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An Established Early Rehabilitation Therapy Demonstrating Higher Efficacy and Safety for Care of Intensive Care Unit Patients

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Statistical Analysis C
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Background: Although survival rates of critically ill patients in Intensive Care Units (ICUs) have improved in recent years, many risk factors cause a few serious complications. This study aimed to evaluate efficacy and safety of comprehensive early rehabilitation therapy for ICU patients.

Material/Methods: This study recruited ICU patients who were diagnosed as having cerebral hemorrhage or traumatic brain injury. ICU patients were randomly divided into an early rehabilitation therapy group (Observation group, n=21) and a Control group (n=21). Patients in the Control group underwent persistent monitoring of respiratory functions and blood oxygen saturation, as well as electrocardiographic monitoring. ICU patients in the Observation group underwent individualized treatments based on conventional treatments. APACHE II scores, MRC scores, and consciousness improvement rates of ICU patients were evaluated. Incidences of adverse events and complications were also assessed.

Results: Early rehabilitation therapy significantly decreased APACHE II scores and significantly increased MRC scores compared to the Control group ($p<0.05$). Early rehabilitation therapy significantly improved consciousness of ICU patients compared to the Control group ($p<0.05$). Early rehabilitation therapy significantly reduced the incidence of complications compared to the Control group ($p<0.05$). Early rehabilitation therapy significantly shortened ICU or total hospital stay and mechanical ventilation time compared to the Control group ($p<0.05$).

Conclusions: Early rehabilitation therapy decreased APACHE II scores, enhanced MRC scores, and improved consciousness of ICU patients. Moreover, early rehabilitation therapy also reduced the incidence of complications and shortened ICU or total hospital stay and mechanical ventilation time of ICU patients. Therefore, early rehabilitation therapy was shown to be effective and safe for ICU patients.

MeSH Keywords: **Consciousness • Intensive Care Units • Rehabilitation • Treatment Outcome**

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Background

In recent years, with the development of critical care medicine and enhancement of diagnostic and therapeutic levels, the success rates of rescue and survival rates of critically ill patients in the Intensive Care Unit (ICU) have significantly improved [1,2]. Due to the severe illness and rapid progression of critically ill ICU patients, they often undergo mechanical ventilation, tracheotomy, catheter indwelling, and application of sedative and analgesic drugs, all of which continuously increase the incidence of complications in ICU patients [3,4]. Therefore, the above risk factors pose difficulties for treatments administered in ICUs.

Early rehabilitation in the ICU means that the patients participate in a series of sports training under a few auxiliary conditions using self-muscular strength and control [5]. However, the early rehabilitation must be implemented under some defined situations in patients, such as blood flow stability, sufficient blood oxygen levels, and stable vital signs [6]. Early rehabilitation can improve systemic dysfunctions and maintain the functions of various systems in critical periods [7,8]. However, the optimal time at which to provide early rehabilitation is controversial. The onset of intervention time ranging from 2 days to 5 days after the critical illness is commonly accepted in clinical treatments [9]. A previous study [10] also reported that the evaluative decision making for early rehabilitation for patients must be conducted within 24 h after entering the ICU.

Early rehabilitation strategy is still in the early stages, in which the clinicians mainly focus on the survival rates of critical ill patients [11]. However, the complications and life quality of ICU patients have never been systematically reported in the previous document [12]. The present study aimed to discuss the safety and efficacy of comprehensively early rehabilitation and intervention for critical ICU patients. This study may provide the basis for deciding on the optimal time to intervene and assesses evaluative and therapeutic methods for early rehabilitation.

Material and Methods

Subjects

This study recruited ICU patients admitted from December 2016 to December 2017 in the Department of Neurosurgery, Second Hospital of Hebei Medical University, Shijiazhuang, China.

Inclusive criteria were: 1) critical patients who were diagnosed with cerebral hemorrhage or traumatic brain injury according to clinical diagnostic standards [13,14]; 2) acute physiology and chronic health evaluation (APACHE II) score more than 15 points; 3) patient age 18–80 years; 4) onset of disease for the first time; 5(provided signed informed consent.

Exclusion criteria were: 1) long-term inability to move independently prior to onset of disease; 2) in the advanced stage of malignant tumors or underwent radiotherapy or chemotherapy of tumors within the last 6 months; 3) imperfect limbs and new fracture was not fixed; 4) needed long-term mechanical ventilation due to neuromuscular diseases; 5) heart rate exceeded the 70% maximum allowable for age; 6) family members did not agree.

Trial grouping

All enrolled patients were randomly divided into an Observation group (n=21) or a Control group (n=21). The basic characteristics are illustrated in Table 1. There were no significant differences in characteristics between the Control group and Observation group. Therefore, the 2 groups were comparable.

Therapeutic strategies

Control group: All of the patients were monitored for respiratory functions and blood oxygen saturation, and were monitored by electrocardiography. Then, according to the needs of patients, the dehydration reducing intracranial pressure, nutritional nerve administration, anti-infective therapy, nutritional support therapy, and regulating balance of water/electrolyte/acid-base were administrated to the patients, while ventilator-assisted ventilation or tracheotomy was also administrated in an emergency. The patients were placed in supine position or lateral decubitus position. Bedsores were prevented by turning over, slapping the back, and massaging skin, and sputum was drained to avoid asphyxia.

Observation group: In this study, the individualized treatments were conducted based on the conventional treatments. The rehabilitation therapy was performed at 2 days after the patient became stable, and therapy was adjusted according to the patients' conditions. The schedule was the followings: once daily, 6 times per week, and the course of treatment was 10 days. After 3 treatment courses, the characteristics were compared between the Observation group and Control group.

The early rehabilitation therapy strategies, including awaking therapy (such as transcranial direct current stimulation (tDCS) [15,16], hyperbaric oxygen therapy [17], comprehensive sensory stimulation therapy [18], and fastigial nucleus stimulation [19]), therapeutic exercise (such as intelligent rehabilitation training system for lower limbs [20], passive activity training/active assistant activity training [21], and electrical stimulation therapy [22] were conducted in this study according to the above documents. Rehabilitation therapy was stopped

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Table 1. General information for the patients in this study.

Groups		Observe group	Control group
Cases (n)		21	21
Age (years, mean ±SD)		58.48±6.38	57.29±6.94
Gender (n)	Male	12	10
	Female	9	11
APACHE II scores (n, mean ±SD)		18.00±1.67	17.43±1.75
GCS scores (n, x±s)		5.67±1.56	5.95±1.49
Course of disease (days, mean ±SD)		3.90±1.22	4.10±1.70
Tracheotomy cases (n)		5	6
Operation cases (n)		13	12
Disease type (n)	Cerebral hemorrhage	12	11
	Traumatic brain injury	9	10

APACHEII – acute physiology and chronic health evaluation; GCS – Glasgow coma scale.

when we encountered the following conditions: 1) heart rate increased by more than 30% at resting position, heart rate less than 30 beats per minute or more than 130 beats per minute; 2) hypertension increased by more than 20% in quiet recumbent position, and mean arterial pressure (MAP) less than 60 mmHg or more than 110 mmHg; 3) respiration less than 5 breaths per minute or more than 40 breaths per minute, and SpO_2 lower than 90% with supplemental oxygen; 4) body temperature more than 38.5°C or less than 36°C; 5) symptoms of decreased consciousness, sweating, abnormal complexion, and pain; 6) patient did not cooperate with the treatments.

Evaluative approaches

The observational indexes were evaluated by clinicians prior to and after the treatments. The evaluated indexes included: completion of rehabilitation treatment program, the changes of vital signs/cardiovascular events/IV line disengagement/falling out of bed, the incidence rates of ICU-AW/deep venous thrombosis (DVT)/pneumonia, APACHE II scores/Medical Research Council (MRC) scores prior to and after treatments, consciousness improvement rates, mechanical ventilation time, hospital stay in ICU, and total hospital stay.

APACHE IIand MRC evaluation

The APACHE IIevaluation was conducted according to a previously published study [23]. The APACHE II scale mainly includes acute physiology score (APS), age, and chronic health score (CHS), with the total scores ranging from 0 to 71 points. When the APACHE IIscores ≥15 points, the patients were assigned as severe cases. More severe patient condition was associated with higher score and worse prognosis.

The MRC evaluation was also conducted according to the method described in a previous study [24]. The MRC scale mainly evaluates 6 pairs of skeletal muscles, including the external oblique muscle of the shoulder (bilateral), flexor elbow, extensor carpi, flexor hip muscle, extensor muscle of knee, and dorsalis pedis muscle. The MRC scale score ranges from 0 to 60 points. For the coma patients, the muscle strength was evaluated by observing the limb movement and limb response to strong stimuli. The ICU-AW was diagnosed when the MRC scores were less than 48 points for the ICU-discharged patients [25].

Evaluation of consciousness improvement rate

The consciousness improvement rates were determined using the GCS scale [26]. The GCS scale system includes eyes-open response, language response, and limb movement. The scores of the GCS score system range from 0 to 15 points. A higher GCS score represents better consciousness of patients. The consciousness improvement mainly includes 4 aspects, including basic cure (consciousness becoming awake, GCS scores=15), markedly effective (signs and symptoms improving markedly, GCS scores ≥12), effective (signs and symptoms with little improvement, GCS scores ≥9), and invalid (no improved signs and symptoms, no enhanced or reduced GCS scores). The consciousness improvement rate=(numbers of basic cures+numbers of marked effectiveness+numbers of effectiveness)/therapeutic patients×100%.

Mechanical ventilation time, hospital stay in ICU, and total hospital stay were also determined to evaluate effects of early rehabilitation on diseases.

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Table 2. Comparison for the APACHE II scores of patients between observation group and control group (mean ±SD).

Group	Prior treatment	Post treatment
Observation group (n=21)	18.00±1.67	8.90±2.07*,**
Control group (n=21)	17.43±1.75	10.24±2.19*

* $p<0.05$ *vs.* prior treatment within group, ** $p<0.05$ *vs.* effects of post treatment in control group. APACHEII – acute physiology and chronic health evaluation.

Assessment of incidence of adverse events and complications

Adverse events, including arrhythmia, cardiac arrest, hemodynamic changes, reduction of oxygen saturation, removal of tracheal intubation/intravascular catheter, and falling, were evaluated in this study. For the implications, the ICU-AW was diagnosed using the MRC score system (MRC scores ≤48) [25], deep vein thrombosis (DVT) formation was confirmed using color Doppler ultrasound, and pneumonia was diagnosed with computed tomography (CT). The incidence rates of the above adverse events and implications were evaluated and compared between the Observation group and Control group.

Statistical analysis

The data were analyzed with the professional SPSS software 21.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were analyzed and compared using Tukey's post hoc test validated by ANOVA among multiple groups. Categorical variables were analyzed using the chi-square test in multiple groups. Statistical significance was defined as $p<0.05$. All data were obtained from at least 6 independent tests or experiments.

Results

Early rehabilitation therapy decreased APACHE II scores

In order to determine the acute physiology and chronic health of patients, APACHE II scale was evaluated in this study. The results showed that the APACHE II scores were significantly lower after treatment than before treatment in both the Observation group and Control group (Table 2, $p<0.05$). Meanwhile, after treatments in both groups, the early rehabilitation therapy (Observation group) significantly decreased the APACHE II scores compared to that in the Control group (Table 2, $p<0.05$).

Table 3. Comparison for the MRC scores of patients between observation group and control group (mean ±SD).

Group	Prior treatment	Post treatment
Observation group (n=21)	47.14±1.85	52.95±3.99*,**
Control group (n=21)	46.38±1.88	50.10±4.21*

* $p<0.05$ *vs.* prior treatment within group; ** $p<0.05$ *vs.* effects of post treatment in control group. MRC – medical research council.

Early rehabilitation therapy enhanced MRC scores

Our findings indicated that the MRC scores were significantly higher after treatment group than before treatment in both the Observation group (early rehabilitation therapy) and Control group (Table 3, $p<0.05$). Moreover, after treatments in both groups, the MRC scores were significantly higher in the early rehabilitation therapy group (Observation group) compared to that in the Control group (Table 3, $p<0.05$).

Early rehabilitation therapy improved consciousness of patients

Consciousness improvement indexes include basic cure, markedly effective, and effective. The results showed that the early rehabilitation therapy (Observation group) significantly increased the basic cure rates, markedly enhanced the effective rates, and increased the effective rates compared to the Control group (Table 4, $p<0.05$). The total effective rate in the Observation group was also significantly higher than in the Control group (Table 4, $p<0.05$).

Early rehabilitation therapy reduced incidence of complications

Although early rehabilitation exhibited higher efficacy, it also caused a few complications. Our results indicated that the incidence rate of ICU-AW was lower in the early rehabilitation therapy group (Observation group) compared to that in the Control group, but the difference was not statistically significant (Table 5, $p>0.05$). Early rehabilitation therapy also decreased the incidence rates of pneumonia and deep venous thrombosis compared to that in the Control group, but the difference was not statistically significant (Table 5, $p>0.05$). Moreover, the total incidence rate of complications in the Observation group was significantly lower than in the Control group (Table 5, $p<0.05$).

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Table 4. Comparison for the therapeutic effects of patients between observe group and control group (%).

Groups	Basic cure GCS=15	Markedly effective GCS >12 scores	Effective GCS >9 scores	Total
Observe group (n=21)	5 (24%)*	10 (48%)*	3 (14%)*	18 (86%)*
Control group (n=21)	2 (9.5%)	5 (24%)	9 (43%)	16 (76%)

* *p*<0.05 *vs.* control group. GCS – Glasgow coma scale.

Table 5. Comparison for the ratios of complications in patients between observation group and control group (%).

Groups	ICU-AW	Pneumonia	Deep venous thrombosis	Total
Observation group (n=21)	1 (4.8%)	1 (4.8%)	2 (9.5%)	4 (19%)*
Control group (n=21)	3 (14%)	3 (14%)	3 (14%)	9 (43%)

* *p*<0.05 *vs.* control group. ICU-AW – Intensive Care Unit acquired weakness.

Table 6. Comparison for the ICU hospital stay, total hospital stay and mechanical ventilation time in patients between observe group and control group (mean ±SD).

Groups	ICU hospital stay (days)	Total hospital stay (days)	Mechanical ventilation time (days)
Observation group (n=21)	11.76±2.63*	31.38±4.006*	3.00±0.71*
Control group (n=21)	14.00±2.19	35.24±5.059	5.17±0.75

* *p*<0.05 *vs.* control group. ICU – Intensive Care Unit.

Early rehabilitation therapy shortened hospital stay and mechanical ventilation time

The early rehabilitation therapy significantly shortened the ICU stay and total hospital stay compared to that in the Control group (Table 6, $p<0.05$). The mechanical ventilation time was also significantly shorter in the Observation than in the Control group (Table 6, $p<0.05$).

Discussion

Cerebral hemorrhage and traumatic brain injury patients have extensive damage to the reticular activation system and cerebral cortex, as well as associated consciousness disorders [27,28]. In the present study, the early rehabilitation therapy was conducted by combining hyperbaric oxygen therapy, tDCS, comprehensive sensory stimulation therapy, fastigial nucleus stimulation, and therapeutic exercises. Previous studies [29–31] have never combined the above therapeutic approaches together for improving the care of ICU patients. Hyperbaric oxygen therapy has been widely employed to enhance blood oxygen levels, increase the blood oxygen diffusion velocity, and inhibit anaerobic glycolysis in damaged brain tissues [29, 30]. Hyperbaric oxygen therapy can also suppress inflammation and alleviate vascular endothelial injury in damaged brain tissues [31]. All of the above functions of hyperbaric oxygen therapy are significant in modulating the intra-cerebral environments. The tDCS is also administrated for triggering early awakening in critically ill patients in the ICU. Previous studies [32–34] reported that the tDCS-treated patients had significantly higher coma recovery scale-revised (CRS-R) scores compared to control patients, which might be associated with the spontaneous neuronal network activity, cortical excitability, synaptic plasticity, and local cerebral blood flow. In this study, comprehensive sensory stimulation therapy was mainly produced by the family members, such as auditory stimulus, visual stimulation, and massage stimulation, all of which can improve the consciousness of ICU patients. The fastigial nucleus stimulation can improve the posterior cerebral circulation and enhance cerebral cortical blood flow, the mechanism of which might be associated with nerve conduction pathways and cerebrovascular auto-regulation [35]. We used APACHE II scores, MRC scores, consciousness, incidence rates of complications, and length of hospital stay and ICU stay to evaluate the effects of the early rehabilitation strategy.

In the present study, early rehabilitation therapy significantly reduced the APACHE II scores and enhanced the MRC scores compared to that in the Control group, which suggested that

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early rehabilitation therapy alleviated the disease severity and improved the consciousness of ICU patients. These results were consistent with former studies [36,37] reporting the effects of various approaches in early rehabilitation therapy on the progression and prognosis of ICU patients.

Due to the long-term bedridden, braking, and sedative/analgesic measures, associated complications always occur in ICU patients. In this study, the complications of ICU-AW, pneumonia, and DVT were evaluated and compared between the Observation group and Control group. ICU-AW is mainly characterized by decreased systemic muscle strength, contracture of joints, decreased muscle endurance, and dysfunctional ventilatory weaning response [38]. A previous study [39] also reported that the incidence rate of ICU-AW in critically ill patients is 25–30%. Braking usually causes decreased diaphragm strength and impaired discharge of secretions, both of which prolong the mechanical ventilation time and induce pneumonia [40]. DVT is caused by the obstruction of venous return and micro-vascular dysfunctions [41]. In this study, the total incidence rate of complications in the early rehabilitation therapy group (Observation group, 19%) was decreased significantly compared to that in the Control group (43%). These results suggest that early rehabilitation helps reduction complications. However, there were no significant differences in occurrence of ICU-AW, pneumonia, and DVT, which might be associated with the lower number of cases and limited therapy approaches. Subsequent studies should have larger sample sizes, increased cardiopulmonary resuscitation, and early initiation of exercise out of bed.

Adler et al. [42] reported that the early exercise of ICU patients is feasible and safe, and can improve the prognosis. In this study, we administrated the rehabilitation therapy at 3.9±1.22 days after the onset of disease, which is significantly earlier than that reported in a previous study [43]. However, early rehabilitation therapy in this study led to significantly shorter ICU stay and total hospital stay, as well as shorter mechanical ventilation time compared to the Control group. These results suggest that rehabilitation conducted at the early stage of disease is effective for ICU patients. Moreover, our results showed that there was only 1 patient with increased heart rate in the early rehabilitation therapy group, which suggests that early rehabilitation therapy does not increase the occurrence of adverse events. In this study, we established a comprehensive early rehabilitation therapy for ICU patients, which demonstrated high efficacy and safety. Compared with previously established approaches, our therapeutic strategy led to decreased APACHE II scores, enhanced MRC scores, and improved consciousness for ICU patients. Early rehabilitation therapy also resulted in decreased incidence of complications and shortened ICU stay and total hospital stay. Our results suggest that comprehensive early rehabilitation therapy improves clinical care of ICU patients.

Although this study verified the effectiveness and safety of early rehabilitation therapy, there were also a few limitations. Firstly, the sample size of this study was relatively small, so our results might not realistically reflect actual outcomes in real conditions. In our next study, we will enlarge the sample size and involve more patients. Secondly, the observation time of patients was relatively short and we did not perform long-term follow-up. Future research on early rehabilitation therapy should include assessment of the therapeutic effects of ultra-early rehabilitation treatment, as well as the effects of early rehabilitation therapy on other disorders.

Conclusions

Early rehabilitation therapy decreased APACHE II scores, enhanced MRC scores, and improved consciousness of ICU patients. Moreover, early rehabilitation therapy also reduced the incidence of complications and shortened ICU stay, total hospital stay, and mechanical ventilation time of ICU patients. Therefore, the early rehabilitation therapy was effective and safe for ICU patients.

Conflict of interest

None.

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