

CLINICAL RESEAPCH

## Analysis of the Effect of Cerebrospinal Fluid Circulation Reconstruction on Serum Indexes and Long-term Prognosis of Patients with sTBI Based on Decompressive Craniectomy

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### Keywords

Severe traumatic brain injury,  
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### Abstract

**Objective** To investigate the effect of decompressive craniectomy combined with cerebrospinal fluid circulation reconstruction on serum indexes and long-term prognosis of patients with severe traumatic brain injury (sTBI). **Methods** A total of 120 patients with sTBI who were treated in our hospital from January 2019 to December 2020 were selected and randomly divided into the control group and the observation group, with 60 cases in each. The control group applied the treatment of decompressive craniectomy, and the observation group applied the treatment of decompressive craniectomy combined with cerebrospinal fluid circulation reconstruction. We compared the intracranial pressure (ICP), serum indexes, complications and prognosis of the two groups before and after treatment. **Results** At 3 days and 7 days after operation, the ICP of the two groups was significantly lower than that before operation ( $P<0.05$ ), and the observation group was significantly lower than that of the control group ( $P<0.05$ ). At 7 days after operation, the levels of cortisol, neuron-specific enolase (NSE) and central nerve-specific protein (S100 $\beta$  protein) in the two groups were significantly lower than those before surgery ( $P<0.05$ ), and the observation group were significantly lower than those in the control group ( $P<0.05$ ). The total incidence of complications in the observation group was significantly lower than that in the control group ( $P<0.05$ ). The prognosis of patients in the observation group was significantly better than that in the control group ( $P<0.05$ ). **Conclusion** Cerebrospinal fluid circulation reconstruction is a safe and reliable treatment modality that could effectively reduce ICP in patients with sTBI, mitigate brain tissue damage, protect neurological function and improve the prognosis of patients.

## Introduction

Traumatic brain injury (TBI) is a traumatic disease caused by external forces acting directly or indirectly on the head, resulting in intracranial injuries, and patients who lose consciousness over 6 hours or lapse into a second coma are defined as having a severe traumatic brain injury (sTBI) [1]. sTBI is a common disease in clinical neurosurgery. After a patient sustains a severe craniocerebral trauma, his sharp elevation of intracranial pressure (ICP) would lead to serious complications such as deformation of the cerebral ventricle, midline shift and cerebral hernia, which have high disability and mortality rates and seriously affect the life and health [2]. Clinical studies have shown that taking effective managements are of importance to improve the prognosis of patients [3]. At present, the clinical treatments of sTBI are mainly aimed at removing intracranial blood clots and lowering ICP, among which decompressive craniectomy (DC) is a commonly performed procedure. Although this management has some efficacy, the occurrence of postoperative brain edema, cerebral infarction and other serious secondary brain injury are still inevitable and more postoperative complications set in, which is not conducive to prognostic treatment [4]. With the development of medical technologies, cerebrospinal fluid circulation reconstruction is gradually moving from theoretical research to clinical practice. Based on the principle of “glymphatic circulation”, the technique could facilitate cerebrospinal fluid circulation and remove extracellular fluid to effectively decrease the ICP by opening the brain cisterns to atmospheric pressure and

reconstructing the current return circuit [5]. In this study, a total 120 cases of patients with sTBI in our hospital were selected to treat with DC alone and DC combined with cerebrospinal fluid circulation reconstruction, respectively, to investigate the effect of this combined treatment on serum indexes and long-term prognosis of patients with sTBI, hoping to provide a reference for the option of clinical treatment modality.

## Information and methods

### General information

A total of 120 cases of patients with sTBI in our hospital selected from January 2019 to December 2020 were randomly divided into the control group (n=60) and the observation group (n=60). There was no difference in the basic information such as gender, age, admission time and leading causes between the observation group and the control group ( $P>0.05$ ), and the data were clinically comparable, as detailed in Table 1. The study was approved by the Ethics Committee of our hospital, with informed consent form signed from family members of all patients. The patients were included from the following: (i) patients with sTBI diagnosed by clinical symptoms, physical signs, CT and other imaging studies; (ii) patients with sTBI met a Glasgow Coma Scale (GCS) score of 3-8; (iii) patients with operation indication. The patients were excluded from the following: (i) patients with most sTBI with persistent dilated pupils; (ii) patients with cerebral penetrating injury; (iii) patients with severe cardiac, hepatic and renal diseases; (iv) patients with incomplete medical records after admission.

Table 1. Comparison of basic information

groups	cases	gender (case)		age (year)	admission time (h)	leading causes (case)		
		male	female			traffic accident	falling object	heavy hit
observation group	60	32	28	40.32±8.34	3.24±1.02	26	20	14
control group	60	34	26	41.20±7.56	3.04±0.96	28	17	15
$\chi^2/t$			0.135	-0.606	1.106		0.352	
$P$			0.714	0.546	0.271		0.839	

## Treatment methods

### Control group

The patients were treated with a standard DC. Briefly, patients under a state of general anesthesia were performed craniotomy according to the cranial CT. The large bone flap craniotomy (frontal, temporal and apical) is completed with DC on the side of haematoma. Then, intracranial haematoma, necrotic and edematous tissues were required to completely remove from the subdural space. After stop bleeding, the cranial cavity was closed and sutured without placing a drainage-tube. Postoperatively, the patients were given symptomatic supportive treatments such as oxygen inhalation and dehydration.

### Observation group

The patients were treated with DC combined with cerebrospinal fluid circulation reconstruction. In short, on the basis of the control group, the anterior skull base was exposed along the extra side approach, and the optic chiasm and the internal carotid artery pool were opened. After lowering the ICP, the dura mater was widely removed, followed by further opening of the brain cisterns. Then, a drainage-tube was placed 10-15 cm above the lateral ventricle before closing the cranial cavity and performing suture. Postoperatively, the nursing staff monitored the patients' ICP and observed fluid volume and color in the drainage-tube. After 3-4 days of drainage, the tube could be removed if the cerebrospinal fluid was circulating smoothly in the circumstance of elevation of the drainage bag or 24-hour-shut of the drainage-tube. Similarly, the patients were given symptomatic supportive treatments such as oxygen inhalation and dehydration after the surgery. All surgical procedures are performed by the same team of surgeons, the same lead surgeon.

### Observation and assessment

(i) ICP monitor (Pressio, SOPHYSA, France) was used to record ICP in both groups before the surgery, at 3 days and 7 days after the surgery. (ii) 5 ml of peripheral venous blood was drawn from all patients in the early morning on an empty stomach. After

centrifugation, the separated serum was stored in a refrigerator at  $-20^{\circ}\text{C}$  for the following test. Enzyme-linked immuno sorbent assay (ELISA) was applied to detect the levels of cortisol, neuron-specific enolase (NSE) and central nerve-specific protein (S100 $\beta$  protein) in the serum, with the help of a microplate reader (Varioskan LUX, Thermo Fisher Scientific, USA). The ELISA kits were brought from the Beijing Leadman Biochemistry Company and were operated strictly according to the protocols. (iii) The occurrence of postoperative complications, including acute intraoperative encephalocele, cerebral edema, incisional hernia and cerebral infarction, was observed and recorded in both groups. The total complication rate in both groups was calculated afterwards. (iv) At six months after surgery, the patient's prognosis was assessed according to the GCS, with good recovery (5 points), mild disability (4 points), severe disability (3 points), vegetative survival (2 points) and death (1 point). Favorable prognosis included good recovery, mild disability, and poor prognosis included severe disability and vegetative survival.

### Statistical analysis

SPSS software (version 20.0, IBM, USA) was used for statistical analysis. Count data were compared using  $\chi^2$  test. Quantitative data was demonstrated as the mean  $\pm$  standard, with comparison using the t-test.  $P < 0.05$  was considered statistically significant.

## Results

### Comparison of ICP

Before surgery, there was no statistically significant difference in ICP between the two groups ( $P > 0.05$ ). At 3 days and 7 days after surgery, ICP levels were significantly lower than preoperative levels in both groups ( $P > 0.05$ ), and was significantly lower in the observation group than in the control group ( $P < 0.05$ ), as shown in Table 2.

### Comparison of serum indexes

Preoperatively, there was no statistically significant difference in serum indexes between the two groups

( $P>0.05$ ). At 7 days after surgery, cortisol, NSE and S100 $\beta$  protein levels were significantly lower in both groups than before surgery ( $P<0.05$ ), and the significant decrease of protein levels was observed in the observation group comparing to the control group ( $P<0.05$ ), as shown in Table 3.

Table 2. Comparison of ICP (mmH<sub>2</sub>O)

groups	cases	pre-operation	3 days after operation	7 days after operation
observation group	60	348.56±45.30	212.38±28.65*	152.64±18.30*
control group	60	352.34±38.56	256.10±32.44*	188.26±20.74*
<i>t</i>		-0.492	-7.825	-9.975
<i>P</i>		0.624	0.000	0.000

Note: compared to pre-intervention, \* $P<0.05$

Table 3. Comparison of serum indexes

groups	cases	Cortisol ( $\mu\text{g/L}$ )		NSE (ng/L)		S100 $\beta$ ( $\mu\text{g/L}$ )	
		pre-operation	7 days after operation	pre-operation	7 days after operation	pre-operation	7 days after operation
observation group	60	395.54±68.30	196.32±48.20*	42.34±8.65	25.38±7.64*	1.32±0.34	0.52±0.15*
control group	60	402.56±75.25	226.34±50.52*	40.60±9.57	32.62±6.36*	1.36±0.40	0.78±0.22*
<i>t</i>		-0.535	-3.330	-1.045	-5.641	-0.590	-7.564
<i>P</i>		0.594	0.001	0.298	0.000	0.556	0.000

Note: compared to pre-intervention, \* $P<0.05$

**Comparison of the occurrence of complications** was significantly lower than that in the control group. The overall complication rate in the observation group ( $P<0.05$ ), as shown in Table 4.

Table 4. Comparison of the occurrence of complications (case (%))

groups	cases	acute intraoperative encephalocele	cerebral edema	incisional hernia	cerebral infarction	total incident
observation group	60	2 (3.33)	4 (6.67)	5 (8.33)	2 (3.33)	13 (21.67)
control group	60	5 (8.33)	8 (13.33)	7 (11.67)	5 (8.33)	25 (41.67)
$\chi^2$						5.546
<i>P</i>						0.019

**Comparison of prognosis** significantly better than that of the control group. The prognosis of the observation group was ( $P<0.05$ ), as shown in Table 5.

Table 5. Comparison of prognosis (case (%))

groups	cases	favorable prognosis	poor prognosis	death
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observation group	60	35 (58.33)	22 (36.67)	4 (6.67)
control group	60	21 (35.00)	29 (48.33)	10 (16.67)
$\chi^2$			7.024	
<i>P</i>			0.030	

## Discussion

STBI is defined as a craniocerebral injury patient whose consciousness deteriorates within 24 hours after the injury and who is in a secondary coma for a certain period of time, with a GCS score of 3-8 [6]. The patients with sTBI are often accompanied with cerebral contusion and intracranial hematomas which oppresses the brain tissue and reduces the intracranial space, leading to the steep elevation of ICP and causing damage to nerve function and even threatening the life of the patients. Currently, the standard DC is the most commonly used management in the clinic that could effectively reduce ICP in patients with TBI. Clinical studies have shown that simple DC has certain advantages in controlling the ICP and removing intracranial hematomas, however, due to the severity of sTBI patients, this treatment cannot alleviate cerebral edema and venous circulatory disturbance caused by the rapidly increasing ICP. Even worse, it may exacerbate the ongoing ischemia and lack of oxygen in brain tissue and cause brain cell death [7]. Therefore, addressing cerebral edema and venous circulatory disturbance is of great importance to improve the prognosis of patients with sTBI. The “glymphatic circulation” is an important part in the pathway of cerebrospinal fluid circulation and extracellular fluid clearance, i.e. half of the cerebrospinal fluid is absorbed by the brain parenchyma instead of the convex subarachnoid cavity, which plays a key role in the absorption of cerebrospinal fluid [8].

By applying microsurgical techniques, cerebrospinal fluid circulation reconstruction is designed to reconstruct the cerebrospinal fluid circulation at the beginning of the glymphatic circulation in the skull of patients with sTBI by opening up the dura mater and the brain cisterns for reducing the fluid pressure so that the cerebrospinal fluid no longer flows through the Virchow-Robin spaces (VRS) and the extracellular

fluid can flow back to the basal pool through the new cerebrospinal fluid circulation system, thus significantly overcoming obstructions of cerebral blood circulation and cerebrospinal fluid circulation caused by the impeded venous return, alleviating cerebral edema, relieving the local pressure on the brainstem and effectively reducing ICP [9]. Our study found that at 3 days and 7 days after surgery, ICP levels were significantly lower in the observation group than in the control group, suggesting that the combination of DC and cerebrospinal fluid circulation reconstruction is more beneficial in decreasing ICP in patients with sTBI, compared with the treatment of DC alone.

A sharp increase in ICP is the leading cause of neurological dysfunction and tissues damage in the brain. When damage occurs to nerve cells in brain tissue, NSE is released from the cytoplasm into the cerebrospinal fluid and crosses the blood-brain barrier into the bloodstream. Thereby, its serum level can reflect the severity of neuronal damage in patients with sTBI. Cortisol is a glucocorticoid that can be regarded as a specific molecular marker to assess brain injury. Clinical studies have found that the level of cortisol in the serum is strongly correlated with the degree of brain injury, showing a positive correlation. S100 $\beta$  is a group of specific proteins expressed in the in the central nervous system, and its expression is deemed contributive to promote neuronal proliferation and growth, but the overexpression of it has been found to produce neurotoxicity and impair neurological function in the brain tissue [10]. In this study, we found that at 7 days after surgery, cortisol, NSE and S100 $\beta$  protein levels were significantly lower in the observation group than before surgery, and the significant decrease of protein levels was observed in the observation group comparing to the control group, indicating that the combined treatment could exert better therapeutic effects in reducing brain

injury and protecting neurological function, compared with the treatment of DC alone. By improving venous drainage and cerebral perfusion pressure, cerebrospinal fluid circulation reconstruction is expected to help patients restore blood and oxygen supply to the brain, increase partial pressure of oxygen in brain tissue, promote the removal of reactive oxygen species, thus effectively preventing the continued necrosis of ischemic and hypoxic brain tissue, inhibiting the level of endogenous harmful factors such as cortisol and S100 $\beta$  after TBI, and protecting the nutrient metabolism and neurological function in brain tissue [11].

The observation of postoperative complications in patients with sTBI is an important factor in determining their long-term prognosis as serious complications such as cerebral edema, cerebral infarction, incisional hernia and acute intraoperative encephalocele usually emerge after sTBI treatment, causing brain tissue damage and impaired neurological function. Our study found that the total incidence of complications in the observation group was significantly lower than in the control group, and its prognosis was significantly better than that of the control group, revealing that this combined treatment has high safety and a better patient prognosis comparing to the application of DC alone. Continuously elevated ICP is one of the main factors affecting the prognosis of patients with sTBI. The application of cerebrospinal fluid circulation reconstruction could minimize the damage caused by cerebral ischemia-reperfusion by sufficiently reducing ICP, restoring blood flow and cerebrospinal fluid circulation after brain tissue injury, and increasing blood oxygen content, which is conducive to repairing damaged brain cells and improving neurological function of the brain [12], thus effectively decreasing serious complications after treatment and improving the prognosis of patients.

In conclusion, cerebrospinal fluid circulation reconstruction has good clinical curative effect in treatment of sTBI, which could significantly decrease ICP, mitigate brain tissue damage, protect neurological function, reduce the incidence of

complications and improve prognosis of patients.

#### Declaration of conflict-of-interest

The authors declare no conflict-of-interest.

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