offer several unique advantages in terms of action and theory [5, 11, 35]. Elevated CSF protein may result from a multitude of causes, including—but not limited to—intracranial infection, encephalitis, meningitis, hemorrhage, and brain cancer or nervous system tumors. Primarily, VSS shunt can treat hydrocephalus with elevated protein and high-content CSF. For patients with hydrocephalus, the eligibility of traditional VP shunts is the outcome of a CSF protein concentration below 0.6 g/L along with a CSF cell count less than 100. Protein and blood in CSF often imply blockage of the catheter [9]. When the measurement of the CSFP and number of CSF cells are not within the normal reference range or continuously fail to achieve qualification for eligibility for shunt surgery after the LD is attempted, externalization of the peritoneal end of the VP shunt is performed, and the tube is connected to a drainage system in vitro for at most 3 months; in this instance, the ventricle is prone to infection and even aggravation of infection. Patients with hydrocephalus commonly present with postinfectious hydrocephalus and CH or OH secondary to intracranial neoplasia. In our study, 8 patients underwent two different methods of shunt surgery within 6 months, and 3 patients underwent three surgeries, but all without success. These experiences of VP shunt failure meant that doctors also had to worry about the function of peritoneal absorption and evaluate the potential unsuitability of such patients for the VP shunt. The VSS shunt was a response to hydrocephalus accompanied by elevated CSFP for 44 patients in our research. Based

on collected data, surgery had satisfactory effects on imaging and clinical symptoms in patients who had no surgery-related shunt failure or complications. The natural drainage of CSF occurs into the dural sinuses. The theory that the SSS is the physiological drainage site supports the advantage of the capacity of the VSS shunt for hydrocephalus with elevated CSFP. Additionally, the viewpoint that elevated protein content in CSF causes the dysfunction of peritoneal absorption mentioned earlier provides a theoretical basis for promoting VSS as a choice for treating VP shunt failure. The flow rate and flow volume of fluid in the bladder are far greater than those in the abdominal cavity. Theoretically, this is not conducive to the deposition of proteins at the distal end of the shunt. This also forms the theoretical basis for VB shunt treatment A. However, in fact, the failure rate of VB shunts is much higher than that of VP shunts, even in cases where the CSFP is normal. The main reasons for failure include a significantly increased risk of bladder stones, a risk of electrolyte depletion, and a biophysical inequivalence between the intrabladder and intracranial pressures.

The major classifications of different causes of hydrocephalus include postinfectious/posthemorrhagic/post-traumatic hydrocephalus [36]. VSS shunt are equally effective in treating all categories of hydrocephalus and can be applied to hydrocephalus patients with failed VP shunts, elevated protein content in the CSF, and CSF extracranial absorption deficiency. During the progression of postinfectious hydrocephalus and neoplasia-related hydrocephalus, the blood–brain barrier of the choroid plexus is destroyed by tumor cells and inflammation, and the increase in permeability leads to the penetration of protein and blood cells from the plasma to the CSF [37, 38]. In some patients, the protein and cells of CSF remain unqualified for shunt surgery after LD, even though the attempt of in-catheter medication injection improving the CSF flow rate of drainage. These patients had undergone LD for at least 3 weeks with the disappearance of infection symptoms such as fever and underwent surgery. However, hydrocephalus remains unresolved, and when shunt surgery is performed with elevated CSF, the risk is high; specifically, protein can easily produce obstruction, which can occur at the distal end and around the valve. Externalizing the VP shunt catheter is a temporary treatment, but it is a challenge for postoperative anti-infection and care. The drainage of elevated protein and cell content in CSF always involves a certain degree of risk despite the normal flow of CSF into the SSS. In most cases, continuously pressing on the reservoir could sustain the function of the VSS shunt system. Therefore, before VSS shunt, CSFP and CSF cell levels should be restored to normal or near normal by employing CSF bedside drainage, and repeated CSF cultures are required.

To ensure safety and compatibility, in the past decade, the VSS shunt was designed to avoid overdrainage and underdrainage of CSF [4, 7]. Behind the drainage principle of the VSS shunt, which closely aligns with the normal physiological drainage of CSF, the pressure gradient between ventricles and the SSS is similar to that of the physiological condition [11]. Shunt-related complications at the extracranial recipient site are unlikely to occur with the strategy of imitating CSF physiological circulation [4]. The VSS shunt partly prevents the impact of gravity on the function of shunt devices under different body positions, with decreased risks of CSF overdrainage caused by the siphoning effect. Subdural fluid collection or subdural hematomas are also avoided. In addition, the shorter pathway of the catheter is an indication of more chances to reduce the possibility of infection and mechanical complications, also shortening the operative time [35]. Furthermore, VSS shunt could be chosen in the acute stage of hydrocephalus under local anesthetic because of its simplicity and minimal surgical trauma [5].

Several ventriculosinus shunt devices and procedures have been investigated early. In an initial study, the ventriculotranverse sinus demonstrated symptomatic and clinical benefits for patients with hydrocephalus [10]. El-Shafei held the view that a retrograde direction approach of the catheter should be implemented to reduce the stagnation and coagulation of blood at the catheter end, thereby lowering ventriculosinus shunt failure rates. Briefly, a prepared catheter is pushed forward into the SSS against the flow of venous blood [5, 39]. The catheter direction of all patients in our study followed the flow of venous blood in the SSS and were carefully monitored after implantation, which took into consideration that the contradiction between the valve and reservoir constituted a shunt system approximately 6 cm long, which offered a confined and limited space from the anterior horn of the lateral ventricle to the frontal hairline. El-Shafei et al. reviewed 8 case series and concluded that the existence of a wake zone and impact zone in the context of the anterograde introduction of the catheter would lead to stagnation and coagulation of venous blood [5, 11]. To address this, a structure of two regular and narrow cracks at the end of the distal tube was used in all patients to prevent the wake effect resulting from catheter placement. At the end of the study, not a single case of VSS shunt failure was caused by a theoretical catheter or mechanical-related complications, such as air embolization and sinus thrombosis. Finally, the improvement in symptoms and the size of the ventricles confirmed the feasibility and efficacy of the anterograde VSS shunt.

The VSS shunt utilizes the physiologic collapse of the internal jugular vein (IJV) to prevent overdrainage of CSF and the siphonage effect [4, 11]. We therefore investigated the clinical effect of VSS shunts for IVP-normal hydrocephalus or iNPH during the period of study design. Indeed, the VSS shunt effectively alleviates the symptoms of iNPH without underdrainage during follow-up.

In our study, the data of 6-month follow-up were not analyzed because eligible participants at six months after shunt operations were not representative and typical enough. Specifically, they did not contain all types of hydrocephalus and causes of elevated CSFP. Moreover, the sample sizes of VP shunt and VB shunt were too small to make meaningful statistical analysis. Furthermore, for hydrocephalus, the size of ventricles could not consistently reflect the state of illness in some hydrocephalus patients. Among eligible participants at six months after shunt operations, the index system to evaluate ventricles size was obviously unevenly distributed and not uniform. Last but not least, for some patients, whether the improvement in symptoms after six months is due to the shunt surgery is an uncertain answer (e.g., rehabilitation training after a cerebral hemorrhage). Although the message that comes out of 6-month follow-up we had not decided to use to compare the clinical effect of VSS shunt, VP shunt and VB shunt, we still yield exciting and promising findings in our work regarding VSS shunt for hydrocephalus with elevated CSFP. Taken together, since the postoperative parameters had improved greatly, we figured the VSS shunt is an extremely effective method for the treatment of hydrocephalus with elevated CSFP, and the clinical outcome is extremely significant.

Limitations of the work

This study had certain limitations. This study was a retrospective observational study, encompassing both the advantages and disadvantages characteristic of this type of study design. First, the sample size was small and nonprobabilistic. This study could not detect the impact of individual differences among patients receiving VSS shunts because of the limited available data. Second, a short follow-up of 3 months was used to investigate the safety and efficacy of VSS shunts but not their specific risk factors and complications. Moreover, the 3-month follow-up was relatively short. Several challenges were encountered during this study, such as we cannot follow up all patients and insufficient follow-up data integrity, specific refers to we cannot simultaneously obtain both image data and questionnaire in some patients. Finally, the case series cited in this study were from a single institution, which may make the results of the study less reliable and scientific. To generalize the adoption of VSS shunt and guarantee the clinical value of the VSS shunt, a multicenter prospective controlled trial is necessary to elucidate the reliability and robustness of the VSS shunt in the future.

Conclusion

In summary, our findings demonstrate the effectiveness of the VSS shunt, which not only provides a recommended new method for treating hydrocephalus with increased protein content but also reduces the probability of shunt complications. The VSS shunt procedure has great potential as a novel research direction for refractory and difficult hydrocephalus cases. To provide insights and guidance for future clinical practice, prospective studies are needed to broaden the analysis and prove the viability of VSS shunt.

Supplementary Information

Additional file 1.
Additional file 2.
Additional file 3.
Additional file 4.
Additional file 5.
Additional file 6.
Additional file 7.
Additional file 8.
Additional file 9.
Additional file 10.

Acknowledgements
Not applicable.

Author contributions
Y.W. wrote the main manuscript text and D.W., Y.T., and Y.Y. prepared Figs. 1, 2, 3, 4, 5 and 6. Q.Y. revised the manuscript. All authors reviewed the manuscript.

Funding
This work was financially supported by the Natural Science Foundation of Liaoning Province (No. 2022-YGJC-70).

Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
All subjects gave their informed consent for inclusion before they participated in the study. This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the institutional review board of Shengjing Hospital of China Medical University.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 1 September 2024 Accepted: 11 February 2025
Published online: 11 March 2025

References

1. Hochstetler A, Raskin J, Blazer-Yost BL. Hydrocephalus: historical analysis and considerations for treatment. Eur J Med Res. 2022;27(1):168.
2. Lee RP, Ajmera S, Thomas F, et al. Shunt failure—the first 30 days. Neurosurgery. 2020;87(1):123–9.
3. Low SYY, Kestle JRW, Walker ML, Seow WT. Cerebrospinal fluid shunt malfunctions: a reflective review. Childs Nerv Syst. 2023;39(10):2719–28.
4. Toma AK, Tarnaris A, Kitchen ND, Watkins LD. Ventriculosinus shunt. Neurosurg Rev. 2010;33(2):147–52; discussion 153.
5. El-Shafei IL, El-Shafei HI. The retrograde ventriculosinus shunt: concept and technique for treatment of hydrocephalus by shunting the cerebrospinal fluid to the superior sagittal sinus against the direction of blood flow. Preliminary report. Childs Nerv Syst. 2001;17(8):457–65; discussion 466.
6. Munthe S, Pedersen CB, Poulsen FR, Andersen MS, Borgesen SE. Ventriculosinus shunt: a pilot study to investigate new technology to treat hydrocephalus and mimic physiological principles of cerebrospinal fluid drainage. J Neurosurg. 2023;139(5):1412–9.
7. Baert EJ, Dewaele F, Vandersteene J, Hallaert G, Kalala JO, Van Roost D. Treating hydrocephalus with retrograde ventriculosinus shunt: prospective clinical study. World Neurosurg. 2018;118:e34–42.
8. McDonald PJ. Ventriculoperitoneal shunt failure from spontaneous knotting of the peritoneal catheter. CMAJ. 2016;188(5):E97.
9. Browd SR, Ragel BT, Gottfried ON, Kestle JR. Failure of cerebrospinal fluid shunts: part I: obstruction and mechanical failure. Pediatr Neurol. 2006;34(2):83–92.
10. Borgesen SE, Pieri A, Cappelen J, Agerlin N, Gjerris F. Shunting to the cranial venous sinus using the SinuShunt. Childs Nerv Syst. 2004;20(6):397–404.
11. El Shafei IL, El Shafei HI. The retrograde ventriculo-sinus shunt (El Shafei RVS shunt). Rationale, evolution, surgical technique and long-term results. Pediatr Neurosurg. 2005;41(6):305–17.
12. Li X, Zheng J. Ventriculosinus shunt as a reliable option in the treatment of failed ventriculoperitoneal shunt: report of 19 cases and review of the literature. Ann Palliat Med. 2021;10(7):7627–33.
13. Oliveira MF, Teixeira MJ, Reis RC, Petitto CE, Gomes Pinto FC. Failed ventriculoperitoneal shunt: is retrograde ventriculosinus shunt a reliable option? World Neurosurg. 2016;92:445–53.
14. Gupta N, Park J, Solomon C, Kranz DA, Wrensch M, Wu YW. Long-term outcomes in patients with treated childhood hydrocephalus. J Neurosurg. 2007;106(5 Suppl):334–9.
15. Browd SR, Gottfried ON, Ragel BT, Kestle JR. Failure of cerebrospinal fluid shunts: part II: overdrainage, loculation, and abdominal complications. Pediatr Neurol. 2006;34(3):171–6.
16. Jayanth A, Benabbas R, Chao J, Sinert R. Diagnostic modalities to determine ventriculoperitoneal shunt malfunction: a systematic review and meta-analysis. Am J Emerg Med. 2021;39:180–9.
17. Ishikawa M, Mori E. Association of gait and cognition after surgery in patients with idiopathic normal pressure hydrocephalus. Sci Rep. 2023;13(1):18460.
18. Williams MA, Nagel SJ, Luciano MG, et al. The clinical spectrum of hydrocephalus in adults: report of the first 517 patients of the Adult Hydrocephalus Clinical Research Network registry. J Neurosurg. 2020;132(6):1773–84.
19. Zhou X, Xia J. Application of evans index in normal pressure hydrocephalus patients: a mini review. Front Aging Neurosci. 2021;13: 783092.
20. Ferreira CD, Matushita H, Silva BR, et al. Proposal of a new method to induce ventricular system dilation to simulate the features of hydrocephalus and provide an anatomical model for neuroendoscopy training. Childs Nerv Syst. 2014;30(7):1209–15.
21. Wilhelmy F, Krause M, Schob S, et al. Cerebrospinal fluid protein concentrations in hydrocephalus. Children (Basel). 2023;10(4).
22. Hikmat O, Naess K, Engvall M, et al. Elevated cerebrospinal fluid protein in POLG-related epilepsy: diagnostic and prognostic implications. Epilepsia. 2018;59(8):1595–602.
23. Nadkarni NA, Maas MB, Batra A, et al. Elevated cerebrospinal fluid protein is associated with unfavorable functional outcome in spontaneous subarachnoid hemorrhage. J Stroke Cerebrovasc Dis. 2020;29(4): 104605.
24. Izutsu N, Hosomi K, Kawamoto S, et al. Lumbar catheter misplacement into the spinal subdural epiarachnoid space causing lumboperitoneal shunt malfunction: report of two cases. NMC Case Rep J. 2021;8(1):183–7.
25. Lopez-Sanchez C, Rozas-Munoz E, Mir-Bonafe JF. Ventriculoperitoneal Shunt Infection. JAMA Dermatol. 2020;156(12):1366.
26. LeHanka A, Piatt J. Readmission and reoperation for hydrocephalus: a population-based analysis across the spectrum of age. J Neurosurg. 2021;134(3):1210–7.
27. Morosanu CO, Filip GA, Nicolae L, Florian IS. From the heart to the bladder-particularities of ventricular shunt topography and the current status of cerebrospinal fluid diversion sites. Neurosurg Rev. 2020;43(3):847–60.
28. Isaacs AM, Yang R, Cadieux M, et al. Characteristics of shunt failure in 38,095 adult shunt insertion surgeries: a systematic review and meta-analysis. Neurosurg Focus. 2023;54(4):E2.
29. Isaacs AM, Ball CG, Sader N, et al. Reducing the risks of proximal and distal shunt failure in adult hydrocephalus: a shunt outcomes quality improvement study. J Neurosurg. 2022;136(3):877–86.
30. Iglesias S, Ros B, Martin A, et al. Surgical outcome of the shunt: 15-year experience in a single institution. Childs Nerv Syst. 2016;32(12):2377–85.
31. Pelegrin I, Lora-Tamayo J, Gomez-Junyent J, et al. Management of ventriculoperitoneal shunt infections in adults: analysis of risk factors associated with treatment failure. Clin Infect Dis. 2017;64(8):989–97.
32. Akay S, Ozutemiz O, Kilic M, et al. Reabsorption of ascites and the factors that affect this process in cirrhosis. Transl Res. 2008;152(4):157–64.
33. Docter TA, Patel BH, Brennan JJ, Castillo EM, Lee RR, Vilke GM. Utility of shunt series in the evaluation of ventriculoperitoneal shunt dysfunction in adults. J Emerg Med. 2020;58(3):391–7.
34. Garegnani L, Franco JV, Ciapponi A, Garrote V, Vietto V, Portillo Medina SA. Ventriculo-peritoneal shunting devices for hydrocephalus. Cochrane Database Syst Rev. 2020;6(6):CD012726.
35. El-Shafei IL, El-Shafei HI. The retrograde ventriculovenous shunts: the El-Shafei retrograde ventriculojugular and ventriculosinus shunts. Pediatr Neurosurg. 2010;46(3):160–71.
36. Oi S. Hydrocephalus research update–controversies in definition and classification of hydrocephalus. Neurol Med Chir (Tokyo). 2010;50(9):859–69.
37. Wang HQ, Han P, Huang QB, Zhang ZL. Clinical characteristics and treatment of early and delayed intra-cranial infection after ventriculoperitoneal shunt in adults: retrospective analysis of nineteen cases. Surg Infect (Larchmt). 2023;24(1):66–74.
38. Sweeney J, Zyck S, Tovar-Spinoza Z, Krishnamurthy S, Chin L, Bodman A. Evidence-based perioperative protocol for ventriculoperitoneal shunt infection reduction at a single institution. World Neurosurg. 2019;128:e814–22.
39. Vandersteene J, Baert E, Planckaert GMJ, et al. The influence of cerebrospinal fluid on blood coagulation and the implications for ventriculovenous shunting. J Neurosurg. 2019;130(4):1244–51.

Publisher's Note