https://doi.org/ 10.33472/AFJBS.6.10.2024.5490-5504

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

The Association Between Prolonged Duration of Mechanical Ventilation and the Incidence of Intensive Care Unit-Acquired Weakness (ICU-AW)

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Article History

Volume 6,Issue 10, 2024

Received:28 Apr 2024

Accepted : 29 May 2024

doi: 10.33472/AFJBS.6.10.2024.5490-5504

Abstract

Background/Aims: The muscle weakness that occurs as a result of critical care in the ICU is referred to as Intensive Care Unit-Acquired Weakness (ICU-AW). Mechanical ventilation is one of the most commonly used therapies in the ICU. Prolonged use of mechanical ventilation can restrict patient movement, leading to immobilization and subsequently causing muscle weakness. This study aims to determine the relationship between the prolonged duration of mechanical ventilation and the occurrence of ICU-AW in the ICU of dr. Hasan Sadikin Hospital Bandung.

Methods: A case-control study was conducted on patients treated in the ICU of dr. Hasan Sadikin Hospital Bandung from July to October 2023. Patients who meet the inclusion and exclusion criteria will undergo muscle strength examination using the Medical Research Council (MRC) scale. Research subjects will be selected using purposive sampling into two groups: the ICU-AW group (n=30) and the Without ICU-AW group (n=30). Data will be collected from medical records.

Results: In the ICU-AW group, there are 12 patients (40.0%) with prolonged mechanical ventilation duration and 18 patients (60.0%) without. In the Without ICU-AW group, there are 3 patients (10.0%) with prolonged mechanical ventilation duration and 27 patient (90.0%) without. This result shows a significant difference with a p-value<0,05.

Conclusion: This study finds a relationship between the prolonged duration of mechanical ventilation and the occurrence of ICU-AW in the ICU of dr. Hasan Sadikin Hospital Bandung. Patients with prolonged mechanical ventilation have a higher incidence of ICU-AW than patients without prolonged mechanical ventilation.

Keywords: ICU acquired weakness, prolonged mechanical ventilation duration

Introduction

Muscle weakness is one of the problems that is often found during and after treatment in the Intensive Care Unit (ICU).[1] Muscle weakness that occurs as a result of critical condition treatment in the ICU is often referred to as ICU-acquired weakness (ICU-AW). Muscle weakness in ICU-AW generally occurs completely, symmetrically, and affects the limbs. Facial and ocular muscles are generally not affected.[1,2] Studies conducted in America estimate that global ICU-AW sufferers could reach one million people. A systematic review reported a median ICU-AW prevalence of 43% from thirty-one studies.[3] In Indonesia, the incidence of ICU-AW is not clearly known.

Several techniques can be used to diagnose ICU-AW. Starting from manual muscle strength measurements (medical research council (MRC) scale, hand dynamometry, 6-minute walking distance, etc.), electrophysiological examinations (nerve conduction study, electromyography), imaging (ultrasonography, computed tomography, magnetic resonance imaging), to muscle and nerve biopsy examinations.[1] The most common and frequently used examination and said to be the "gold standard" for diagnosing ICU-AW is the Medical Research Council (MRC) scale.[1,2] The MRC scale assesses limb strength in a group of muscles from value 5 (normal) to value 0 (no contractions). The diagnosis of ICU-AW is made if the total score is <48 or the mean muscle score that can be assessed is <4 on the MRC scale assessment.[1,4,5] Patients with ICU-AW have poor short-term and long-term effects.[1,6]

Patients with ICU-AW had poor short-term and long-term effects.[1,6] In short-term effects, patients with ICU-AW had a higher risk of ICU and hospital death, risk of prolonged duration of mechanical ventilation, extubation failure, postextubation dysphagia, longer duration of ICU care, and higher hospital care costs. During the first week in the ICU, patients with ICU-AW can experience muscle mass loss of up to >10% which can result in functional impairment.[7,8] Previous research had stated that as many as 60-80% of ICU patients still had functional limitations due to ICU-AW.[9] Even after discharge from the hospital, patients with ICU-AW still have a higher risk of death and long-term muscle weakness which results in chronic functional disability.[1,3,10,11]

Mechanical ventilation is a mechanical aid that functions to provide breathing assistance by providing positive air pressure to the lungs of patients experiencing respiratory failure in the ICU.[12] Research conducted in America previously stated that using mechanical ventilation for more than seven days can result in weakness in the strength of respiratory muscles and limb muscles due to immobilization.[13] It is estimated that at least 25% of patients who receive prolonged mechanical ventilation suffer from ICU-AW.[3,14] Weakness of the limb muscles and diaphragm muscles is the main factor causing the prolonged duration of mechanical ventilation and causing long-term complications up to death.[9] Therefore, prolonged duration of mechanical ventilation is associated with immobilization and is reciprocally related to the risk of ICU-AW and weaning failure.[3]

Patients who do not move muscles during treatment are at high risk of developing muscle weakness and atrophy. Skeletal muscle atrophy begins to occur when the patient begins to be inactive for 4 hours and gets worse after that.[15] Not using the muscles for movement will result in atrophy produced by reduced myofibril tension.[9] There is no specific therapy for ICU-AW, therefore the focus is on preventing certain risk factors to reduce the incidence of ICU-AW. [17,18] Currently there is no research regarding the relationship between prolonged duration of mechanical ventilation and the incidence of ICU-AW at RSUP dr. Hasan Sadikin Bandung, so from this background, the author intends to conduct research to determine the relationship between prolonged duration of mechanical ventilation and the incidence of ICU-AW at RSUP dr. Hasan Sadikin Bandung.

Materials and Methods

Patients and Sample Size

We enrolled patients treated in the ICU of dr. Hasan Sadikin Hospital Bandung from July to October 2023 who were selected based on inclusion and exclusion criteria. The inclusion criteria included patients aged ≥18 years, received mechanical ventilation therapy for ≥ 24 hours, and agreed to take part in the research and signs informed consent. Patients with neuromuscular weakness (e.g. Myasthenia Gravis, Guillain Barre Syndrome), patient with stroke, brain stem lesion, spinal cord injury, patients with unilateral or bilateral limb injuries that do not allow for muscle strength examination, patients with a Barthel Index score < 70 (functional ability before illness), and patients with GCS < 15 were excluded. Patients with incomplete medical record data were also excluded from this study. The sampling technique used was purposive sampling. This technique was a non-probability sampling. By using the formula for determining sample size for unpaired categorical analytical research, the sample formula was used to test hypotheses between two populations with the sample size 2.0 program from Hosmer and Lemeshow. Thus the minimum number of samples for each group was 30 samples. So the total sample for both groups was 60 patients. This study was approved by Health Research Ethics Committee Faculty of Medicine Padjadjaran University / Dr. Hasan Sadikin Hospital Bandung.

Study Design

This study was an analytical observational study with a case control study design. All samples that met the inclusion and exclusion criteria were included as study subjects. Data on the characteristics of subjects were obtained from medical records. A case control study design was used to assess the role of the risk factors play in the incidence of disease (cause effect relationship). In case control, the Odds Ratio (OR) value will appear. Judging from the relationship between variables, this study was a causal or cause-effect study, i.e. a study conducted to explain the relation between variables that one variable causes or determines the value of another variable. In this study, the independent variable was the prolonged duration of mechanical ventilation, and the dependent variable was ICU Acquired Weakness and without ICU Acquired Weakness.

Definition

ICU Acquired Weakness (ICU-AW) was muscle weakness due to critical care in the ICU which was confirmed if the MRC scale value is <48 or the MRC scale average is <4. Without ICU-AW meant there was no muscle weakness due to ICU critical care, MRC scale value ≥ 48 or average MRC scale ≥4. Prolonged duration of mechanical ventilation was the duration of use of mechanical ventilation while in the ICU ≥7 days.

Measurement

Muscle strength measurements will be taken when the patient was released from the intensive care room. A physiotherapist, blinded to other parameters, assessed muscle strength when the patient was conscious and able to follow instructions (Richmond Agitation and Sedation Scale/RASS values between -1 and 1). The physiotherapist had received an explanation regarding the previous assessment of muscle strength. Muscle strength measurements were carried out using the MRC scale. The MRC scale assessed bilaterally in six muscle groups: wrist dorsiflexors, elbow flexors, shoulder abductors, hip flexors, knee extensors, and ankle dorsiflexors. The MRC scores for each muscle group were added up and then divided by the number of muscle groups that can be tested to get the average MRC scale value. The diagnosis of ICU-AW was made when the sum of the MRC scale is <48 out of a maximum score of 60 or the average MRC value was <4.

Researcher will collect data regarding the duration of mechanical ventilation through the patient's medical records. Apart from that, data during ICU stay will also be collected for the characteristics of the subjects in this study, including APACHE II scores to determine the severity of illness, history of sepsis or not, lactate levels, gender, age, history of sedation accompanied by neuromuscular blockade agents, hyperglycemia conditions (, administration of vasoactive, aminoglycoside antibiotics, corticosteroids, and early parenteral nutrition during ICU stay. Data will be collected by researchers for data processing.

Statistical Analysis

The data already collected was processed computerized to convert the data into information. Data were presented as percentages (%) for categorical variables and mean ± standard deviation (SD) for numerical variables. Statistical analysis began with a normality test which aims to determine whether the data was normally distributed or not normally distributed. Then statistical analysis according to research objectives and hypotheses. The significance test to compare the characteristics of two research groups used the unpaired t test if the data was normally distributed and the Mann Whitney test as an alternative if the data was not normally distributed.

Meanwhile, statistical analysis for categorical data was tested using the chi-square test, if the Chi-Square requirements were met, if not met, then Fisher's Exact test was used for 2 x 2 tables and Kolmogorov Smirnov for tables other than 2 x 2. The Chi Square requirement was that there was no expected value less than 5 in 20% of the table. Then, because it was a case control study, the Odds Ratio (OR) value will appear, i.e measuring the strength of the cause and effect relationship. The significance criteria used were p value, $p \leq 0.05$ was significant or statistically significant, and $p > 0.05$ was insignificant. The data obtained was recorded in a special form and then processed using the SPSS version 24.0 for Windows program.

Results

Demographic data

General characteristics of subjects based on high severity illness, sepsis, hyperlactatemia, female gender, old age, administration of sedation accompanied by neuromuscular blockade agents, administration of vasoactive substances, administration of aminoglycosides, administration of corticosteroids, hyperglycemia conditions, and administration of early parenteral nutrition (Table 1).

Table 1. Comparison of Characteristics of Study Subjects in Both Groups

Variable	Group		P value
	ICU-AW N=30	Without ICU-AW N=30	
High severity illness	30(100.0%)	27(90.0%)	0.237
Sepsis	16(53.3%)	11(36.7%)	0.194
Hyperlactatemia	17(56.7%)	20(66.7%)	0.426
Female gender	11(36.7%)	15(50.0%)	0.297
Old age	8(26.7%)	3(10.0%)	0.095
Administration of sedation accompanied by neuromuscular blockade agents	2(6.7%)	5(16.7%)	0.424
Administration of vasoactive substances	18(60.0%)	14(46.7%)	0.301
Administration of aminoglycosides	5(16.7%)	1(3.3%)	0.195
Administration of corticosteroids	5(16.7%)	0(0.0%)	0.052
Hyperglycemia conditions	2(6.7%)	1(3.3%)	1.000
Administration of early parenteral nutrition	0(0.0%)	0(0.0%)	1.000

Note: For categorical data, the p value was calculated based on the Chi-Square test with the alternative Kolmogorov Smirnov and Fisher's Exact tests if the Chi-Square requirements were not met. The significance value was based on p value <0.05.

In the ICU-AW group, high severity illness (APACHE II ≥ 15) was found at 30 or 100.0%, sepsis at 17 or at 56.7%, hyperlactatemia (lactate serum > 2 mmol/L) at 17 or at 56.7%, female gender at 11 or at 36.7%, old age (age > 50) was 8 or 26.7%, administration of any sedation combined with neuromuscular blockade agents during ICU stay was 2 or 6.7%, administration of any vasoactive agents during ICU stay was 18 or 60.0%, administration of any aminoglycosides during ICU stay was 5 or 16.7%, administration of any corticosteroids agents during ICU stay was 8. 5 or 16.7%, hyperglycemia conditions (blood sugar > 200 mg/dL during ICU stay) was 2 or 6.7%, and early parenteral nutrition (initiation parenteral nutrition < 48 hour after ICU admission) was 0 or 0.0%.

In the Without ICU-AW group, the disease severity was 27 or 90.0%, sepsis was 6 or 20.0%, hyperlactatemia was 22 or 73.3%, female gender was 15 or 50.0%. , old age 3 or 10.0%, sedation accompanied by neuromuscular blockade agents 5 or 16.7%, vasoactive administration 14 or 46.7%, administration of aminoglycosides 1 or 3.3%, administration of corticosteroids 0 or 0.0%, hyperglycemia conditions 1 or 3.3% and early parenteral nutrition 0 or 0.0%.

The P value for the high severity illness variable, hyperlactatemia, female gender, old age, sedation accompanied by neuromuscular blockade agents, vasoactive administration, aminoglycoside administration, corticosteroid administration, hyperglycemia conditions and early parenteral nutrition were > 0.05 which meant it was insignificant, thus it can be explained that there was no statistically significant difference in proportion between the variables of high severity illness, sepsis, hyperlactatemia, female gender, old age, administration of sedation accompanied by neuromuscular blockade agents, administration of vasoactive substances, administration of aminoglycosides, administration of corticosteroids, hyperglycemia conditions and provision of early parenteral nutrition in the ICU-AW and without ICU-AW groups.

Association between prolonged duration of mechanical ventilation and the incidence of ICU-AW

In the ICU-AW group, there were 12 patients with prolonged duration of mechanical ventilation or 40.0% and 18 patients or 60.0% who did not. In the Without ICU-AW group, there were 3 patients with prolonged duration of mechanical ventilation or 10.0% and 27 patients without it or 90.0% (Table 2).

Table 2. Association between prolonged the duration of mechanical ventilation and the incidence of ICU-AW

Variable	Group		OR CI 95%	P Value
	ICU-AW N=30	Without ICU-AW N=30		
Prolonged duration of mechanical ventilation				
Yes	12(40.0%)	3(10.0%)	6.000	0.007*
No	18(60.0%)	27(90.0%)	(1.482-24.299)	

Note: For categorical data, the p value was calculated based on the Chi-Square test with the alternative Kolmogorov Smirnov and Fisher's Exact tests if the Chi-Square requirements were not met. The significance value was based on p value <0.05.

For analysis of categorical data in Table 2, it was tested using the Chi Square statistical test, i.e lengthening the duration of mechanical ventilation. The results of statistical tests in the study group showed that the P value for the variable prolonged duration of mechanical ventilation was smaller than 0.05 (P value <0.05), which meant that it was statistically significant, thus it can be explained that there was a statistically significant difference in proportion between the variable of prolonged duration of mechanical ventilation in the ICU-AW and Without ICU-AW groups.

The results of the Odds Ratio calculation in Table 2 show six results which showed that the probability of patients with prolonged duration of mechanical ventilation to experience ICU-AW was six times compared to patients who did not have prolonged duration of mechanical ventilation.

Results of MRC Scale Examination and Comparison of Duration of Mechanical Ventilation in Both Groups

The results of the MRC scale examination of patients treated in the ICU at dr. Hasan Sadikin Hospital Bandung obtained an average MRC scale value of 50.43 ± 8.840 (Table 3).

Table 3. Descriptions of MRC Scale Examination Results in ICU patients at dr. Hasan Sadikin Hospital Bandung

Variable	N=60
MRC Scale	
Mean±Std	50.43±8.840
Median	51.50
Range (min-max)	23.00-60.00

Note: Categorical data was presented in number/frequency and percentage, while numerical data was presented in mean, median, standard deviation and range.

Data on the duration of mechanical ventilation was collected for each group, in the ICU-AW group the average value of mechanical ventilation duration was 8.27 ± 9.815 and in the without ICU-AW group it was 4.33 ± 2.893 (Table 4).

Table 4. Comparison of Duration of Mechanical Ventilation in Both Groups

Variable	Group		P Value
	ICU-AW N=30	Without ICU-AW N=30	
Duration of Mechanical Ventilation (day)			
Mean±Std	8.27±9.815	3.97±2.822	0.026*
Median	4.00	3.00	
Range (min-max)	2.00-45.00	2.00-13.00	

Note: For numerical data, the p value was tested using the unpaired T test if the data was normally distributed with the alternative Mann Whitney test if the data was not normally distributed. Categorical data p values were calculated based on the Chi-Square test with the alternative Kolmogorov Smirnov and Fisher's Exact tests if the Chi-Square requirements were not met. The significance value was based on p value <0.05.

Discussion

Demographic data

The research was conducted on 60 patients treated in the ICU of dr. Hasan Sadikin Hospital Bandung which was divided into two groups, each consisting of 30 subjects. The general characteristics of research subjects in this study were divided based on high severity of illness, sepsis, hyperlactatemia, female gender, old age, sedation accompanied by neuromuscular blockade agents, vasoactive administration, aminoglycoside administration, corticosteroid administration, hyperglycemia conditions, and early parenteral nutrition.

Intensive Care-Acquired Weakness (ICU-AW) was associated with high illness severity.[1,16] Severity of illness can be assessed at the time of initial admission to the ICU using the Acute Physiology and Chronic Health Evaluation (APACHE) II score. The APACHE II score assessed clinical, physiological, and laboratory signs performed within the first 24 hours when the patient was admitted to the ICU. APACHE II assessment results ranged from 0 – 71 with higher scores corresponding to higher severity of illness and higher risk of death. Previous research in India which calculated severity of illness using the APACHE II value showed that a value of ≥ 15 was associated with the risk of ICU-AW.[17] A study conducted in Germany stated that patients with severe severity of illness experienced immobilization which could result in loss of muscle mass.[18]

Sepsis is defined as a life-threatening condition due to organ dysfunction caused by dysregulation of the body's response to infection.[19] A number of patients with sepsis in the ICU showed signs of severe muscle loss to ICU-AW.[20] In the condition of sepsis itself there was a decrease in protein synthesis contributed by pro-inflammatory cytokines. such as IL-6 and TNF-α and results in a condition called sepsis-induced muscle atrophy. In conditions of sepsis there was also an increase in protein degradation through several mechanisms such as the ubiquitin proteasome system (UPS) and lysosomal systems, which increased the apoptotic pathway and result in the breakdown of myofibrillar proteins and proteasome degradation. An imbalance between muscle protein synthesis and muscle protein degradation resulted in the loss of muscle mass, which was thought to be the main mechanism causing muscle atrophy, which results in ICU-AW.[20,21]

Lactate is the main metabolite of the anaerobic glycolysis process which was caused by tissue hypoperfusion and hypoxia. Examination of serum lactate levels was routinely carried out in critical patients and helps clinicians predict and detect serious disease at the start of treatment. An increase in lactate levels indicated dysfunction in the mitochondria.[22] Studies in China showed that hyperlactatemia (lactate levels > 2 mmol/L) measured when the patient was admitted to the ICU was an independent risk factor for the formation of ICU-AW in adult critical patients.[23]

Various previous studies stated that female gender was a risk factor for ICU-AW that cannot be modified.[1,16,24] Physiological differences in body composition, muscle strength, and energy metabolism were thought to contribute to ICU-AW. Women had lower muscle mass than men so women were more susceptible to experiencing ICU-AW.[16] Research conducted in Germany hypothesized that in female critical patients there would be changes in insulin sensitivity to lower levels as well as differences in muscle fiber in muscle morphology which could disrupt energy metabolism, resulting in occurrence of ICU-AW.[24]

One of the risk factors for ICU-AW was old age when undergoing critical care.[1,16,25] As age increased, older patients experienced a decrease in muscle mass secondary to sarcopenia, lack of protein intake, and a sedentary lifestyle. Older people also experience muscle atrophy due to less frequent muscle use compared to young people. Critical Illness Myoneuropathy (CINM) is type of ICU-AW that often occurs in elderly patients.[26] Although CINM could occur at various ages, generally the patient was over 50 years old.[25]

The relationship between giving sedation accompanied by neuromuscular blockade agents and muscle weakness did not occur directly. It was due to immobilization and bed rest which had the potential to increase ICU-AW.[15] Skeletal muscle atrophy can occured when the patient began to be inactive for 4 hours and becomes more severe after that. In addition, protein synthesis and degradation occurs which results in a decrease in muscle mass, muscle fiber diameter and the number of fibers per muscle. In a study in Belgium, of COVID-19 patients who required ICU care, ICU-AW occurred in patients with prolonged sedation.[27] Sedation was generally needed to prevent ventilator asynchrony and ventilator-related lung injury. Neuromuscular blockade agents were one of the drugs used in the ICU to help facilitate the use of mechanical ventilation. Several case reports stated prolonged muscle weakness after the use of aminosteroid and benzylisoquinolone in critical patients. Research in animal models stated that the use of neuromuscular blockade agents accompanied by sedation results in ICU-AW.[28] One study estimated a 5-10% risk of prolonged muscle weakness if neuromuscular blockade agents were used for more than 24 hours.[29]

Vasoactive drugs were commonly used during the care of critical patients in the ICU with shock or life-threatening conditions of circulatory failure.[14] Vasoactive drugs were used to maintain perfusion to vital organs until the main cause of shock can be treated. The use of vasoactive drugs was known to be a risk factor for ICU-AW.[1,16] The relationship between vasoactive drugs and critical illness-related polyneuropathy had been attempted to be elucidated, but little is known about the mechanisms leading to muscle weakness.[14] In addition, animal studies have stimulated the β receptors with high doses of adrenergics can result in apoptosis and necrosis in skeletal muscle and cardiac myocytes.[30] This can link the use of vasoactive drugs and skeletal muscle injury which can increase the risk of ICU-AW. Administration of catecholamines was also known to result in transcellular transfer of electrolytes. Disturbances in potassium homeostasis can trigger muscle weakness. 56 Studies conducted in America show that there was an independent relationship between the cumulative dose of norepinephrine and the risk of ICU-AW.[14]

Antibiotics were commonly used daily in ICU care. Aminoglycosides are broad-spectrum antibiotics that have strong bactericidal activity against a number of gram-negative aerobic bacteria and staphylococcus. Aminoglycoside antibiotics had a strong bactericidal effect and low resistance rates, so aminoglycosides were often used in the care of critical patients. The relationship between aminoglycoside therapy and ICU-AW remains controversial. Aminoglycosides can inhibit neuromuscular transmission by inhibiting the presynaptic release of acetylcholine. Aminoglycoside antibiotics can also inhibit voltage-dependent calcium channels, which interfere with neuromuscular transmission. A meta-analysis conducted in China stated that there was a significant relationship between the use of aminoglycosides and ICU-AW, however further research was still needed regarding the total dose and duration of medication needed to be a risk factor for ICU-AW. [31]

A systematic review stated that the use of corticosteroids was associated with the risk of ICU-AW. Corticosteroids was often used in the care of critical patients because they had strong anti-inflammatory and anti-fibrotic effects. The relationship between ICU-AW and the role of corticosteroid therapy was still being investigated. A meta-analysis conducted in China on eighteen studies showed a significant association between corticosteroid use and ICU-AW.[32] Corticosteroid therapy was found to trigger changes in the expression of specific genes that can inhibit protein synthesis and increase muscle wasting. Administration of corticosteroids can also stimulate the mitogen activated protein kinase (MAPK) pathway along with the protosome pathway which results in loss of muscle mass.[33] The effect of corticosteroids on ICU-AW was also complex and depended on the duration and cumulative dose of corticosteroids.[32]

Hyperglycemia during ICU care can be caused by stress from critical illness with or without a history of diabetes.[1,8] Hyperglycemia will result in damage to neurons and skeletal muscles which can result in muscle atrophy even though glucose levels have been restored. Direct toxic effects to mitochondria stimulated by hyperglycemia contribute to the development of ICU-AW.[8,34]

Providing nutrition was important to prevent anorexia related to critical illness or gastrointestinal dysfunction which can result in muscle atrophy and weakness. However, providing enteral nutrition accompanied by early parenteral nutrition to achieve calorie targets increased complications and recovery from critical illness compared to delaying parenteral nutrition in the first week of treatment in the ICU.[8,35] Studies conducted in Belgium stated that providing early parenteral nutrition (< 48 hours since entering the ICU) has a longer recovery time and has higher complications compared to providing advanced parenteral nutrition (after seven days from entering the ICU).[35] Early parenteral nutrition was also associated with higher ICU-AW rates and longer dependence on mechanical ventilation in the ICU. Early parenteral nutrition was known to suppress autophagy in muscle which was the mechanism of ICU-AW.[34,35]

When comparing the characteristics of the two groups of research subjects, statistically p value of >0.05 was obtained for each characteristic of the research subjects. It can be concluded that both groups were similar or there were no differences in characteristics at the start of the examination. This showed that the two groups were homogeneous.

Association between prolonged duration of mechanical ventilation and the incidence of ICU-AW

In this study, it was found that the subjects who experienced a prolonged duration of mechanical ventilation had a significant relationship with the incidence of ICU-AW compared to the subjects who did not experience a prolonged duration of mechanical ventilation. These results were in accordance with research in America that patients with prolonged duration of mechanical ventilation are at risk of experiencing ICU-AW.[14] Furthermore, the previous study stated that duration of mechanical ventilation of more than one week can result in changes in respiratory muscle strength and limb muscles caused as the main result of immobilization which causes muscle weakness.[9] Furthermore, the previous study stated that a duration of mechanical ventilation of more than one week can result in changes in respiratory muscle strength and limb muscles caused by immobilisation, which causes muscle weakness.[9]

Prolonged duration of mechanical ventilation had a reciprocal relationship with the incidence of ICU-AW. The ICU-AW condition was associated with failure to wean from mechanical ventilation.[10,36] Failure to wean from mechanical ventilation was also correlated with an increased risk of death, meaning patients on ICU-AW can have poor outcomes. When a patient experiences critical illness, weakness of the respiratory muscles and peripheral muscles will cause immobilization.[3] If muscles were not moved, their function will weaken and even atrophy. Skeletal muscles will begin to atrophy when the patient began to be inactive for 4 hours and will get worse in the future.[15] Muscles that did not move will become atrophic due to reduced myofibril tension.[9]

In patients receiving mechanical ventilation therapy, skeletal muscle weakness began to occur after respiratory muscle weakness. This was in accordance with this study that limb muscle weakness occured after a prolonged duration of mechanical ventilation, which indicated respiratory muscle weakness. Respiratory muscle weakness itself began due to excessive load due to acute respiratory failure experienced before the patient was intubated.[37] A cohort study conducted in Canada stated that in critically ill survivors, quadriceps muscle atrophy appeared in all patients after 7 days of ICU treatment.[38] This was also consistent with the fact that in patients who have undergone mechanical ventilation for seven days or more, patients can experience muscle atrophy. which resulted in ICU-AW. However, to objectively prove muscle atrophy, research needs to be carried out with objective measurements of muscle mass such as muscle biopsy. After undergoing critical therapy accompanied by rehabilitation, muscles can experience regrowth which varies for each individual, however, the majority of patients can still have muscle atrophy up to 6 months after leaving the ICU.[37]

Even though there have been many studies that early mobilization even for mechanically ventilated patients had high benefits, there were still many factors that can hinder patients from mobilizing.[9] Cultural factors in the ICU itself were an obstacle in almost 60% of studies because the staff in the ICU did not view early mobilization as a priority for patient or lack of knowledge regarding the benefits of early mobilization and the techniques needed to treat the patient's condition.[39] The presence of an endotracheal tube was also an obstacle that exists in mechanical ventilation patients. A previous study conducted in America explained in detail the steps for carrying out mobilization interventions from one day after intubation and found no incidents related to interference with the catheter used by the patient.[40] The increasing need for ICU staff and costs generally became obstacles to mobilization, however, the research conducted in America states that there was no increase in costs for providing a special mobilization team, and even better there was a reduction in the risk of re-admission to the ICU after leaving the intensive care unit.[41] Early mobilization in the ICU had also been proven to be safe as long as existing guidelines were followed. The potential cumulative incidence, such as hemodynamic events and oxygen saturation instability, was 2.6%. Initial screening criteria for starting mobilization and stopping mobilization needed to be provided in each ICU.[9]

Our study found that patients with prolonged duration of mechanical ventilation without ICU-AW were also patients without prolonged duration of mechanical ventilation who experienced ICU-AW (Table 2). The ICU-AW condition is muscle weakness that occurs due to multifactorial causes.[1] In critical patients there were changes in pharmacokinetics such as changes in drug absorption and metabolism, which results in the response to various drugs being different in each critical patient.[42,43]

Other Findings

We obtained an average MRC scale of 50.43 ± 8.840 with the lowest value being 23 and the highest value being 60 (Table 3). This showed that there were still patients with ICU-AW conditions even though they have received treatment and rehabilitation therapy in the ICU of dr. Hasan Sadikin Hospital Bandung. This finding deserved attention because patients with ICU-AW needed to receive special treatment immediately to prevent worse outcomes. The first signs of ICU-AW can be found starting from the first two days after admission when a decrease in muscle and nerve excitability can be observed. Initiation of therapy at this time can be more effective because the abnormalities were still reversible.[6]

We also found that the average duration of patients experiencing ICU-AW was 8.27 ± 9.815 days. Standard deviation data that exceeded the mean value indicated that there was a lot of variation in the data. Patients who experienced ICU-AW had a duration of mechanical ventilation ranging from two days to forty-five days. This could be due to the diverse population of patients treated in the ICU of dr. Hasan Sadikin Hospital Bandung. Research conducted in America states that the surgical ICU patient population was prone to experiencing post-operative muscle weakness. This could be caused by residue from neuromuscular blockade agents, opioid therapy, inflammation, surgical location, and type of surgery (for example, open surgery or laparoscopic).[44]

Early mobilization in the ICU is defined as patient mobilization within the first 72 hours after the patient enters the ICU.[9] Early mobilization and physical rehabilitation were known to increase muscle strength which was associated with a reduced number of ICU-AW events and a higher survival rate after discharge from the hospital. Previously conducted studies stated that active mobilization and rehabilitation increased muscle strength when the patient was discharged from the ICU, increased ability to walk without assistance when discharged from the hospital, and a higher survival rate after discharge from the hospital.[13,45] High dose rehabilitation in the ICU also showed improvements in various aspects of quality of life up to the sixth month, the latest study showed a reduced risk of ICU-AW compared to patients with regular routine rehabilitation or without rehabilitation. Barriers that can occur in clinical practice can include the patient's desire to carry out physical activity, safety for patients, staff and care providers, lack of equipment and staff who can provide rehabilitation programs.[13,45]

In conclusion, our study showed there was a relationship between prolonged duration of mechanical ventilation and the incidence of ICU-AW in the ICU of dr. Hasan Sadikin Hospital Bandung. Patients who experienced prolonged duration of mechanical ventilation had a higher rate of ICU-AW events compared to patients without prolonged duration of mechanical ventilation. Based on our results, the likelihood of patients with prolonged mechanical ventilation experiencing ICU-AW was six times compared to patients who did not have prolonged duration of mechanical ventilation. In addition, the average duration of patients treated at ICU of dr. Hasan Sadikin Hospital Bandung who suffered from ICU-AW was 8.27 days. We suggest further study with a larger group of subjects.

Limitations

This study has limitation. The assessment of the muscle strength scale using the MRC scale was not carried out periodically to monitor the improvement of muscle strength after leaving the ICU. Patients still need rehabilitation therapy and regular monitoring of muscle strength after leaving the ICU which can worsen the patient's quality of life.

Acknowledgements

None.

Author Contributions

Army Zaka Anwary is responsible for the designed the research, data analysis, and preparation of the manuscript. Suwarman and Ezra Oktaliansah critically revised the manuscript for important intellectual content and extracted the compund used in this study. All authors approved the final content for journal submission and publication.

Funding Sources

This research was supported by Faculty of Medicine, Padjadjaran University.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of Interest to declare.

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