European Review for Medical and Pharmacological Sciences 2020; 24: 5627-5632

Effects of comprehensive rehabilitation on complications and long-term prognoses of patients in vegetative and minimal consciousness states

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Abstract. – OBJECTIVE: To understand the clinical characteristics, prognoses, and prognostic factors of vegetative state (VS) and minimal consciousness state (MCS) patients hospitalized for comprehensive rehabilitation.

MATERIALS AND METHODS: The data of VS and MCS patients admitted in the past six years were retrospectively analyzed. Age of onset, etiology, course of disease, complications, and retention of tracheal intubation, gastric tube, and urethral catheter were recorded. All patients were followed for one year after onset, and their Glasgow Outcome Scale (GOS) scores were assessed. Long-term prognostic factors were analyzed using logistic regression.

RESULTS: The proportion of patients with traumatic brain injuries in the MCS group was higher than in the VS group ($p<0.05$), while hypoxic-ischemic encephalopathy accounted for a higher proportion in the VS group; the differences were statistically significant between the two groups. The occurrence of infection was the highest in both groups, followed by spasticity and epilepsy. The occurrence of other complications was slightly different between the two groups but did not reach statistical significance ($p>0.05$). Age, etiology, and consciousness at admission had a significant impact on the long-term prognoses of VS or MCS patients ($p<0.05$), and the age of onset was the most important factor (the highest OR).

CONCLUSIONS: Infection, spasticity, and epilepsy are common complications in both VS and MCS patients. Recovery of consciousness after one year was shown to be affected by age, etiology, and consciousness at admission.

Key Words:

Disturbance of consciousness, Vegetative state, Minimal consciousness state, Rehabilitation, Prognosis.

Introduction

Advances in emergency and neurosurgical procedures have increased survival in patients with severe traumatic brain injuries. It has been estimated that the prevalence of severe craniocerebral trauma is about 170 per million in the United States, and the prevalence of patients in a vegetative state (VS) is about 40 to 168 per million[1]. In the United Kingdom, the incidence of patients in a VS is about 14 per million per month after trauma, eight per million three months after trauma, and five per million six months after trauma[2]. There are no data on the incidence or prevalence of patients in a minimal consciousness state (MCS).

A disturbance of consciousness (DOC) illustrates the complexity of ongoing care and medical needs and has long been one of the most challenging topics in neurorehabilitation. Although some patients have spontaneous or stimulated eyesight (awakening), they lack awareness and understanding of internal or external conditions and cannot effectively communicate (i.e., the so-called lack of consciousness). This state has long been referred to as a VS, and later concepts of persistent and permanent VS have been proposed, all of which differ in the duration of the VS. When the VS features very limited consciousness, and not enough for reliable communication, it is called a MCS[3].

The misdiagnosis rate of a VS is very high, and many comatose patients have been misdiagnosed as being in a VS[4]. With the standardization and wide acceptance of diagnostic methods, the misdiagnosis rate has gradually decreased; however, the prevalence of the VS and MCS is still very difficult to determine, and many rehabilitation departments

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do not strictly distinguish between them. We began to use the Coma Recovery Scale-Revised (CRS-R) earlier than our peers to standardize assessment and grouping of hospitalized DOC patients. This study retrospectively analyzed the clinical status and complication of patients admitted to the Department of Neurology and Rehabilitation of the China Rehabilitation Research Center in the past six years. All patients were followed and their factors influencing long-term prognosis analyzed to guide future rehabilitation.

Patients and Methods

General Information

According to the diagnostic criteria for a persistent VS in 2001 and the CRS-R scale, 52 DOC patients hospitalized in the Department of Neurology and Rehabilitation of China Rehabilitation Research Center from January 2010 to December 2016 were retrospectively analyzed. Of the 52 DOC patients, 30 were in a VS, and 22 were in a MCS. The age of onset, etiology, course of disease, complications (i.e., infections, malnutrition, epilepsy, venous thrombosis of the lower extremities, hydrocephalus, ectopic ossification, stress ulcers, and spasticity), and retention of tracheal intubation, gastric tube, and urethral catheter were recorded in detail. All patients were followed for one year after onset, and the Glasgow Outcome Scores (GOSs) were recorded. This investigation was approved by the Ethics Committee of Capital Medical University School of Rehabilitation Medicine. Signed written informed consent was obtained from all participants before the study.

Comprehensive Rehabilitation Methods

All patients were given comprehensive rehabilitation as follows: 1) drug treatment (oral mecobalamin tablets, 0.5 mg 3 times a day; oxiracetam capsules, 0.8 g 3 times a day; donepezil hydrochloride, 5 mg once a day; and other medications were administered as indicated); 2) hyperbaric oxygenation (multiperson air ballast tank, oxygen mask [oxygen concentration of 99.2%-99.7%, pressure of 0.2 MPa, pressure increase in 20 min, stable for 80 min, and decompression for 20 min once daily]); 3) physical therapy and sensory input stimulation (visual stimulation, alternate color and intensity, as well as location within the field of vision; outdoor activities; exposure to the environment and nature; auditory stimulation; communication, such as using the patient's name or offering verbal encouragement; playing the patient's favorite music, TV, or broadcast programs; giving commands (15 min at a time several times a day); taste stimulation using a cotton swab dipped in different foods to stimulate the patient's taste buds (patients without difficulty swallowing were fed a small amount of liquid with different flavors); stimulation of the lips and mouth areas, gradually increasing to three times a day; smell stimulation by placing the patient's favorite food by the nose for 15 s a time several times a day; and sense of depth stimulation in which family members stroked and massaged the patients from time to time; and stimulation of the extremities with alternating hot and cold application); 4) exercise therapy (i.e., switching the patient to the supine position once every 2 h, helping the patient maintain good posture on the bed, providing passive joint exercise of the patient's limbs for full range of movement, and stand training [supine position → sitting → standing] 30 min a time, twice a day); and 5) one acupuncture treatment daily.

Statistical Analysis

Counting data are shown as absolute values and percentages, and measurement data are expressed as the mean ± standard deviation. All data were statistically analyzed using Statistical Product and Service Solutions (SPSS) 16.0 software (SPSS Inc., Chicago, IL, USA), and a Chi-square test was used to analyze the category data. A $p<0.05$ was considered statistically different, and a $p<0.01$ was considered as statistically significant difference.

Results

General Information on the VS and MCS

There was no significant difference between the two groups with respect to sex, age, course of disease, or duration of comprehensive rehabilitation intervention ($p>0.05$). The proportion of patients with traumatic brain injuries in the MCS group was higher, while the prevalence of ischemic hypoxic encephalopathy in the VS group was higher. The differences were statistically significant ($p<0.05$; Table I).

Patient Complications in the VS and MCS Groups

The occurrence of infections was the highest in both groups, followed by spasticity and epilepsy. The occurrence of other complications was slightly different between the two groups but did not reach statistical significance ($p>0.05$). Only

Table I. Comparison of general patient information on the vegetative and minimal consciousness states.

	VS (n=30)	MCS (n=22)	*p*-value
Gender (male/female)	22:8	16:6	0.325
Age of onset (years old)	35.23±14.16	33.42±13.38	0.208
Course of disease (days)	102.45±23.56	99.74±30.13	0.117
Etiology (traumatic brain injury, cerebrovascular disease, hypoxic ischemic encephalopathy)	10:8:12	14:7:1	0.046
Duration of comprehensive rehabilitation	56.34±15.54	59.23±18.23	0.468

three patients had no complications, while 49 patients had at least one complication, and 24 patients had at least two complications (Table II).

Clinical Characteristics of the Conscious Recovery and Unconscious Non-Recovery Groups 1 Year After Onset

All patients were followed for one year after onset to evaluate their GOS scores. Of the patients, two died; their causes of death were pulmonary infection and pulmonary embolism. Eighteen patients were in a persistent VS, while 26 had severe disabilities, six had moderate disabilities, and no patients recovered completely. Patients who died or were in a persistent VS were considered part of the unconscious non-recovery group, while those with a severe or moderate disability were considered part of the conscious recovery group. The clinical characteristics of the two groups with different prognoses were compared (Table III).

Analysis of the Impact of Factors on Prognosis

According to the GOS scores one year after the onset of the disease, death or a persistent VS was regarded as ineffective, and severe or moderate disability was regarded as effective. A logistic regression model was used to analyze age, sex, etiology, course of disease, consciousness at admission (VS or MCS), duration of comprehensive rehabilitation intervention, and number of complications (Table IV). Based on the results, age at onset, etiology, and consciousness (VS or MCS) at admission had a significant effect on the long-term prognosis of patients ($P<0.05$), and age at onset was the most important factor (the highest OR). There was no significant correlation between sex, duration of disease, duration of comprehensive rehabilitation intervention, number of complications, or prognosis ($p>0.05$).

Discussion

Currently, it is believed that VS and MCS are due to cortical or subcortical contact interruption caused by cortical or reticular damage, while brainstem function is relatively intact. As a result, cortical and brainstem functions appear to separate. While awakening ability still exists, no conscious activities or reactions occur. The treatment of a DOC is more challenging than the diagnosis;

Table II. Comparison of patient complications in the vegetative and minimal consciousness state groups.

Complications	VS (n=30)	MCS (n=22)	*p*-value
Infections (lung, intracranial, urinary system)	15 (50%)	12 (54.54%)	0.436
Spasticity	12 (40%)	10 (45.46%)	0.425
Epilepsy	8 (26.67%)	7 (31.82%)	0.328
Lower extremity venous thrombosis	5 (16.67%)	3 (13.64%)	0.311
Anemia	5 (16.67%)	2 (9.09%)	0.120
Shoulder hand syndrome	6 (20%)	4 (18.18%)	0.387
Heterotopic ossification	3 (10%)	1 (4.55%)	0.086
Hypoproteinemia	5 (16.67%)	4 (18.18%)	0.411
Breathing disorders (long-term tracheal intubation)	6 (20%)	4 (18.18%)	0.406
Swallowing disorders (long-term nasal feeding tube)	8 (26.67%)	5 (22.73%)	0.393
Urination disorders (long-term retention catheter)	6 (20%)	5 (22.73%)	0.287
Paroxysmal sympathetic hyperactivity (PSH)	3 (10%)	2 (9.09%)	0.535

Table III. Comparison of clinical characteristics of the conscious recovery and unconscious non-recovery groups 1 year after onset.

Complications	Unconscious group	Conscious group	*p*-value
Gender (male/female)	15:5	23:9	0.440
Age of onset (years old)	38.17±15.73	31.06±17.25	0.014
Course of disease (days)	113.43±25.88	96.86±27.05	0.076
Etiology (traumatic brain injury, cerebrovascular disease, hypoxic ischemic encephalopathy)	6:11:10	18:4:3	0.023
Duration of comprehensive rehabilitation	57.66±13.29	58.19±15.08	0.825
VS: MCS	16:4	14:18	0.007
Infections (lung, intracranial, urinary system)	11 (55%)	16 (50%)	0.377
Anemia	8 (40%)	14 (43.75%)	0.402
Hypoproteinemia	7 (35%)	13 (40.63%)	0.330
Lower extremity venous thrombosis	3 (15%)	5 (15.63%)	0.634
Spasticity	4 (20%)	3 (9.38%)	0.076
Shoulder hand syndrome	5 (25%)	5 (16.63%)	0.229
Heterotopic ossification	1 (5%)	3 (9.38%)	0.102
Epilepsy	2 (10%)	7 (21.88%)	0.045
Breathing disorders (long-term tracheal intubation)	6 (30%)	4 (12,5%)	0.129
Swallowing disorders (long-term nasal feeding tube)	6 (30%)	7 (21.88%)	0.209
Urination disorders (long-term retention catheter)	3 (15%)	8 (25%)	0.114
Paroxysmal sympathetic hyperactivity (PSH)	4 (20%)	1 (3.13%)	0.038

thus, sometimes the words "hopeless" and "frustrating" are used to describe the prognoses of some patients. Even so, many measures, including rehabilitation, hyperbaric oxygenation, drug therapy, and acupuncture, can still be used in the treatment of DOC and achieve curative effects. In addition, some electrical and magnetic stimulation technologies are currently available to treat a DOC, but the exact effects remain to be evaluated[5-9].

Clinically, a combination of methods is usually used to maximize benefits. Our study used drugs, hyperbaric oxygenation, physical factors, acupuncture, exercise therapy, and other comprehensive rehabilitation methods to treat patients. Comprehensive rehabilitation is key, including a somatic treatment strategy and treatments that promote consciousness. Somatic treatment strategy refers to promotion of the functional status of the body to prevent and treat complications. Treatments that promote consciousness include different forms of stimulation (e.g., relatives calling their name, music therapy, increasing contact with the environment) to induce a wide range of behavioral responses[10-12].

Due to prolonged bed rest and a nasogastric diet, patients with a DOC are particularly prone to repeated complications during the course of the disease. If serious complications occur, their condition may deteriorate rapidly. Complications (e.g., fever, epilepsy) greatly increase brain tissue oxygen and glucose consumption to such a degree that some original dying neurons are further damaged. Some patients who have started to recover re-enter VS after a serious complication[13-16]. If compli-

Table IV. Analysis of the impact of factors on prognosis.

	β	SE	*p*-value	OR (95%CI)
Age of onset	-2.125	0.972	0.006	3.254 (1.256-9.324)
Gender	-0.533	0.721	0.589	0.229 (0.122-2.398)
Etiology	-1.414	0.856	0.037	1.336 (0.723-3.404)
Duration of disease	-0.980	0.453	0.102	0.554 (0.212-5.331)
Consciousness (VS or MCS)	-1.886	0.732	0.013	1.823 (0.215-4.353)
Duration of comprehensive rehabilitation	1.232	0.556	0.086	0.772 (0.118-1.244)
Number of complications	-0.387	0.442	0.154	0.256 (0.034-1.233)

cations occur, it is necessary to actively treat both DOC and complications, which can lead to sharply rising medical expenses. Therefore, understanding the occurrence of complications and their impact on rehabilitation is of great significance to both physicians and patients' families.

Many reports have explored the factors that influence the long-term prognoses of patients with a DOC. According to an American Association of Vegetative State Working Group Study, the following three factors were closely related to patient rehabilitation: patient age; etiology; and duration of the VS[17]. Typically, children have a better prognosis than adults, and the prognosis for trauma patients is better than for non-trauma patients[18]. As the duration lengthens, the possibility of recovering consciousness gets smaller and smaller.

Giacino et al[19] also wrote that the duration of comprehensive rehabilitation intervention and complications affect the prognoses of patients; however, these subjects are usually early coma patients. The subjects in the study were patients with a DOC at rehabilitation centers who tended to have diseases of a relatively long duration. With the use of comprehensive rehabilitation, these patients were managed holistically, and the complications were better controlled. The patients also underwent a longer rehabilitation intervention. Consciousness is one of the most important features of human life, and after more than one year, the recovery rate of consciousness of VS patients was very low. Even patients with recovery of consciousness often have a severe disability and poor quality of life with a lack of effective treatment options[20]. Therefore, when patients are diagnosed with a persistent VS, physicians should explain the situation to their families to facilitate understanding.

Conclusions

In summary, infection, spasticity, and epilepsy are common complications in both VS and MCS patients. Recovery of consciousness after one year was shown to be affected by age, etiology, and consciousness at admission.

Funding Acknowledgements

This study was supported by the Basic Research Fund of China Rehabilitation Research Center (No. 2018ZX-28) and the National Natural Science Foundation of China (No. U1809209).

Conflict of Interests

The authors declare that they have no conflict of interests.

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