Review

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Early Mobilization and Rehabilitation of Critically-Ill Patients

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Abstract

Post-intensive care unit (ICU) syndrome may occur after ICU treatment and includes ICU-acquired weakness (ICU-AW), cognitive decline, and mental problems. ICU-AW is muscle weakness in patients treated in the ICU and is affected by the period of mechanical ventilation. Diaphragmatic weakness may also occur because of respiratory muscle unloading using mechanical ventilators. ICU-AW is an independent predictor of mortality and is associated with longer duration of mechanical ventilation and hospital stay. Diaphragm weakness is also associated with poor outcomes. Therefore, pulmonary rehabilitation with early mobilization and respiratory muscle training is necessary in the ICU after appropriate patient screening and evaluation and can improve ICU-related muscle weakness and functional deterioration.

Keywords: Rehabilitation; Critical Care; Intensive Care Unit-Acquired Weakness; Early Mobilization

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Introduction

Increased survival rates after intensive care unit (ICU) treatment owing to improved critical care technology have increased the interest in long-term complications after ICU treatment. A study on the survival of 109 patients who received ICU treatment for acute respiratory distress syndrome showed that pulmonary function recovered close to normal at 5 years. However, physical function does not return to normal, even in young patients[1]. The physical, cognitive, and psychological impairments that occur during treatment in the ICU or after ICU discharge comprise post-intensive care syndrome (PICS), which affects not only the long-term prognosis of patients treated in the ICU but also their families[2].

PICS often presents with symptoms of cognitive decline, such as delirium, dementia, and depression; decline in physical function, such as ICU-acquired weakness (ICU-AW); and psychiatric disorders, such as depression, anxiety, and post-traumatic stress syndrome. In addition, it affects mental health, causing anxiety, depression, and post-traumatic stress for family members who are guardians, as well as ICU survival. It also affects social health, such as family social responsibility, resulting in PICS-family[3,4].

The ABCDE bundle is widely known to prevent PICS and comprises: A, aawakening; B, breathing, which means daily interruption of a mechanical ventilator and spontaneous breathing attempt; C, ccoordination; D, delirium monitoring; and E, early mobility and exercise. These are also risk factors for PICS. Recently, FGH has been added to prevent PICS, where F indicates family involvement, follow-up referrals, and functional reconciliation; G indicates good handoff communication; and H indicates handout material on PICS and PICS-family[3,5]. This bundle has beneficial effects that reduce deep sedation, immobilization, and anxiety[6,7]. This review focuses on rehabilitation in the ICU, including early mobilization, as a strategy for preventing and treating PICS.

ICU-AW

ICU-AW is defined as limb muscle weakness in patients treated in the ICU and is reported in 33% to 59.6% of cases. ICU-AW may be due to the period of mechanical ventilation[8-10]. According to a study published in 2013, 63 patients treated in the ICU who were expected to undergo intubation for more than 48 hours were recruited within 24 hours. The cross-sectional area of the thigh muscle (rectus femoris) was measured on the 1st, 3rd, 7th, and 10th days and showed a significant reduction of 10.3% (95% confidence interval [CI], 6.1% to 14.5%) on day 7 and −17.7% (95% CI, −20.9% to −4.8%) on day 10[11]. According to a recently published prospective observational study, 59.6% of patients showed a decrease of ≥10% in the rectus femoris cross-sectional area when comparing the 1st and 7th days of ICU admission[10]. Biopsy of the skeletal muscles of patients with prolonged critical illness revealed changes in muscle properties. Protein synthesis at the gene expression level decreased, and proteolysis increased[12]. Muscle atrophy continued to decline for up to 4 weeks, and the decrease in cross-sectional area in the arms was greater than that in the legs[13].

The pathophysiology of ICU-AW is thought to be caused by various factors, including microvascular ischemia, catabolism, and immobility, which can lead to skeletal muscle wasting. In contrast, microvascular injury resulting in nerve ischemia, sodium channel dysfunction, and nerve mitochondrial injury can contribute to critical illness-related neuropathy and myopathy[14].

ICU-AW is commonly divided into critical illness polyneuropathy (CIP), critical illness myopathy (CIM), critical illness neuromyopathy (CINM), and muscle deconditioning[15]. CIP is a symmetrical distal sensorimotor axonal polyneuropathy that affects the limb muscles, respiratory muscles, sensory nerves, and autonomic nerves. Extremity weakness is observed more distally, and distal sensory impairments may occur[16]. CIM preserves sensory nerves but causes weakness in the limb and respiratory muscles. Similar to CIP, flaccid paralysis is noted, but muscle weakness is more severe in the proximal than in the distal muscles[16]. CIP and CIM share certain characteristics in CINM[3].

The ICU-AW diagnostic criteria were presented by Stevens et al.[8] in 2009. Systemic weakness occurs after the onset of severe disease and is symmetrical and flaccid, including both proximal and distal muscles; however, the cranial nerves are usually preserved. It can be diagnosed if tested twice or more over 24 hours, and the Medical Research Council (MRC) score is <48 out of 60 points and less than 4 points for all tested muscles. In addition, a diagnosis can be made even when a ventilator is used, and no other existing diseases can explain this weakness. The manual muscle strength test is conducted on six muscle groups: arm abduction, forearm flexion, wrist extension, hip flexion, knee extension, and foot dorsiflexion. It is measured on both sides and based on a score of 0–5, so the total score was 60 points. A score of <48 out of 60 indicates ICU-AW and a score of less than 36 indicates severe ICU-AW[17].

A hand-held dynamometer is a more straightforward method, and a diagnosis is made when the weight is <11 kg in men and <7 kg in women[18-20]. However, since these examination methods are only possible with the patient's cooperation, if muscle weakness is suspected clinically, a diagnosis of ICU-AW can be made according to a decrease in handgrip strength and an MRC sum score <48 after identifying whether there was preceding muscle weakness, and if the patient's evaluation was valid and reliable. If these clinical assessments are unreliable, a diagnosis can be made through objective studies such as electrophysiological studies or muscle/nerve ultrasound[21].

Diaphragm Weakness in the ICU

As early mobilization of limb muscles is performed to prevent immobility due to ICU-AW, respiratory muscles also experience muscle weakness due to unloading while using a mechanical ventilator. Muscle weakness in the ICU does not appear in the same pattern in the limb and respiratory muscles but occurs more rapidly and severely. Diaphragm atrophy, a representative of inspiratory strength, occurs rapidly in 50% of patients, with a 20% loss in diaphragm thickness on the 3rd or 4th day after mechanical ventilation. This progresses rapidly and more profoundly than the approximately 10% decrease in quadriceps muscle thickness in the first week of mechanical ventilator use[22,23]. Diaphragmatic atrophy progresses rapidly without the use of the respiratory muscles during mechanical ventilation. Histological results from biopsy indicate that this is caused by increased diaphragm proteolysis during inactivity[23,24]. In addition to the excessive loading applied to the diaphragm due to acute respiratory failure during early ICU treatment and extreme muscle unloading after mechanical ventilation, various causes such as critical illness, polymyoneuropathy, sepsis, exposure to pharmacological agents, malnutrition, metabolic factors, and bed rest during the entire period are thought to contribute to this respiratory weakness[25].

Respiratory muscle weakness in the ICU does not occur solely in the diaphragm. One study showed that maximal expiratory pressure (MEP), an index of expiratory muscle strength, decreased significantly after mechanical ventilation in the ICU, although expiratory muscles are mainly related to coughing rather than inspiratory ability[26].

As with the limb muscle test, some methods can only be used to diagnose ICU-AW of the respiratory muscles when the patient is fully cooperative, in addition to non-volitional tests and imaging. If a patient cooperates, measuring maximal inspiratory pressure (MIP) and MEP at the bedside is the best way to estimate respiratory muscle strength[27]. However, MIP represents inspiratory muscle activity and is not specific to the diaphragm. As the examination is possible only when the patient cooperates, poor test results may be due to poor cooperation. In addition to measuring MIP in the ICU, diaphragm strength can be measured by transdiaphragmatic pressure, and maximal transdiaphragmatic pressure less than 60 cmH_2O indicates diaphragmatic weakness. Unlike MIP, this method has the advantage of specific measurement of the diaphragm but has the disadvantage of requiring invasive procedures such as esophageal and gastric balloon insertion[28,29].

If the patient does not cooperate fully, non-volitional functional tests, such as transdiaphragmatic pressure in response to bilateral twitch phrenic nerve stimulation or endotracheal tube pressure in response to bilateral phrenic nerve stimulation, are performed during airway occlusion. Recently, diaphragmatic excursion using ultrasonography, or a method for measuring diaphragmatic weakness by measuring the degree of the thickening fraction, has been widely used. Ultrasound is easy to perform at the bedside and is noninvasive; however, it has limited value during assisted breathing[28-30].

Risk Factors and Prognosis of ICU-AW

Risk factors for ICU-AW include sepsis in female patients, catabolic state, multiple organ failure, systemic inflammatory response syndrome, long-term mechanical ventilation, immobility, hyperglycemia, glucocorticoids, and neuromuscular blocking agents[14]. ICU-AW is a complication in patients treated in the ICU in the short and long-term. Short-term complications include increased ICU stay, increased hospitalization costs, failure to perform tracheal intubation, increased duration of ventilator use, and swallowing disorders. Complications include increased mortality after ICU treatment, decreased physical function, reduced discharge to home, and increased discharge to hospitals or rehabilitation facilities[31].

ICU-AW showed more severe weakness in the proximal than distal muscles. The period on a ventilator and the length of ICU stay were significantly longer, with more deaths occurring at a follow-up of ≤9 months compared to patients without ICU-AW. ICU-AW affects long-term outcomes[32] and is an independent predictor of mortality after ICU treatment. It is thought to be significantly associated with low physical function in survivors 6 months after they leave the ICU[33]. In addition, even after 2 years, the survival rate was significantly lower than that of patients without ICU-AW[34]. The cumulative survival rate at 1 year was significantly lower when the MRC cutoff was 48 and significantly lower compared to three groups in the no ICU-AW, ICU-AW, and severe ICU-AW groups[31]. Therefore, ICU-AW is considered an independent prognostic factor of mortality and is thought to increase the probability of death[35].

Weakness of the respiratory muscles, such as diaphragm atrophy, is a clinically important prognostic factor associated with decreased diaphragm function, increased risk of prolonged mechanical ventilation, and poor outcomes such as reintubation and tracheostomy[36].

An MIP of −30 cmH_2O is the cutoff value suggesting respiratory muscle weakness, and a less negative value than −30 cmH_2O is associated with prolonged weaning and weaning failure[26]. Unlike ICU-AW, which occurs in limb muscles, respiratory muscle weakness is not related to 5-year mortality but is associated with 5-year morbidity, such as decreased physical function, grip strength, and walking distance[37].

Pulmonary Rehabilitation in the ICU

1. Evaluation

Evaluation before rehabilitation in the ICU can be divided into three categories: assessment of disease severity, degree of sedation and delirium, and functional levels. An ICU physician mainly assesses disease severity. The Acute Physiology and Chronic Health Evaluation II (APACHE II), simplified Acute Physiology Score (SAPS), and Sepsis-related Organ Failure Assessment Score (SOFA) are the most commonly used scores[38-40]. The Richmond Agitation-Sedation Scale (RASS) is most frequently used to evaluate the degree of sedation in patients. Scores of 0, −1, −5, +1, and +4 indicate alertness, drowsiness, unarousableness, restlessness, and combativeness, respectively. Sedated patients are provided verbal stimulation by calling their names and asking them to open their eyes; if there is no response, a physical stimulus, such as shaking their shoulders or rubbing their sternum, is administered[41]. The RASS can be evaluated quickly, and changes in sedation status can be detected when repeatedly assessed[42].

In addition, the degree of delirium should be evaluated. For this, the Confusion Assessment Method (CAM)-ICU is mainly used. In the first step, the level of consciousness was evaluated using the RASS; in the next step, the content of consciousness was assessed to confirm delirium[43]. The RASS and CAM-ICU are mainly used to evaluate consciousness before rehabilitation starts and are often used to determine whether or not to receive rehabilitation treatment.

There are several evaluations of functional status, such as the MRC manual muscle test, grip strength test using a hand-held dynamometer, Physical Function in Intensive care test scores (PFIT-s), Functional Status Score for the ICU (FSS-ICU), ICU mobility scale (IMS), and Chelsea Critical Care Physical Assessment tool[44-48].

The PFIT-s scores the four items of shoulder flexion and knee extension strength, sit-to-stand assistance, and step cadence on a scale of 0–3 and scores on an ordinal scale of 0–12. The FSS-ICU scores 0–7 points according to the patient's ability to perform five functional items: rolling, transfer from supine to sitting, sitting at the edge of the bed, transfer from sitting to standing, and walking, and scores from 0 to 35. A score of 0 indicates total inability and a score of 35 indicates a functionally independent state. The Korean FSS-ICU validation study was published in 2019[49].

The IMS evaluates the maximum level of mobility of ICU patients by categorizing the state of being unable to move actively on the bed as 0 points and the state of being able to walk independently without a walking aid as 10 points. The IMS is divided into 11 levels according to the level of mobility and assistance and has a more detailed classification of mobility and assistance levels compared to other functional assessments. The Chelsea Critical Care Physical Assessment tool scores 10 items from 0–5, giving a total score of 50. Compared to other functional assessments, it is differentiated by specific respiratory functions and cough items. These functional evaluations indicate the functional level of ICU patients and can be used as a guide for rehabilitation treatment prescriptions.

The optimal timing for these evaluations is when patients are awake during ICU care with or without mechanical ventilator use, discharged from the ICU or hospital, and during follow-up because these tests require patient cooperation.

2. Early mobilization

Daily interruption of sedation and early mobilization of mechanically ventilated patients have been emphasized in the ABCDE bundle in the ICU to prevent PICS and ICU-AW. Although there is no clear consensus on the definition of early mobilization, mobility is thought to mean more than edge sitting back to the bed. Some studies defined early mobilization as mobilization within 5 days after admission to the ICU[50,51]. It is used interchangeably with physical therapy, early mobility, and rehabilitation. It has been reported that improving the patient's mobility through physical and occupational therapy from an early stage in such an ICU can aid return to ambulation. In addition, the impact of reducing ICU length of stay and hospital length of stay has been reported[52-54]. A randomized controlled trial on the effect of early mobilization in the ICU was first published in 2009, in which the intervention group underwent physical and occupational therapy within 72 hours of ICU admission, and the control group received usual care. The early physical and occupational therapy intervention groups returned to independence better than the control group. It showed significantly favorable outcomes in terms of functional status at hospital discharge, ICU delirium, hospital delirium, and duration of mechanical ventilation[55]. Early mobilization in the ICU results in greater muscle strength at ICU discharge[56], improved physical function, reduced ICU and hospital stay[57], decreased incidence of ICU-AW at hospital discharge, increased number of patients who are able to stand, increased number of ventilator-free days during hospitalization, increased distance of unassisted walking at hospital discharge, increased discharged-to-home rate, and improved quality of life[58,59]. In a recently published randomized controlled trial, no significant difference was observed in outcomes such as days alive, mortality at day 180, and ventilator-free days at day 28 between the early mobilization group and the usual care group. Adverse events were even significantly higher in the early mobilization group. However, the early mobilization group received an average of 20.8 minutes per day compared to 8.8 minutes per day in the usual care group, both of which were lower than the generally administered ICU rehabilitation dose. Moreover, the usual care group implemented active and high-level functional exercises such as active sitting, standing, transfer, assisted walking, and independent walking. Therefore, the observed lack of significant differences between the groups may be attributed to the relatively low treatment dose in both arms. Considering the current reality of rehabilitation therapy in domestic settings where most rehabilitation sessions are conducted at a passive exercise level within 10 minutes due to the lack of specific insurance coverage for ICU rehabilitation, it is suggested that the benefit of early mobilization compared to current usual care should not be underscored without careful consideration of trial details[60].

The recently published recommendations for rehabilitation as a treatment method for PICS emphasize the importance of screening critically-ill patients receiving ICU care for more than 48 hours after leaving the ICU, before and after rehabilitation, and even outpatients.

Recently published guidelines for PICS rehabilitation included 16 recommendations: (1) as ought to or ought not to are early mobilization within the first few days in the ICU, multimodal sensory, cognitive, and emotional stimulation for delirium prevention, and ICU diary use; (2) as should or should not are inspiratory muscle training (IMT), standardized swallowing assessment, computer-based cognitive therapy, interventions for stress reduction, non-use of haloperidol, and psychological intervention. Additionally, supplemental bed cycling, wheelchair cycle ergometer training, strength training, and electrical stimulation are considered potential therapeutic options[61].

When performing rehabilitation in the ICU, the degree of physiological and hemodynamic stability, adequate ventilation, sedation interruption, and delirium management should be assessed before each treatment session to determine whether treatment should be included. The screening criteria for rehabilitation inclusion varied slightly from those reported in the literature. When a hospital plans to start ICU rehabilitation, the inclusion/exclusion criteria should be established first, followed by proper patient care for safety. For rehabilitation and early mobilization, such as active-assisted range of motion and active sitting without back support, patients should be alert and able to cooperate to some extent. In addition, since there is a possibility of acute deterioration in the ICU, it is necessary to observe the patient's condition daily to determine whether to treat or advance the treatment to a higher or lower level. This highlights the importance of establishing the safety criteria, inclusion/exclusion criteria, and screening for every session.

After bedside active range of motion is achieved in the supine position, early mobilization can be advanced to the upright edge sitting, standing, transferring, and walking positions. If any adverse event occurs during these rehabilitation sessions, it is held once, re-evaluated, and treated the next day or session. Early mobilization and rehabilitation in the ICU are considered safe and feasible. The occurrence of safety events in the mobilization/rehabilitation sessions is less than 1% (approximately 0.6%), including hemodynamic changes, tube/catheter removal, and desaturation. These adverse events should immediately be corrected, and no other treatment is required[52,62,63].

Respiratory Muscle Training in the ICU

As respiratory muscle weakness occurs due to respiratory muscle unloading through mechanical ventilator use, selecting an appropriate ventilator support level is important for reducing such unloading. It is crucial to determine the inspiratory effort level within the target range that appropriately lowers the risk of poor outcomes, diaphragm injury, sedation, and ventilator support. This is known as diaphragm-protective ventilation[36]. However, the level of evidence for this is still low, and it is not a routine practice. In addition to controlling the inspiratory level of a mechanical ventilator, there is IMT for improving inspiratory muscle reconditioning. In a randomized controlled trial conducted on patients 48 hours after successful weaning, MIP was significantly higher in the group that received IMT for 2 weeks than in the usual care group[64]. A systematic review and meta-analysis reported that MIP significantly increased in patients with IMT compared to usual care[65]. There are two IMT methods: pressure threshold and flow-resistive loading. A practical guide published by Australian Critical Care in 2018 explained that the flow-resistive loading method depends on the flow generated by the patient, making training intensity variable, depending on effort. Therefore, using a threshold-loading device is recommended[27].

IMT can be applied to both ventilator-dependent and recently weaned patients, and the proper indication for IMT application in the ICU includes the patient's alertness and cooperation and adequate range of positive end expiratory pressure, fraction of inspired oxygen, and respiratory rate. Owing to the possibility of fatigue through IMT training on weak inspiratory muscles, it is recommended to implement a low-repetition, high-intensity protocol, which involves six breaths in one set, five sets, and an intensity of at least 50% of the MIP[27].

Conclusion

After ICU admission, functional deterioration of the limb and respiratory muscle weakness may occur. To prevent and treat these conditions, a multidisciplinary team approach, including an ICU physician, rehabilitation physician, nurse, physical therapist, and occupational therapist, is needed in the ICU. The team should perform screening and proper rehabilitation intervention according to the patient's functional ability and limb/respiratory muscle strength when the patient wakes up, when leaving the ICU, when discharged from the hospital, and during follow-up in an outpatient clinic. In the ICU, spontaneous breathing trials after interrupting sedation are performed daily to prevent delirium, and daily early mobilization and respiratory muscle training are conducted to prevent and treat muscle weakness and functional deterioration. Therefore, active intervention is needed. Rehabilitation in ICU care is not optional but essential.

Authors' Contributions

Conceptualization: all authors. Methodology: all authors. Formal analysis: all authors. Data curation: all authors. Software: all authors. Validation: all authors. Investigation: all authors. Writing - original draft preparation: all authors. Writing - review and editing: all authors. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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