

Review

Rehabilitation Management of Intensive Care Unit-acquired Weakness (ICU-AW): A Narrative Review

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ABSTRACT

Background: Intensive Care Unit-acquired weakness (ICU-AW) is one of the most common neuromuscular disorders affecting intensive care unit (ICU) patients' outcomes and clinical course. ICU-AW is found in 30-50% of patients and increases to 67% in sepsis-critically ill patients. Prolonged ICU stay, the difficulty of weaning from the ventilator, higher hospitalization costs, and an increase in mortality, as well as long-term morbidity, are associated with ICU-AW. ICU-AW causes skeletal muscle weakness, including respiratory muscles, which results in complications that continue even years after being discharged from the hospital.

Aim: To describe the rehabilitation management of ICU-AW and provide the information needed clinically to manage these patients.

Methods: The authors reviewed all types of articles without time filtering using PubMed and Google Scholar databases with "ICU-AW", "ICU-related weakness", "rehabilitation", and "early mobilization" used as keywords.

Results: Rehabilitation management can be done as early as possible, beginning while the patient is still in the ICU. Early mobilization programs require teamwork consisting of doctors, therapists, and nurses. Physical activity and early mobilization in the ICU must be carried out with consideration for safety. Monitoring patient safety before and during mobilization is an essential factor to be considered. Any mobilization program should be the decision of the ICU care team. Implementation of rehabilitation programs and early mobilization improves outcomes for patients with ICU-AW and should be continued until the follow-up period.

Conclusion: The rehabilitation management aiming at preventing and treating ICU-AW should be done since the patient was still in the ICU and under careful consideration of safety aspects.

Keywords: *Critical Illness, Intensive Care Unit, Mechanical Ventilation, Muscle Weakness, Rehabilitation, Respiratory Muscles*

INTRODUCTION

Over the last few decades, the prognosis of patient care in the Intensive Care Unit (ICU) has improved with the advancement of technology and science. Mortality in critically ill patients is decreased, and the number of survivors with an impaired functional ability to return to normal life is increased.⁽¹⁾ ICU survivors with multi-organ failure are highly susceptible to physical morbidity, with a loss of muscle mass of up to 30% in the first 10 days since ICU admission.⁽²⁾ Loss of muscle mass is associated with weakness or reduced muscle strength.⁽³⁾

Intensive Care Unit-acquired weakness (ICU-AW) is the most common neuromuscular disorder that affects the outcomes and clinical course of ICU patients. ICU-AW is found in 30-50% of patients and increases to 67% in sepsis-critically ill patients.⁽⁴⁾ The prevalence of ICU-AW in patients on mechanical ventilation for 48 hours or more is 25-40%.⁽²⁾ Prolonged ICU stay, difficulty in weaning from the ventilator, higher hospitalization costs, and an increase in mortality, as well as long-term morbidity,

are associated with ICU-AW.⁽⁴⁾ Muscle weakness that occurs in ICU-AW may persist for months or even years after the patient is discharged from the hospital.⁽³⁾ ICU-AW patients have a poorer prognosis, both during hospitalization and after being discharged. Among patients requiring mechanical ventilation for 5 days, the existence of ICU-AW was associated with a 2-fold increase in mechanical ventilation duration and a 2- to 5-fold increase in mortality during hospitalization. Two years after acute respiratory distress syndrome (ARDS), ICU-AW patients also showed a decreased quality of life compared to patients without ICU-AW.⁽⁵⁾

Implementation of rehabilitation programs and early mobilization improves the outcomes of ICU-AW patients. Patients with ICU-AW who underwent an early mobilization program were more likely to return home after hospitalization without admission to a rehabilitation center, compared with patients who did not undergo structured physical therapy. Passive mobilization prevents the effects of prolonged bed rest. Diaphragmatic and breathing exercises,

which were performed daily, increased the weaning ability. Modalities and techniques to maintain joint range of motion and muscle strength improve ventilatory function.⁽⁶⁻⁸⁾

Rehabilitation management requires multi-disciplinary collaboration to provide safe mobilization programs for ICU patients.⁽⁸⁾ Early mobilization has been associated with improved healthcare outcomes and serves as a safe procedure for critically ill patients.⁽⁹⁾ Rehabilitation management is carried out from the ICU to an outpatient clinic.⁽¹⁰⁾ To the author's knowledge, there is no standard guideline for rehabilitation management in patients with ICU-AW. This review attempted to describe rehabilitation management of ICU-AW to provide information needed clinically to manage these patients.

METHODS

Articles were reviewed to obtain data about rehabilitation management in patients with ICU-AW. Articles were collected using PubMed and Google Scholar databases without limiting the year or type of article publication. Keywords

used were "ICU-AW", "ICU-related weakness", "rehabilitation", and "early mobilization". Articles that were not available in full text and were not written in English were excluded.

RESULTS AND DISCUSSION

ICU-AW

Definition

ICU-AW is generalized muscle weakness that occurs during ICU care, and no other causes are identified other than the critical illness itself.⁽¹¹⁾ There are several pathologies to describe ICU-AW, including critical illness polyneuropathy (CIP), critical illness myopathy (CIM), or both, which is called critical illness neuromyopathy (CINM).^(3,12) ICU-AW may be observed when there is tetraplegia or tetra paresis, muscle weakness, hyporeflexia, difficulties of weaning, and negative tendon reflexes. Weakness in ICU-AW can affect peripheral and respiratory muscles.⁽⁸⁾

ICU-AW is associated with morbidity and mortality in critically ill patients. Recent data suggests that ICU-AW can also

result in long-term consequences. It is known that ICU-AW is an important contributor to the occurrence of post-intensive care syndrome (PICS), which is a phrase used to describe the occurrence of mental, cognitive, and physical dysfunctions. PICS resulted in permanent disabilities that extend beyond the acute care period. It has a major impact on the quality of life of ICU survivors.⁽¹³⁻¹⁵⁾

Pathophysiology

Skeletal muscle morphological changes that occur in ICU patients include loss of thick filaments (myosin), muscle fiber regeneration, necrosis, and atrophy. In CIP patients with electrophysiological characteristics, the common neuropathology is axonal degeneration, mainly in the distal axons. It involves motor and sensory fibers without any evidence of inflammation or demyelination.

Peripheral nerve atrophy and compressive neuropathy can also cause the loss of functional innervation and muscle

dysfunction. A muscle biopsy shows denervation features and signs of myopathy. Changes in muscle contractility, switch of muscle fiber, muscle protein synthesis and aerobic capacity, as well as the electromechanical properties of the neuromuscular complex, have all been found to be significant in experimental studies of critically ill patients. All of these biological changes result in decreased muscular strength and fatigue resistance.^(3,16,17) The differences in the pathophysiology of CIP, CIM, and CIMN are described in Table 1.⁽¹⁸⁾

In critically ill patients, there are also signs of anabolic metabolism in the form of disruption of the sarcomere along with decreased slow- and fast-twitch muscle fibers. There is a decrease in the number of satellite cells and mitochondria, while the rate of proteolysis and autophagy is increased in the Quadriceps muscles. After being discharged from the ICU, there is persistent atrophy of Quadriceps muscles with fewer satellite cells than before.^(3,19,20)

Table 1. Pathophysiology of CIP, CIM, and CIMN

Examination	CIM	CIP	CINM
Physical Examination	<ul style="list-style-type: none"> • Normal sensory • Proximal muscle weakness • Decreased or normal deep tendon reflexes 	<ul style="list-style-type: none"> • Distal sensory deficit • Distal muscle weakness • Decreased or normal deep tendon reflexes 	<ul style="list-style-type: none"> • Distal sensory deficit • Distal and proximal muscle weakness • Decreased deep tendon reflexes
Neurological Assessment	<ul style="list-style-type: none"> • EMG shows low amplitude activity and short duration • Normal SNAP and decreased CMAP • Decreased MUAP 	<ul style="list-style-type: none"> • Near normal or normal conduction velocity • Decreased SNAP and CMAP • Normal MUAP 	<ul style="list-style-type: none"> • EMG shows low amplitude activity and short duration • Normal SNAP and decreased CMAP • Decreased MUAP
Histology Examination	<ul style="list-style-type: none"> • Loss of thick filaments (myosin), atrophy, and necrosis of type 2 muscle fibers 	<ul style="list-style-type: none"> • Distal axonal, nerve, and sensory degeneration 	<ul style="list-style-type: none"> • Evidence of loss of thick filaments (myosin) and axonal degeneration, type 2 muscle fiber necrosis, and atrophy
Pathophysiology	<ul style="list-style-type: none"> • Oxidative stress • Dysfunction of mitochondrial • Ubiquitin-proteasome proteolysis • Sodium channel abnormalities 	<ul style="list-style-type: none"> • Nerve microvascular injury • Nerve ischemia • Sodium channel abnormalities • Nerve mitochondrial injury 	Mixed

CIP, *critical illness polyneuropathy*; CIM, *critical illness myopathy*; CINM, *critical illness neuromyopathy*; CMAP, *compound muscle action potential*; MUAP, *muscle unit action potential*; EMG, *electromyography*; SNAP, *sensory nerve action potential*

Risk Factors

Factors that placed critically ill patients at risk for ICU-AW include bed rest, hyperglycemia, sepsis, multi-organ failure, and the use of neuromuscular blocking agents (NMBA) and corticosteroids. Other factors are old age, female gender, increasing disease severity, systemic

inflammatory syndrome, use of aminoglycosides, parenteral nutrition, prolonged use of mechanical ventilation, catabolic status, and a combination of these factors.^(4, 5, 8, 21, 22)

Bed rest was found to be the only factor consistently related to the occurrence of ICU-AW in a study of acute lung injury

patients. This is assumed to be caused by inflammation and atrophy with muscle catabolism, which is more common in the traditional treatment model in which the patient is sedated and immobilized for an extended period of time. Muscle catabolism causes systemic inflammation and weakness, especially in sepsis patients. In ARDS patients, multi-organ failure is associated with poor quality of life for up to 5 years and long-term physical dysfunction.^(11, 23, 24)

The most frequent identified risk factor in ICU-AW is hyperglycemia. One study showed that in the management of hyperglycemia patients, assessment and management of ICU-AW through early intervention are more important than managing patients with strict glycemic control. Several prospective cohort studies looking for an association between corticosteroid use and NMBA with ICU-AW found no association between the two.

The use of NMBA in the early phase (first 48 hours) can diminish lung injury, so treatment with these drugs should still be considered.^(5, 25) In mechanically ventilated patients for a minimum of 10 days, the incidence of ICU-AW is up to 67%. A study

found that the prevalence of ICU-AW in ICU patients admitted for a minimum of 24 hours was 11%, and when the ICU stay continued for 7-10 days, the prevalence increased to 24-55%. In awake ARDS patients, the prevalence of ICU-AW was 60% and the incidence is still high at hospital discharge (36%).^(4, 5, 11)

Diagnosis

History

The history should include clinical history and neuromuscular symptoms associated with risk factors.⁽³⁾ Symptoms of ICU-AW include symmetrical limb weakness with more significant flaccidity in the proximal muscles than the distal. Face and eyes muscles are usually preserved. Weakness usually occurs in 26%-65% of patients who were mechanically ventilated for 5-7 days, and 25% among this remain weak for at least 7 days after awakened.⁽¹¹⁾

Physical Examination

A neurological examination is a significant component of the ICU-AW examination. Neurological examination should cover functional domains such as cognitive and consciousness, cranial nerves, reflexes, coordination, sensory, and motor functions.⁽³⁾ Patients with ICU-AW usually

respond to painful stimuli with facial expressions (grins) and very little or no response to limb withdrawal reactions.⁽¹¹⁾ Reduced tendon reflexes are commonly found, although sometimes they can be normal. In CIP cases, there may be sensory symptoms, including loss of temperature, vibration, and sensitivity to pain. Sensory function examination in critically ill patients is usually difficult. Examination of muscle strength should include the respiratory muscles because these muscles are often affected in ICU-AW, resulting in difficulty of weaning from the ventilator. Autonomic

dysfunction is common in critically ill patients, so the physical examination also includes examining autonomic symptoms such as heart rate variations. Many confounders influence blood pressure variations, so autonomic dysfunction is not an optimal indicator in the diagnosis of ICU-AW.⁽¹¹⁾

The Medical Research Council (MRC) is muscle strength examinations that depending on the patient's cooperation and efforts (Table 2). Muscle strength presented with various values from 0 (no muscle contraction) to 5 (full strength).⁽⁵⁾

Table 2. Medical Research Council (MRC): Manual Assessment of Muscle Strength

Grade	Clinical Presentation Assessed by The Patient's Effort
0	No visible movement
1	Only minimal visible movement in the form of twitching, or visible muscle fasciculation, or palpable muscle movement
2	Muscles move only if no resistance to gravity (e.g. the elbow can maximally bend only if the arm is kept in the frontal plane)
3	Reduced muscle strength so the joint can only be moved against gravity and cannot at all withstand the resistance of the examiner (e.g. the elbow joint can be moved from full extension to flexion with the initial position of the arm hanging)
4	Decreased muscle strength but muscle contraction can still move the joint against resistance
5	Normal muscles contraction against full resistance

The MRC muscle examination established the diagnosis of ICU-AW. The total score obtained from the sum of strength of six muscle groups includes shoulder joint abduction, wrist flexion, elbow flexion, knee joint extension, hip joint flexion, and ankle dorsi flexion, with a total score varying from 0 to 60 (defined as complete paralysis and normal muscle strength, respectively). The total MRC score (left and right) of less than 48 recorded in more than two examinations with a difference of 24 hours in the conscious state was defined as ICU-AW.⁽⁵⁾

Electrophysiological examinations are also routinely used to assess the peripheral nervous system, including nerve conduction studies (NCS), neuromuscular junction testing, and needle electromyography (EMG).

Another muscle strength parameter is the assessment of isometric strength and dorsiflexor torque to stimulate the peroneal and ulnar nerves. Phrenic and diaphragmatic nerve conduction assessments were also performed.⁽³⁾

Differential Diagnosis

The differential diagnosis of ICU-AW included metabolic neuropathy, Guillan-Barre Syndrome (GBS), nutritional deficiency-induced neuropathy, and toxic neuropathy. Symptoms of GBS are usually symmetrical, ascending and progressive paralysis, areflexia, and sensory abnormalities. Decreased nerve conduction velocity is a hallmark of GBS. Decreased action potential and normal nerve conduction velocity are features of axonal neuropathy that can be seen in axonal variations in GBS and CIP.⁽⁸⁾

Complications

The most common ICU-AW manifestations are the use of mechanical ventilation and prolonged ICU care. This can occur due to weakness of the diaphragm and chest wall muscles. One study found that >50% of patients who were >48 hours on mechanical ventilation and suffered from ICU discharge experienced ICU-AW. The presence of ICU-AW on discharge from the ICU was related to poor long-term outcomes, including an increased 90-day mortality rate

compared to patients without ICU-AW. One cohort study found that an increased incidence of muscle weakness on ICU discharged was related to an increased risk of death after 12 months. In addition, ICU-AW is also related to poor quality of life in years following treatment.^(11, 26, 27)

Prognosis

Functional healing of nerves and muscles that was good in ICU survivors was found to be highest in young patients who were formerly healthy with good support from caregivers. A greater burden of comorbid disease, increasing age, cognitive/mood dysfunction, longer ICU stay, increased caregiver dysfunction, or a combination of any of these factors negatively affect the ability of patients to return to functional independence.⁽²⁰⁾

FUNCTIONAL ASSESSMENT OF ICU-AW

Assessment of Musculoskeletal Function

Musculoskeletal assessment includes an examination of the presence of edema, muscle atrophy, contractures, deformities, pressure ulcers, and other injuries. Several

methods that can be used in determining muscle mass include: 1) dual-energy X-ray absorptiometry; 2) computed tomography and magnetic resonance imaging; 3) neutron activation analysis; 4) anthropometric measurements; 5) measurement of endogenous metabolites; 6) measurement of a bioimpedance analyzer (BIA); and 7) ultrasound.⁽²⁸⁾

The measurement of BIA is non-invasive, inexpensive, fast, portable, and very acceptable to patients. It is easy to do at the bedside, and this method does not expose the patient to radiation, so it is more applicable. However, other factors influence BIA measurements, including skin temperature and body position. Anthropometric measurement is a simple and inexpensive technique that is easy to apply in clinical practice, but this examination takes a long time and is very dependent on the state of hydration, so it cannot be relied upon as a marker of muscle mass loss in ICU patients.^(28, 29)

Assessment of Neuromuscular Function

The recommended neuromuscular function assessment in ICU-AW patients includes functional assessment: 1)

awareness with the Richmond Agitation Sedation Scale (RASS); 2) cooperation with the Standardized Five Questions; 3) muscle strength with Medical Research Council (MRC) scores and hand-held dynamometer or hand-grip strength (Jamar); 4) muscle tone with the Modified Ashworth Scale; and 5) sensation with the Modified Nottingham Sensory Assessment.⁽²⁹⁾

Assessment of Mobilization Functions and Activity of Daily Living (ADL)

Mobilization function assessment includes an assessment of functional capacity and physical function. Physical function can be measured using the Functional Status Score for the ICU (FSS-ICU), Chelsea Physical Assessment Tools (CPAx), the ICU Mobility Scale (IMS), or the Physical Function in the ICU Test Score (PFIT). The choice of this instrument depends on the purpose of the assessment; for example, 1) IMS for mobility assessment only; 2) PFIT or CPAx for strength and mobility checks; 3) CPAx for examination of respiration and mobility; 4) FSS-ICU, PFIT for detailed physical function examination. Examinations are carried out at least once a week and/or upon discharge

from the ICU. Activities of daily living (ADL) function assessment can be done using Katz, Lawton Instrumental ADL (IADL), Functional Independent Measure, and FSS-ICU baseline evaluation.^(2, 30)

RESULTS

Rehabilitation Management of ICU-AW

Early mobilization is defined as an effort to mobilize critically ill patients in the first 24-48 hours of ICU care. Early mobilization in critically ill patients prevents the deleterious effects of prolonged bed rest, such as muscle weakness and decreased physical function.⁽³¹⁾

Early mobilization in the ICU indicates the success of the therapy and exercise process, as well as the use of tools during treatment. Research proves that early mobilization is safe for ICU patients, although there are several obstacles, such as monitoring devices, central venous catheters, endotracheal tube placement, and therapies to prolong life. Delirium, length of ventilator use, and length of ICU stay can also be reduced by early mobilization.⁽³¹⁾

Occupational therapy and physical therapy for ICU patients can improve

muscle function and reduce atrophy. To strengthen muscles in patients who are sedated and immobilized, electrical stimulation, or neuromuscular electrical stimulation (NMES), is often used. The benefits of NMES can reduce muscle mass loss and prevent polyneuropathy, but the effects are short-term. The use of NMES is usually concurrent with conventional therapy. The bicycle ergometer can be used for exercises that can be started passively, with progression to include more resistant motion. A study found that patients who were trained with a bicycle ergometer experienced an increase in the force of the quadriceps muscle and 6-minute walking test distance upon discharge compared to patients who were given standard therapy in the form of a range of motion exercises of the lower and upper extremities, which were increased to walking exercise as tolerated.⁽³¹⁾

Exercises on dynamic tilt tables enable severely deconditioning individuals to engage in active exercise. This device allows the patient to stand at various angles to perform closed-chain exercises and increase the weight bearing of the lower

extremities. The weight bearing obtained varies from 2% to 75%, depending on the slope of the table. Utilizing a dynamic tilt table minimizes the burden of manually lifting heavy, deconditioned patients.⁽³¹⁾

Inspiratory muscle exercise is used to increase the strength of the diaphragm muscle due to ICU-AW. A systematic review of 10 studies including 394 subjects discovered that inspiratory muscle training using a threshold pressure device increased the maximum inspiratory pressure, the index of rapid and shallow breathing, and the success of weaning. Another study showed that in patients who were given inspiratory muscle training, there was a greater increase in inspiratory muscle strength, but there was no difference in the fatigue resistance index compared to the control group who received standard care.⁽⁵⁾

Early Mobilization and Exercise to Prevent ICU-AW

Monitoring patient safety before and during mobilization is a very important factor to be considered.⁽³¹⁾ The safety criteria for the early mobilization of critically ill patients using ventilators can be seen in Table 3.⁽²⁹⁾

Walking exercises in ICU patients also require special attention to safety, hemodynamic changes, use of breathing apparatus, and termination of exercise. Safety precautions before carrying out the walking training program include: 1) must be accompanied by a nurse to supervise assistive devices; 2) the patient is connected to portable telemetry to monitor heart rate; 3) all necessary equipment must be readily available and all catheters must be secure; 4) must use a safety belt for all transfer and walking re-education activities; 5) availability of filled oxygen cylinders; 6) a wheelchair is provided for the patient during exercise if the patient wants to rest in the middle of the exercise; and 7) there must be sufficient power available to ensure patient safety.⁽³²⁾ In mobilizing an ICU patient, it is also necessary to assess physiological changes to determine how well the activity can be tolerated by the patient. This assessment is carried out through a head-to-toe examination with a system approach.⁽³¹⁾

One of the standard patient mobilization and exercise programs during ICU care developed by Perme et al. can be

seen in Table 4. This program consists of 4 successive phases according to the improvement of the patients' medical condition.⁽³²⁾

Early mobilization programs require teamwork consisting of doctors, therapists, and nurses. Any mobilization program should be the decision of the ICU care team. In each program implementation, the doctor regulates the need for mechanical ventilation, the therapist runs an early mobilization program, and the nurse monitors vital signs, prepares a treatment plan, or prepares medications if needed.⁽³²⁾

Changes in oxygen saturation, respiratory rate, blood pressure, heart rhythm, pulse, oxygen saturation, complaints of fatigue, and breathing pattern during exercise should be assessed during walking exercises. Before beginning exercise, patients who require mechanical ventilation must be ensured that the ventilator is safe to use, the endotracheal tube and tracheostomy are safe, and there is an appropriate communication strategy in place because patients on artificial respiration cannot speak.⁽³²⁾

Table 3. Safety Criteria for Early Mobilization

Criteria	Variable	Parameter	
Cardiovascular	Heart rate	>40 times/minute and <130 times/minute	
	Mean arterial pressure	>60 mmHg	
	Systolic blood pressure	<180mmHg	
	Hemodynamic stability	-	
	No usage of vasoactive medication	-	
	No myocardial ischemia	-	
	No increase in vasopressor dose over the last 2 hours	-	
	No repetition of anti-arrhythmic agents	-	
	Do not use a femoral artery catheter	-	
Respiratory	Peripheral oxygen saturation	>88%	
	Respiratory rate	>5 times/minute and <40 times/minute	
	Airway protection	-	
	Mechanical ventilation parameters	FiO2 <0.6 and/or PEEP <10 cmH2O	
Neurology	Level of consciousness	Not in a coma Not agitated Understand and carry out orders correctly Eye-opening response when given a verbal stimulus Respond to verbal stimuli	
	Intracranial pressure	Not increasing	
	No neurologic and/or neuromuscular disease that limits mobility	-	
	Orthopaedic	No unstable fracture	-
		No bone instability	-
		No orthopedic contraindications to mobilization	-
Others	Not in the use of neuromuscular blocking agents	-	
	No open abdominal surgery wound	-	
	Not in palliative care	-	
	No deep vein thrombosis	-	
	Not on continuous hemodialysis	-	
	Body temperature	<38.5 °C	
No active gastrointestinal bleeding	-		
No active bleeding	-		

Table 4. Mobilization and Exercise Program in ICU

Criteria	PHASE			
	1	2	3	4
	<ul style="list-style-type: none"> Subacute/acute phase patients with several medical problems Patient is unstable The patient is unable to participate fully in therapy 	<ul style="list-style-type: none"> Subacute/acute phase patients with several medical problems Patients can participate better in exercise 	<ul style="list-style-type: none"> Subacute/acute phase patients with medical problems or medical problems being treated Patients who can actively participate in therapy 	Subacute patients who have been weaned on mechanical ventilation and are actively participating in therapy

	<ul style="list-style-type: none"> • Patients without medical problems but with inability to walk, weakness, and/or limited activity tolerance included 	<ul style="list-style-type: none"> • The patient is in stable condition • The patient is weak but can stand 	<ul style="list-style-type: none"> • The patient is weak but has tolerance for increased activity levels 	
Target	<ul style="list-style-type: none"> • The patient sits at the edge of the bed without assistance or minimal assistance • Start standing with a walker and assistance • Start walking activities if possible 	<ul style="list-style-type: none"> • Start transfer with a walker • Start re-education to walk with a walker 	<ul style="list-style-type: none"> • Start self-transfer with a walker • Progressive walking re-education 	<ul style="list-style-type: none"> • Improves progressive transfer and walking independence • Increase patient and family independence with exercise and mobilization programs
Criteria for the next stage	<ul style="list-style-type: none"> • Patients follow orders • Hemodynamically stable • Adequate oxygen • The patient stands with a walker and has good tolerance for pre-walking activities including weight shifting on both legs, upright standing posture 	<ul style="list-style-type: none"> • Patients follow orders • Hemodynamically stable • Adequate oxygen • Transfer to the chair with a walker and assistance 	<ul style="list-style-type: none"> • Patients follow orders • Hemodynamically stable • Adequate oxygen • Patient tolerates progressive walking and increased activity level 	
Education	Educate patients and families about the importance of positioning, exercise programs, and early mobilization	Phase 1 plus education on the use of walkers, the importance of increasing the duration of sitting in chairs, and safety during transfers	Phase 2 plus education about the need of phased mobilization and safety during transfers and progress	Education about exercise plans and targets, training families to mobilize in bed, transfer and walk, safety issues during walking and transfers, exercises at home for program improvement and monitoring

PHASE

	1	2	3	4
Positioning	Focus on preventing injuries, especially on the heels and sacrum	Same as Phase 1		
Bed mobilization	<ul style="list-style-type: none"> • Tilt to the side • Bridging • Supine to sitting • Sitting with breathing 	Same as Phase 1	Reduce support gradually until the patient is self-sufficient.	Focus on patient independence

	exercises, leg exercises, self-care activities, balance exercises, sitting without support			
Transfer	<ul style="list-style-type: none"> Transfer to chair exercises with assistance Start the sit-up exercise using the walker with full assistance 	Transfer exercises to assistance with moving to a chair and use the walker, bedside commode, bed	Begins to reduce assistance until the patient can move independently into a chair or commode	<ul style="list-style-type: none"> Self-transfer with or without a walker Train the family if needed
Walking	<ul style="list-style-type: none"> The patient does not walk Focus on standing exercises using a walker and preparation for walking 	Start walking with a walker and assistance	<ul style="list-style-type: none"> Walking exercises with a focus on gradually increasing distance and endurance Gradually walk independently without assistive devices gradually 	<ul style="list-style-type: none"> Gradually walk independently without assistive devices gradually Practice walking on different surfaces as needed including stairs, carpets, and bends
Exercise	One or a combination of the following exercises: Passive and active range of motion, stretching exercises, resistance training with leg press and lightweight (0.45-2.25 kg), and deep breathing exercises	Same as Phase 1	Same as Phase 1	Further strengthening and resistance exercises include: an arm ergometer or stationary bike inspirational muscle training
Duration	15-30 minutes according to tolerance	15-45 minutes according to tolerance	30-60 minutes according to tolerance	30-60 minutes according to tolerance
Frequency	<ul style="list-style-type: none"> 1 time a day 1-7 times a week 2 times a day as needed (patient still has medical problems that affect the ability to tolerate exercise) 	<ul style="list-style-type: none"> Once a day 5-7 times a week Twice a day if needed 	<ul style="list-style-type: none"> Once a day 5-7 times a week Twice a day if needed 	<ul style="list-style-type: none"> Once a day 5-7 times a week Twice a day if needed

Criteria for Termination of Early Mobilization and Exercise

Early mobilization is terminated when oxygen saturation is <88%, hypotension is accompanied by dizziness, excessive

sweating and/or fainting, a heart rate that exceeds the maximum heart rate, changes in breathing patterns and heart rhythm, changes in breathing pattern with increased use of accessory muscles of breathing and

nostril breathing, excessive fatigue or intolerable shortness of breath with a respiratory rate > 20 breaths per minute, significant chest pain, pallor, or redness, and the patient asks to stop. ⁽³²⁾

Post-ICU Rehabilitation

Guidelines for post-ICU rehabilitation prepared by the National Institute of Health and Clinical Excellence stated that post-ICU rehabilitation is a continuation of the program provided during hospital admission. The education provided is in the form of patient preparation and family support so that patients can carry out ADL while at home. Outpatient rehabilitation provided after the patient is discharged from the hospital includes education, training, cognitive rehabilitation, and psychological therapy. Education after the patient is discharged from the hospital includes education about the disease, motivation, exercise at home, and cognitive and psychological rehabilitation that can be done at home. ⁽¹⁰⁾

Exercise is given for a maximum of three weeks after discharge from the hospital. A delay in starting an exercise

program will reduce the effect of the exercise. Types of exercise that can be provided include cardiopulmonary resistance training and resistance training, which can be combined with cognitive and psychological rehabilitation. Exercise prescription starts with low to heavy doses with a duration of 20 to 90 minutes. Cardiopulmonary resistance exercise can be done by doing walking exercises at home for 20-30 minutes with a frequency of 5 times. The resistance training given is the same as resistance training in general. ⁽³³⁾

Cognitive training aims to improve executive function, which is most often affected after ICU admission. Increasing goal-oriented behaviour and assisting patients in learning to make decisions regarding particular tasks execution are two ways that provided by exercise. An example of this exercise is performing a complex task by dividing it into several simple tasks. Cognitive training combined with physical therapy for 12 weeks resulted in an increase in execution function after three months. ⁽³⁴⁾

Psychological therapy can be given with cognitive behavioural therapy (CBT) to help the patient's thought processes and

improve emotions related to trauma memory during ICU admission, relieving stress, and improving behaviour. The CBT technique is carried out by restructuring cognition or behavioural experience to change the patient's assessment of trauma and unpleasant experiences during ICU care. ⁽³⁴⁾

CONCLUSION

Because the majority of patients receiving ICU care experience weakness, it is a serious issue. The impact of ICU-AW, which causes skeletal muscle weakness, including respiratory muscles, causes further complications in the form of a prolonged ICU stay and difficulty weaning from the ventilator. Complications of ICU-AW can continue even after discharge from the ICU or outpatient treatment.

Diagnosis of ICU-AW during ICU care are important from the beginning of treatment, so that rehabilitation management can be carried out as early as possible. Several examinations were carried out aimed at determining the clinical manifestations of the ICU-AW, either clinical or supporting examinations.

Rehabilitation management in the form of physical activity and early mobilization in the ICU must be carried out based on thorough consideration of patient readiness, staff, and identification of patient safety risks. Several mobilization aids were developed to facilitate the ICU-AW rehabilitation program. Teamwork is needed so that the ICU-AW rehabilitation program can be started as early as possible and be successful. The ICU-AW rehabilitation program does not stop when the patient is discharged from the ICU because of the possibility of post-ICU treatment syndrome, so the patient requires a further rehabilitation program. As a conclusion, the rehabilitation management of ICU-AW should be done since the patient is still in the ICU to prevent and treat it.

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Conflict of Interest

No conflict of interest to be stated

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Author Contribution

Arnengsih Nazir has contributed to all processes in this review, including preparation data gathering and analysis, drafting, editing, and approval for publication of this manuscript. Gabriela Anggraini has contributed to editing and approval for publication.

REFERENCES

1. Kondo Y, Fuke R, Hifumi T, Hatakeyama J, Takei T, Yamakawa K, et al. Early rehabilitation for the prevention of postintensive care syndrome in critically ill patients: a study protocol for a systematic review and meta-analysis. *BMJ Open*. 2017;7(3):e013828.
2. Parry SM, Huang M, Needham DM. Evaluating physical functioning in critical care: considerations for clinical practice and research. *Crit Care*. 2017;21(1):249.
3. Barreiro E. Models of disuse muscle atrophy: therapeutic implications in critically ill patients. *Ann Transl Med*. 2018;6(2):29.
4. Piva S, Fagoni N, Latronico N. Intensive care unit-acquired weakness: unanswered questions and targets for future research. *F1000Res*. 2019;8:F1000 Faculty Rev-508.
5. Hodgson CL, Tipping CJ. Physiotherapy management of intensive care unit-acquired weakness. *J Physiother*. 2017;63(1):4-10.
6. Cameron S, Ball I, Cepinskas G, Choong K, Doherty TJ, Ellis CG, et al. Early mobilization in the critical care unit: A review of adult and pediatric literature. *J Crit Care*. 2015;30(4):664-72.
7. Hashem MD, Parker AM, Needham DM. Early mobilization and rehabilitation of patients who are critically ill. *Chest*. 2016;150(3):722-31.
8. Godoy DA, de Mello LV, Masotti L, Di Napoli M. Intensive Care Unit Acquired Weakness (ICU-AW): a brief and practical review. *RHC* 2015;6(1):9-35.
9. Conceição TMA, Gonzáles AI, Figueiredo FCXSd, Vieira DSR, Bündchen DC. Safety criteria to start early mobilization in intensive care units. Systematic review. *Rev Bras Ter Intensiva*. 2017;29(4):509-19.
10. Connolly B, Douiri A, Steier J, Moxham J, Denehy L, Hart N. A UK survey of rehabilitation following critical illness: implementation of NICE Clinical Guidance 83 (CG83) following hospital discharge. *BMJ open*. 2014;4(5):e004963.
11. Hermans G, Van den Berghe GJCC. Clinical review: intensive care unit acquired weakness. *Crit Care*. 2015;19(1):274.
12. Lipshutz AK, Gropper MA. Acquired neuromuscular weakness and early mobilization in the intensive care unit. *Anesthesiology*. 2013;118(1):202-15.
13. van Wagenberg L, Witteveen E, Wieske L, Horn J. Causes of mortality in ICU acquired weakness. *J Intensive Care Med*. 2020;35(3):293-6.
14. Rawal G, Yadav S, Kumar R. Post-intensive care syndrome: an overview. *J Transl Int Med*. 2017;5(2):90-2.
15. Yuan C, Timmins F, Thompson DR. Post-intensive care syndrome: a concept analysis. *Int J Nurs Stud*. 2021;114:103814.
16. Zhou C, Wu L, Ni F, Ji W, Wu J, Zhang H. Critical illness polyneuropathy and myopathy: a systematic review. *Neural Regen Res*. 2014;9(1):101-10.
17. Rajagopalan S, Baghshomali S, Navarro JC, Kalanuria AA. Intensive care management of the neuromuscular patient. *Textbook of Neuroanesthesia and Neurocritical Care: Springer*; 2019. p. 63-96.
18. Puthuchery Z, Harridge S, Hart N. Skeletal muscle dysfunction in critical care: wasting, weakness, and rehabilitation strategies. *Crit Care Med*. 2010;38(10 Suppl):S676-S82.
19. Dos Santos C, Hussain SN, Mathur S, Picard M, Herridge M, Correa J, et al. Mechanisms of chronic muscle wasting and dysfunction after an intensive care unit stay. A pilot study. *Am J Respir Crit Care Med*. 2016;194(7):821-30.
20. Batt J, Dos Santos CC, Cameron JI, Herridge MS, medicine cc. Intensive care unit-acquired weakness: clinical

phenotypes and molecular mechanisms. *Am J Respir Crit Care Med.* 2013;187(3):238-46.

21. Yang Z, Wang X, Wang F, Peng Z, Fan Y. A systematic review and meta-analysis of risk factors for intensive care unit acquired weakness. *Medicine (Baltimore).* 2022;101(43):e31405-e.

22. Zorowitz RD. ICU-acquired weakness: a rehabilitation perspective of diagnosis, treatment, and functional management. *Chest.* 2016;150(4):966-71.

23. Jolley SE, Bunnell AE, Hough CL. ICU-acquired weakness. *Chest.* 2016;150(5):1129-40.

24. Koukourikos K, Tsaloglidou A, Kourkouta L. Muscle atrophy in intensive care unit patients. *Acta Inform Med* 2014 Dec; 22(6): 406–410. 2014;22(6):406-10.

25. Patel BK, Pohlman AS, Hall JB, Kress JP. Impact of early mobilization on glycemic control and ICU-acquired weakness in critically ill patients who are mechanically ventilated. *Chest.* 2014;146(3):583-9.

26. Wang W, Xu C, Ma X, Zhang X, Xie P. Intensive care unit-acquired weakness: a review of recent progress with a look toward the future. *Front Med (Lausanne).* 2020;7:559789.

27. Saccheri C, Morawiec E, Delemazure J, Mayaux J, Dubé B-P, Similowski T, et al. ICU-acquired weakness, diaphragm dysfunction and long-term outcomes of critically ill patients. *Ann Intensive Care.* 2020;10(1):1-9.

28. Joskova V, Patkova A, Havel E, Najpaverova S, Uramova D, Kovarik M, et al. Critical evaluation of muscle mass loss as

a prognostic marker of morbidity in critically ill patients and methods for its determination. *J Rehabil Med.* 2018;50(8):696-704.

29. Sommers J, Engelbert RH, Dettling-Ihnenfeldt D, Gosselink R, Spronk PE, Nollet F, et al. Physiotherapy in the intensive care unit: an evidence-based, expert driven, practical statement and rehabilitation recommendations. *Clin Rehabil.* 2015;29(11):1051-63.

30. Hruska P. Early mobilization of mechanically ventilated patients. *Crit Care Nurs Clin North Am.* 2016;28(4):413-24.

31. Koester K, Troeller H, Panter S, Winter E, Patel JJ. overview of intensive care unit-related physical and functional impairments and rehabilitation-related devices. *Nutr Clin Pract.* 2018;33(2):177-84.

32. Perme C, Chandrashekar R. Early mobility and walking program for patients in intensive care units: creating a standard of care. *Am J Crit Care.* 2009;18(3):212-21.

33. Connolly B, Salisbury L, O'Neill B, Geneen LJ, Douiri A, Grocott MP, et al. Exercise rehabilitation following intensive care unit discharge for recovery from critical illness. *Cochrane Database Syst Rev.* 2015(6):CD008632.

34. Schandl AR, Brattström OR, Svensson-Raskh A, Hellgren EM, Falkenhav MD, Sackey PV. Screening and treatment of problems after intensive care: a descriptive study of multidisciplinary follow-up. *Intensive Crit Care Nurs.* 2011;27(2):94-101.