

## Hydrocephalus in Persistent Vegetative State

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**Objective:** The authors investigated the clinical influence of a shunt operation in hydrocephalic patients with persistent vegetative state (PVS) patients.

**Methods:** 39 patients with hydrocephalic PVS were included in this study. We analyzed the clinical outcome and prognosis according to clinical parameters, especially in relation to the shunt operation.

**Results:** In 39 patients with hydrocephalic PVS, 26 underwent a shunt operation and 13 were treated conservatively. At the time of diagnosis of hydrocephalus in PVS, the mean Glasgow Coma Scale (GCS) and ventriculocranial ratio (VCR) were  $5.31 \pm 0.85$  and  $0.24 \pm 0.05$  in the conservative group, and  $5.00 \pm 0.75$  and  $0.23 \pm 0.04$  in the operative group. On the brain CT taken upon making the diagnosis of hydrocephalus, there were less cerebral infarctions ( $p=0.001$ ) and more subarachnoid space (SAS) effacement ( $p=0.018$ ) in the shunt operation group compared to the conservative group. After six months from an event causing PVS, the operative group showed an increased GCS score than the conservative group, a mean increase of  $2.38 \pm 0.48$  vs.  $0.54 \pm 0.14$  ( $p=0.002$ ), and a decreased VCR, with a decrease in VCR  $0.07 \pm 0.03$  vs.  $0.01 \pm 0.01$  ( $p=0.021$ ) respectively. With regard to the outcome, according to GOS, the younger aged and post-traumatic patients showed a better prognosis, especially those younger than 60 years ( $p=0.016$ ) and the operation did good in the highly selected group than those in conservative care ( $p=0.009$ ). But CSF flow study grade was not significant prognostic factor.

**Conclusion:** In hydrocephalic PVS patients, a better outcome and GOS may be anticipated in the case of highly selected patients of a younger age, less cerebral infarction and more SAS effacement preoperatively.

**Key Words:** Hydrocephalus · Persistent vegetative state · Shunt operation



### INTRODUCTION

Persistent vegetative state (PVS) is defined as a vegetative state (VS)-state of preservation of autonomic function and primitive reflexes, without the ability to interact meaningfully with the external environment, present one month after an acute traumatic or non-traumatic brain injury<sup>23,26,31,34</sup>. In the literature, Jennett et al<sup>16</sup> reported an 77% incidence of hydrocephalus in VS, but not all ventriculomegaly is true hydrocephalus<sup>28</sup>. These hydrocephalus cases may be caused by abnormality of secretion, circulation or absorption of CSF or secondary ventricular dilatation due to atrophy<sup>1,4,5,11,14,17,19</sup>.

In these PVS patients, comprehensive evaluation of hydrocephalus is difficult. Although diagnosis of ventriculomegaly seen with a follow-up imaging study may be easy, the clinical course is sometimes obscure and most of the time, accurate clinical signs of increased intracranial pressure (IICP) out of associated hydrocephalus can not be easily obtained<sup>1,3,6,7,10,13,15</sup>. In the case of hydrocephalic PVS, it is important to know which patients will benefit from the shunt operation procedure<sup>22,24,26,29,30</sup>.

In this study, the authors studied the clinical influence of a shunt operation in hydrocephalic PVS and tried to induce the beneficial factors affecting the outcome in hydrocephalic PVS retrospectively.

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### MATERIALS AND METHODS

#### 1. Patient selection and management

This a study is retrospective one, and concerned 39 patients

with PVS in whom hydrocephalus was diagnosed with follow-up brain CT during March 2000 to April 2003. All patients that could be followed for a minimum of 6 months from the initial diagnosis of hydrocephalic PVS were included. In this study, factors to consider for the shunt operation in patients with hydrocephalic PVS were: ① aged 60 or younger, ② progressive hydrocephalus with follow-up brain CT, ③ higher isotope CSF flow abnormality, ④ less intracranial infarction, and ⑤ normal or increased subarachnoid space (SAS) effacement. Surgery was planned when 4 or more above factors met.

## 2. Brain CT findings

Hydrocephalus was graded as 4 tier according to ventriculo-cranial ratio (VCR) described by Vassilouthis<sup>33</sup>. For practical purposes, in our study, ratios between 1/5 and 1/6.5 were taken to represent minimal ventricular enlargement, 1/4 to 1/5 moderate, and above 1/4 marked ventricular dilatation. Along with VCR, the extent of cerebral infarction was divided three groups. focal is one cerebral arterial territory infarction, multiple is two or more cerebral arterial territories infarction, and the degree of SAS effacement divided into three groups according to sulcal-gyral patterns of convexity<sup>14</sup>.

## 3. CSF flow study

To obtain the CSF scan, <sup>99m</sup>Tc of diethylenetriamine-pentacetic acid (DTPA) were introduced into the subarachnoid space through a standard lumbar puncture technique. Images of the head were obtained by means of a scintillation gamma camera at 1-, 3-, and 24-hour intervals. The results of the scan were analyzed by an experienced observer and designated according to their features, into grade I to grade IV defined groups (Table 1)<sup>2</sup>. No side effect was observed in the patients who underwent the procedure.

**Table 1.** Grading of cerebrospinal fluid flow study (<sup>99m</sup>Tc-DTPA)

Grade	Ventricular filling	Flow over the convexities
I	No	Yes
II	Yes; out by 24h	Yes
III	Yes; persistent at 24h	Yes
IV	Yes; persistent at 24h	No

## 4. Follow-up studies

At 6 months after the initial causative events, the 39 patients still alive were reassessed by a follow-up brain CT and GCS. Outcome was also evaluated according to the Glasgow Outcome Scale (GOS) as a good recovery (GR), moderate disability (MD), severe disability (SD), PVS and dead.

## 5. Statistical analysis

The post-operative status at an at least six months follow-up evaluation was compared with the pre-operative status in the shunt operation group and in the conservative group. Data was processed by SPSS (10.0 Korean version), and a p-value of less than 0.05 obtained through the student t-test and regression analysis was considered statistically significant.



## RESULT

### 1. Demographic data

In 39 hydrocephalic PVS, there were 26 males and 13 females with a median age of 51.5 years (mean 51.7 years, range 28~75 years). 26 patients underwent the shunt operation. Among these, 22 patients had the ventriculo-peritoneal shunt and 4 took the lumbo-peritoneal shunt. Conservative care was carried out with the remaining 13 patients. The etiology of hydrocephalus were 19 post-trauma, 18 with post-cerebrovascular disease and 2 of

**Table 2.** Clinical parameters between operative and conservative group

Factors		Group	
		Operative	Conservative
Age (yrs)*	Mean	47.79±9.75	60.23±9.34
	Range	28 ~ 65	44 ~ 75
Pre-op GCS**		5.00±0.75	5.31±0.85
Pre-op VCR***		0.24±0.75	0.23±0.04
CSF flow study†		3.68±0.01	3.00±0.22
Follow-up (months)‡	Mean	10.92±2.87	10.38±2.72
	Range	7 ~ 18	7 ~ 17

GCS: Glasgow coma scale, VCR: ventriculocranial ratio, CSF: cerebrospinal fluid, \*p=0.002, \*\*p=0.386, \*\*\*p=0.323, †p=0.440, ‡p=0.842

**Table 3.** Brain CT findings in hydrocephalic PVS

Group	Brain CT findings								
	Infarction*			SAS effacement**			Ventricular dilatation***		
	none	focal	multiple	+	NL	– <sup>§</sup>	minimal	moderate	marked
Operative	10	15	1	14	10	2	5	8	13
Conservative	1	5	7	1	1	11	4	3	6

SAS: subarachnoid space, \*p=0.001, \*\*p=0.018, \*\*\*p=0.770, <sup>§</sup> enlarged subarachnoid space

"other".

## 2. Clinical parameters and the CSF flow study

In this study, the age of the operative group was younger than the conservative group (p=0.002). But there was no difference in pre-operative GCS and pre-operative VCR between the two groups. The operative group had a mean grade of  $3.68 \pm 0.01$  in the isotope CSF flow study and the conservative group had a grade of  $3.00 \pm 0.22$ , which did not suggest a significant difference (p=0.440, Table 2).

## 2. Brain CT of hydrocephalic PVS

At the time of diagnosis of hydrocephalus in PVS, there was less cerebral infarction (p=0.001) and more SAS effacement (p=0.018) in the shunt operation group compared to the conservative group. But there showed no significant difference in the degree of ventricular dilatation between the two groups (Table 3).

## 3. Relationship between shunt operation and outcome

Compared to the conservative group, the operative group showed a significant increase in the change of the GCS score (p=0.002, Table 4) and the reduction in VCR (p=0.021, Table 5). With regard to the outcome according to GOS, the younger aged patients showed better results, especially those that were 60 or younger (p=0.016) and the operation did good in the highly selected group than those in conservative care (p=0.009, Table 6). 11 patients in the operative group and two in the conservative group recovered from SD or MD. And two patients with the shunt operation who recovered were able to live independently but were not capable of achieving a high level of performance. 9 out of 19 patients (47%) with traumatic hydrocephalic PVS recovered consciousness, and 4 out of 20 (20%) non-traumatic hydrocephalics recovered consciousness. Recovery of consciousness from hydrocephalic PVS was noted at 33.3% as a total, for the operative group 42.3%, while the conservative group was at 18.2%. One patient in the conservative group died of pneumonia.

**Table 4.** GCS vs. treatment modality and age

Group	Pre-op GCS	Follow-up GCS	GCS change*
Operative	5.00±0.75	7.38±1.79	2.38±0.48
Conservative	5.31±0.85	5.85±1.07	0.54±0.14

GCS: Glasgow coma scale, \*p=0.002

**Table 5.** VCR change vs. treatment modality and age

Group	Pre-op VCR	Follow-up VCR	VCR change*
Operative	0.23±0.04	0.17±0.03	0.07±0.03
Conservative	0.24±0.05	0.23±0.05	0.01±0.01

VCR: ventriculocranial ratio, \*p=0.021



## DISCUSSION

In neurosurgical practice, it is important to check through the patient's correctable condition in order not to delay neurological recovery, and the situation is same in patients with PVS.

Giacino et al<sup>9)</sup> reported a recovery rate from PVS: 6 out of 11 patients with traumatic PVS recovered consciousness (53%), and non-traumatic patients 3 out of 11 recovered consciousness (27%).

In the Multi-Society Task Force on PVS<sup>26)</sup>, which included 434 patients with traumatic head injury, 52% of the patients had recovered consciousness while 48% died or remained in VS. Among 434 patients, one-year outcome according to the GOS

**Table 6.** GOS vs. treatment modality and age

Group*	Age**	GOS				
		GR	MD	SD	PVS	Dead
Operative	below 40	0	1	3	0	0
	41 to 60	0	1	5	3	0
	above 60	0	0	1	12	0
Conservative	below 40	0	0	0	0	0
	41 to 60	0	0	2	5	0
	above 60	0	0	0	5	1

GOS: Glasgow outcome scale, GR: good recovery, MD: moderate disability, SD: severe disability, PVS: persistent vegetative state, \*GOS vs. treatment modality,  $p=0.009$  \*\*GOS vs. Age,  $p=0.016$

was as follows: 33% died, 15% in PVS, 28% SD, 17% MD and 7% GR. And of the 169 patients caused by non-traumatic injury, only 15% had recovered consciousness; 85% remained in VS or had died. In this study, the authors stated that recovery of function was extremely poor compared to that of consciousness.

In our study, 9 out of 19 patients (47%) with traumatic hydrocephalic PVS recovered consciousness, and 4 out of 20 (20%) non-traumatic hydrocephalic PVS regained consciousness.

Ventriculomegaly is commonly seen at post-mortem in patients who have died in VS<sup>29</sup>. Jennett et al<sup>16</sup> reported the neuropathological findings in 35 VS patients and 30 SD cases at the time of death. They reported the incidence of hydrocephalus in VS at 77%, SD at 73%. But the figure of 77% for "hydrocephalus" probably represents both hydrocephalus ex vacuo as well as true hydrocephalus. This supposition is born out by the incidence of both diffuse axonal injury and thalamic abnormalities of 80%<sup>28</sup>.

Nevertheless, in these PVS patients, recognition of ventricular dilatation with serial follow-up brain imaging such as brain CT or MRI may be easy. In the literature, CT scanning has been reported to show ventricular dilatation in some 25~51% of patients in VS although the definition of ventriculomegaly has differed between the reports<sup>8,12,19-21,24,25,27</sup>.

As one may expect, the clinical course in hydrocephalic PVS may not always be consistent. Moreover, detection of accurate clinical symptoms and signs of increased intracranial pressure from hydrocephalus cannot be made early in this level of PVS.

Kahlon et al<sup>18</sup> studied the efficacy of the lumbar infusion test and the CSF tap test in order to predict the outcome of the

shunt operation in hydrocephalic patients. In their 68 patients, CT or MRI showed widening of the ventricular system relative to the age-matched ventricular index. In their study, they reached conclusions that increased CSF outflow on the lumbar infusion test and improved clinical parameters after CSF removal on the CSF tap test could predict a good prognosis of shunt operation.

Pickard et al<sup>28</sup> suggested that a favorable response to the shunt operation might be expected in patients with normal pressure hydrocephalus where there is no superficial cortical atrophy, the third ventricle is enlarged, and there is periventricular hypodensity suggestive of edema due to CSF extravasation and reversal of drainage of interstitial fluid. However, there are many exceptions and periventricular changes in chronic state are more likely to represent periventricular gliosis and infarcted white matter rather than the edema of acute hydrocephalus. In these situations, consideration should be given to assessing their intracranial pressure and CSF dynamics. So, the authors recommended a CSF infusion test in order to ascertain the presence of elevated intracranial pressure and/or high resistance for CSF absorption which are suggestive of good shunt-response.

Tribl et al<sup>32</sup> reviewed 48 patients with post-traumatic hydrocephalus who had the shunt operation. Out of the 18 patients presenting with PVS before the shunt operation, six (33.3%) improved from PVS to SD after the operation. Out of the 30 patients presenting with SD before the shunt operation, 19 patients (63.3%) improved after implantation, 6 patients from SD to MD and 13 patients had clearly improved, but did not enter MD. The doctors also performed CSF scintigraphy in 13 patients. 11 of 13 patients showed markedly delayed resorption, one

slightly delayed resorption and one only signs of cerebral atrophy. However, only six (46.2%) of them improved after the shunt operation. In their article, contrary to our study, the patients' ages did not seem to influence the outcome. They concluded that the best predictive parameter for outcome after the shunt operation was the preoperative status and, similar to our study, isotope cisternography did not seem to be of additional help.

Mazzini et al.<sup>23)</sup> analyzed 63 patients with post-traumatic hydrocephalus. The level of hydrocephalus was evaluated by MRI with a score from normal to severe, according to the patterns of sulci and ventricles, when compared with expected size in a person of the same age. The level of hypoperfusion in cerebral territories was scored from absent to severe by SPECT. Ventriculo-peritoneal shunt was done in 13 patients with severe hydrocephalus. In these patients, SPECT showed severe hypoperfusion of the temporal lobe and frontal lobe. Before the shunt operation, 5 of 13 patients were PVS. Afterwards, 3 patients improved, but 2 in PVS. The remaining 8 patients were in SD, 4 patients improved after the shunt operation, but 4 in SD. In this SPECT study, they described that the improvement in temporal perfusion after shunting was a good prognostic factor.

In this study, we reviewed 39 patients with hydrocephalic PVS. 11 (42%) out of 26 patients with the shunt operation were improved, but only 2 (15%) of the 13 with conservative management were improved ( $p=0.009$ ). At the beginning of our study, we tested parameters such as age, brain image findings and isotope CSF flow patterns. Contrary to Tribl et al., younger age ( $\leq 60$ ) was a good prognostic factor in our study ( $p=0.016$ ).

Though the degree of ventricular dilatation was similar between the groups, the operative group had less infarction ( $p=0.001$ ) and more SAS effacement ( $p=0.018$ ) than the conservative group, meaning good prognostic factors that might be brought to bear when considering shunt operation in hydrocephalic PVS.

In our study, though the operative group had a better outcome than the conservative group, overall outcome of hydrocephalic PVS was not significantly different or better than other studies on outcome of PVS<sup>9,28)</sup>. Hence, it is likely that the outcome of PVS is mainly affected by initial causative event rather than hydrocephalus itself.

As might be expected, the outcome of hydrocephalic PVS may be different in relation to initial causative events. To induce

more acceptable results, a population might be included in a further study, especially in the case of delineating the outcome of hydrocephalic PVS according to an individual disease entity.

Finally, other than conventional brain CT or MRI, it may be helpful to include functional studies such as a CSF infusion test and/or various cerebral blood flow studies in order to testify the efficacy of the shunt operation in patients with hydrocephalic PVS.



## CONCLUSION

Treatment of hydrocephalus even in PVS may be beneficial to a patient's awakening. Those who underwent the shunt operation showed a more increased GCS score and more decreased VCR than those who received the conservative treatment. In hydrocephalic PVS patients, a better outcome may be anticipated in the case of highly selected patients of a younger age, less cerebral infarction and more SAS effacement preoperatively.



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