Correlation of Measuring Diaphragm Capacity Using Ultrasonography on the Success of Ventilator Removal in ICU-Acquired Weakness (ICU-AW) Patients at RSUD Dr. Soetomo Surabaya

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KEYWORDS

Diaphragmatic excursion, Diaphragmatic thickness, Intensive Care Unit-Acquired Weakness, Diaphragm dysfunction

ABSTRACT:

Introduction: Generalized muscle weakness that occurs in intensive care unit-acquired weakness (ICU-AW) patients and in the diaphragm muscles leads to increased duration of mechanical ventilation, length of stay, and mortality. The diagnostic modality of changes in diaphragmatic capacity measured using diaphragmatic ultrasound accompanied by motor examination using Medical Research Council (MRC) scoring is effective as an early diagnosis of ICU-AW and diaphragmatic dysfunction. The need for comprehensive healthcare is made part of the universal healthcare package. **Objectives:** The purpose of this research is to analyze diaphragm capacity in the form of diaphragmatic thickness and excursion using diaphragm ultrasound on the success of getting off the ventilator for ICU-AW patients. **Methods:** 23 ICU-AW patients underwent diaphragm ultrasound examination during the Spontaneous breathing trial/T-piece process. The correlation between diaphragmatic thickness and excursion scores on success in getting off the ventilator was analyzed statistically. **Results:** There is a significant difference between the results of diaphragmatic excursion (p=0.001) and thickness (p=0.006) with the success rate of getting off the ventilator. **Conclusions:** Patients who experience diaphragm muscle dysfunction or weakness have an increased risk of failure to get off the ventilator. The potential benefits of measuring diaphragm capacity using ultrasonography can be considered as a diagnostic tool or early diagnostic in ICU-AW patients need to be explored in further studies with control indicators and larger sample sizes.

1. Introduction

Approximately 13-20 million people worldwide undergo ICU treatment annually, with 25-31% (3.2-6.2 million patients) developing ICU-acquired weakness (ICU-AW) each year. The occurrence of ICU-AW fluctuates based on factors such as age, gender, existing medical conditions, and treatments received in the ICU. During ICU care, 56-74% of patients exhibit clinical symptoms of ICU-AW [1].

In other studies, ICU-AW has been found in 30-50% of patients in the intensive care unit, and this number can rise to 67% in critically ill patients, particularly those suffering from sepsis, and remained detectable in 36% of patients after ICU discharge [2]. Research on ARDS patients with ICU-AW showed increased mortality rates of up to 60% [3]. ICU-Acquired Weakness (ICU-AW) has become an increasing concern for healthcare providers in the ICU [4]

A study revealed that muscle weakness, which impacts both the respiratory and peripheral skeletal muscles, is experienced by 25-55% of patients who are undergoing mechanical ventilation. Skeletal muscle atrophy and dysfunction, particularly in the extremities, respiratory muscle weakness can continue for a number of months following the resolution of acute respiratory failure. It is the most important risk factor for prolonged use of ventilation and contributes to higher rates of both illness and death [5]. Although respiratory and skeletal muscle weakness are often assumed to be part of the same pathological process, several studies indicate they are independent occurrences. First, from a temporal perspective, there are differences in muscle structural changes. In the quadriceps, the thickness of muscles decreases by around 10% following one week of being on a ventilator, whereas the atrophy of the diaphragm happens at a faster rate. Around half of the patients experience a 20% reduction in diaphragm thickness by the third or fourth day of mechanical ventilation. Diaphragm atrophy develops earlier and more frequently than extremity muscle atrophy [6].

Assessing the function of the diaphragm is crucial for determining if patients will be able to be taken off ventilators and breathe spontaneously. The diaphragm is a key muscle involved in breathing, serving as the main muscle responsible for inhaling. It is responsible for the majority of ventilation while at rest, making it a critical component of the respiratory system. This function becomes impaired in conditions of hypotension, hypoxemia, systemic infection, and mechanical ventilation use. Diaphragm atrophy and dysfunction can develop quickly after the initiation of ventilation and may progressively worse, influenced by the ventilator mode and other previously mentioned risk factors [7]. Ultrasonography (USG) is recommended for clinical diagnosis of diaphragm dysfunction. An impairment in the diaphragm is linked to a higher likelihood of needing extended mechanical breathing support and difficulty in transitioning off the ventilator, similar to ICU-AW [8]. Other studies have also reported that both ICU-AW and diaphragm dysfunction correlate with prolonged ventilator weaning, increased hospital costs, longer hospital and ICU length of stay, and increased ICU mortality rates [9].

The recommended clinical diagnosis for ICU-AW involves bedside muscle strength examination using a scoring system based on Medical Research Council (MRC) guidelines. The rating system goes from 0 to 5 for 12 different muscle groups, with a range of scores from no contraction to normal muscle strength. These muscle groups, which are assessed on both sides of the body, include shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and ankle dorsiflexion. The overall MRC score can vary from 0 to 60, and a diagnosis of ICU-AW is made when the total score falls below 48 [10], [11]. Early diagnosis and a multidisciplinary approach are essential in preventing ICU-AW and diaphragm dysfunction, with management techniques focusing on minimizing or avoiding risk factors such as controlling inflammation and sepsis, minimizing sedation and relaxants, strict glycemic control, and encouraging patients to move and undergo therapy early on can help prevent muscle deterioration [4].

2. Objectives

The primary goal of this study was to establish the correlation between diaphragm capacity measured by ultrasound and the success rate of ventilator weaning in ICU-AW patients. The research took place in the ICU of the combined surgical facility at Dr. Soetomo General Hospital in Surabaya, starting from July 2024 and ending in October 2024.

3. Methods

Selection Criteria

The study utilized an observational approach and a cross-sectional analytical survey design. Individuals in the intensive care unit who met certain requirements were enrolled in the investigation. The number of patients participating in the study was 23 individuals, with no subjects dropping out during the research period. The research received the green light from the ethics committee at Dr. Soetomo Hospital in Surabaya. Eligibility requirements included being hospitalized in the ICU for over 48 hours, aged between 18 and 60, needing ventilator support for more than 24 hours, and having ICU-acquired weakness with an MRC score below 48. Individuals with neurological and muscular conditions, individuals who have suffered a stroke, those with brain or spinal cord injuries, individuals with a body mass index over 35 kg/m², people with peripheral vascular disease, patients with paralysis prior to their admission to intensive care, individuals with fractures in their extremities, individuals with leg swelling, patients with wounds where electrodes are placed, those with cognitive impairments, individuals who are heavily sedated, individuals with stiffness or spasticity in their limbs, and those who use pacemakers were not included in the study.

Study Protocol

The study hypothesized that diaphragm capacity measurement using ultrasonography can determine the success rate of ventilator weaning in ICU-AW patients. Patients who met the criteria were evaluated at first by using the Medical Research Council Scale for Muscle Strength (MRC-SS) and Manual Muscle Testing (MMT). Patients whose clinical conditions improved and underwent ventilator weaning process were subjected to diaphragm ultrasound examination when Spontaneous Breathing Trial (SBT) was successful. Once the patients successfully completed the 30-minute SBT, the medical team determined that extubation could be performed. Throughout the SBT, the ultrasound physician closely observed and documented the movement of the diaphragm, ensuring that all ultrasound images were saved and measurements were conducted multiple times. Throughout the entire SBT procedure, the rate at which medications and other treatments were administered stayed consistent. The patient was observed using an ECG monitor to document fluctuations in heart rate (HR), mean arterial pressure (MAP), respiration rate (RR), and pulse oxygen saturation (SPO2), as well as changes in mental alertness. The individuals were separated into two groups based on the success or failure of extubation. Different data and weaning factors like FiO2, PaO2, and PaCO2 were gathered in advance. Healthcare providers were unaware of the ultrasound findings.

Successful extubation is determined by the ability to sustain spontaneous breathing for a minimum of 48 hours without needing ventilatory assistance. On the other hand, unsuccessful extubation involves reconnecting to a ventilator within 48 hours, either invasive or noninvasive, due to respiratory failure

or other causes. The decision to extubate and reconnect to the ventilator was based on the results of the Spontaneous Breathing Trial and the clinical judgment of the doctors. Patients who underwent extubation were evaluated periodically and assessed for either successful extubation or the need for reintubation within 48 hours.

Diaphragmatic Ultrasound

The ultrasound used was the Vivid™ iq series from GE Health Care, where diaphragm atrophy and contractility were evaluated by measuring diaphragmatic thickness (Tdi) and diaphragmatic thickening fraction (TFdi). Tdi was measured using a high-frequency linear probe (>10 MHz) placed at the zone of apposition (ZOA), where the diaphragm contacts the thoracic cavity. The probe was placed at a right angle to the side of the chest and positioned between the middle of the armpit and the front of the armpit at the 8th or 9th rib space. The space between the skin and the diaphragm was approximated to range from 0.8 to 4.9 cm. The thickness of the diaphragm is influenced by the amount of muscle mass present and is linked to forced vital capacity. If the thickness decreases, it can be identified through a low amplitude on electromyography, suggesting diaphragmatic atrophy. A thickness variation of less than 20% can indicate a likelihood of unsuccessful weaning from mechanical ventilation [7].

Diaphragmatic excursion (E) is measured using a low-frequency convex or phased array probe (1-5 MHz), positioned in the subcostal region, specifically between the midclavicular and anterior axillary lines. While low-frequency probes offer good depth penetration, their resolution may not be optimal. The left and right hemidiaphragms can be assessed using the liver and spleen as acoustic windows. To evaluate the movement of the right hemidiaphragm, the ultrasound probe is angled appropriately to capture B-mode images. The right hemidiaphragm appears as a thick, curved line on the ultrasound screen. After this, M-mode is employed to measure the maximum excursion by placing the probe perpendicularly to the diaphragm. Patients are then asked to breathe quietly (QB), deeply (DB), and also to sniff voluntarily (SV) during the examination [8]. Diaphragmatic dysfunction is diagnosed if the excursion is <10-15 mm during tidal breathing or if the TFdi (max) is <20% [12].

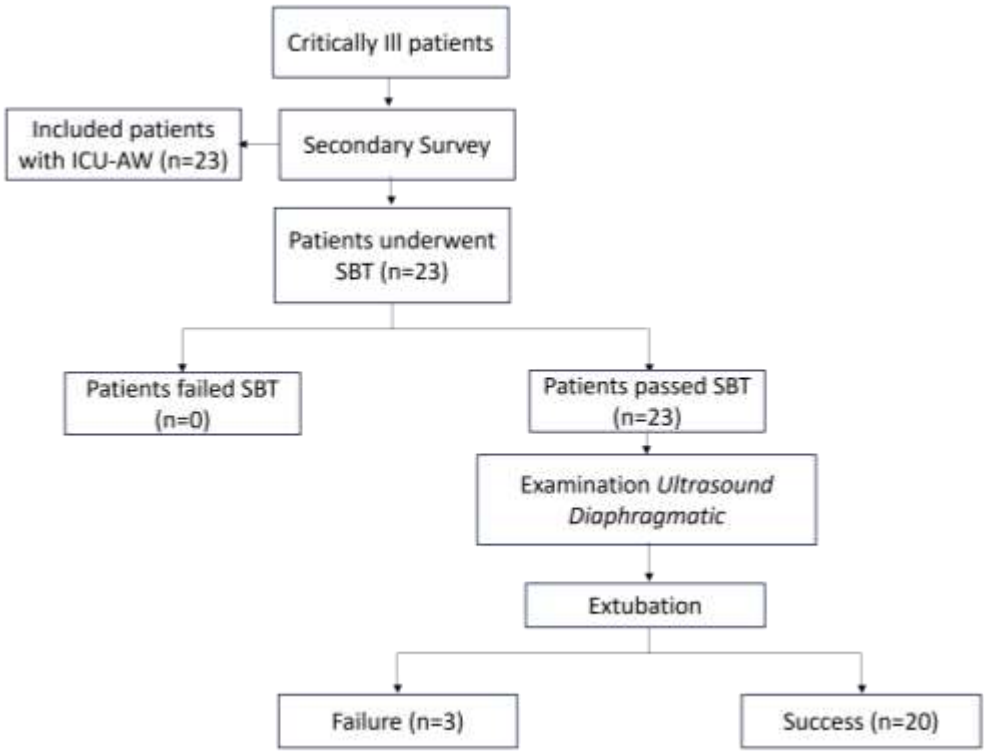

Figure 1: Research flow

Data Analysis

The collected data were processed using computer software (SPSS 26). Descriptive statistics were used to summarize the demographic characteristics data, including age and gender. The information about the measurements was given in two different formats: either as mean ± standard deviation or as median with interquartile range. To check for normality, the Shapiro-Wilk test was used. The correlation analysis between diaphragmatic excursion and extubation success rate was conducted using the Paired T-test, while the analysis between diaphragmatic thickness and extubation success rate was performed using the Mann-Whitney U test, as the diaphragmatic thickness data were not normally distributed.

4. Results

Population Main Characteristics

This study involved 23 patients who received treatment in the intensive care unit over a period of 4 months, with no subjects experiencing dropouts. The number of subjects who completed the study was 23, which exceeded the minimum sample size calculated at the beginning of the study. No adverse events were reported among the subjects during the research period. Overall, the study subjects consisted of 10 males (43.5%) and 13 females (56.5%) (see Table 1). Female gender was identified as an independent predictor of ICU-acquired weakness (ICU-AW) paresis and diaphragmatic dysfunction.

Table 1: Main Characteristics of 23 Patients

Characteristic	Median (Range)	Mean + SD	Normality Test Significance
Age	37 (16 – 64)	36.96 + 13.796	0.516
Body Mass Index	24.9 (14.5 - 33.2)	24.73 + 4.4644	0.159
Predicted Body Weight	52.4 (43.3 – 66)	3.578 + 6.6585	0.148
Sistol	110 (90 – 162)	115.13 + 17.195	0.023
Diastol	69 (35 – 91)	69.52 + 16.192	0.186
Mean Arterial Pressure	86 (58 – 125)	84.65 + 16.036	0.648
PF Ratio	347 (150 – 500)	323.57 + 96.374	0.789
Length of Stay	4 (2 – 6)	3.65 + 0.982	0.028
Durasi Ventilator	4 (2 – 6)	3.7 +1.063	0.012
MRC	40 (20 – 48)	40 + 9.723	0.000
Sex			
Male	10 (43.5%)		
Female	13 (56.6%)		

Diaphragmatic Dysfunction

The diaphragm excursion had a mean value of 14.522 ± 4.8698, with normality testing indicating a normal distribution (p = 0.493). In contrast, diaphragm thickness had a median value of 27.8 mm (range: 10–75 mm), but normality testing revealed a non-normal distribution (p = 0.007) (see Table 2). The distribution of diaphragm excursion categories showed that the majority of respondents had no impairment, with 18 individuals (78.3%), while 5 individuals (21.7%) exhibited weakness (≤15 mm). For diaphragm thickness, 19 individuals (82.6%) had no impairment, while 4 individuals (17.4%) showed weakness (≤20%).

Table 2: Diaphragm Muscle Strength and Skeletal Muscle Characteristics of 23 Patients

Variable	Median (Range)	Mean + SD	Normality Test Significance
Diaphragm Excursion	15 (5 – 27)	14.522 + 4.8698	0.493
Diaphragm Thickness	27.8 (10 – 75)	32.404 + 17.2499	0.007
Diaphragm Excursion			
No	18 (78,3 %)		
Weak (<=10 mm)	5 (21,7 %)		
Diaphragm Thickness			
No	19 (82,6 %)		
Weak (<=20%)	4 (17,4 %)		
MRC Score			

Variable	Median (Range)	Mean + SD	Normality Test Significance
Mild	11 (47.8%)		
Moderate	8 (34.8%)		
Severe	4 (17.4%)		
Incidence of Reintubation			
No	20 (87%)		
Yes	3 (13%)		

Analysis of Diaphragmatic Ultrasound Examination on the Incidence of Reintubation

The analysis results indicate a significant difference in Diaphragm Excursion values between patients requiring reintubation and those who do not, as determined by an independent t-test (p = 0.001) (see Table 3). Similarly, a significant difference was also observed in Diaphragm Thickness values between the two groups, as evidenced by the Mann-Whitney test (p = 0.006) (see Table 4).

Table 3: Diaphragm Excursion Difference Test Based on Reintubation

Reintubation	N	Mean	Std. Deviation	Levene's Test Significance	t test Significance
No	20	15.700	4.0013	0.266	0.001
Yes	3	6.667	1.5275		

Table 4: Diaphragm Thickness Difference Test Based on Reintubation

Reintubation	N	Median	Range	Mann Whitney test significance
No	20	28.850	18.3 - 75.0	0.006
Yes	3	12.000	- 12.5	

Analysis of Diaphragmatic Ultrasound Examination on MRC Score

This study found that 18 respondents (78.3%) had normal Diaphragmatic Excursion, while 5 respondents (21.7%) exhibited weak Diaphragmatic Excursion (≤10 mm), with varying distributions across different MRC score categories. The analysis results indicate a significant association between the MRC score and Diaphragm Excursion values, as determined by Fisher's Exact Test (p = 0.000) (see Table 5). Furthermore, 19 respondents (82.6%) were classified as having normal Diaphragmatic Thickness, whereas 4 respondents (17.4%) had low Diaphragmatic Thickness (≤20%). The analysis also revealed a significant association between the MRC score and Diaphragm Thickness values, based on Fisher's Exact Test (p=0.000) (see Table 6).

Table 5: Cross-tabulation of MRC score with Diaphragm Excursion

MRC Category	Diaphragm Excursion Category		Total	Fisher's Exact Test
	Normal	Weak (<=10mm)		
Mild	11	0	11	0.000
	100.00%	0.00%	47.83%	
Moderate	7	1	8	
	87.50%	12.50%	34.78%	
Severe	0	4	4	
	0.00%	100.00%	17.39%	
Total	18	5	23	
	78.30%	21.70%	100.00%	

Table 6: Cross tabulation of MRC score with Diaphragm Thickness

MRC Category	Diaphragm Thickness Category		Total	Fisher's Exact Test
	Normal	Low (<=20%)		
Mild	11	0	11	0.000
	100.00%	0.00%	47.83%	
Moderate	8	0	8	
	100.00%	0.00%	34.78%	
Severe	0	4	4	
	0.00%	17.40%	17.39%	
Total	19	4	23	
	82.60%	17.40%	100.00%	

5. Discussion

In general, the study subjects consisted of 10 males (43.5%) and 13 females (56.6%). Female sex is considered an independent predictor of ICU-AW paresis and diaphragmatic dysfunction. Physiological variances in body composition, muscle strength, and energy metabolism could play a role in the development of ICU-AW and problems with the diaphragm. Additionally, impaired insulin sensitivity index has been found to be more prevalent in critically ill female patients. An investigation based on gender reveals that women who are critically ill are more likely to experience a decrease in insulin sensitivity, increasing the chances of losing muscle mass [13]. The average age of the participants in the research was 37 years old, and they were all hospitalized in the ICU. The mean body mass index (BMI) was 24.73 kg/m², which, according to WHO classification, falls within the overweight category. However, BMI may not serve as an accurate marker due to excess body fat in critically ill patients, making it challenging to determine muscle mass gain or loss [14].

The main factors that are consistently linked to ICU-AW are connected to how severe the illness is, such as experiencing shock, sepsis, and the extent of multiple organ failure. This indicates that ICU-AW can be seen as another form of multiple organ dysfunction syndrome. Cohort studies on critically

ill patients have demonstrated an association between sepsis and ICU-AW. Several ICU-related interventions or exposures have been identified as potential risk factors for ICU-AW, including corticosteroid administration, neuromuscular blocking agents, glycemic control, aminoglycoside therapy, and prolonged immobilization. Increased use of fluids and blood transfusions in a liberal manner could potentially play a role in the onset of ICU-acquired weakness [9]. Extended periods of immobility can result in muscle wasting as a result of inactivity, causing alterations in the size, length, and power of the muscles. In healthy individuals, muscle fiber shortening begins within four hours of immobilization. After one week of complete immobilization in healthy volunteers, postural muscle strength decreases by 5% to 10%, with an average daily loss of 1% to 1.3% of total muscle strength [15].

The Medical Research Council (MRC) scale is highly regarded and commonly used for evaluating peripheral muscle strength, making it the preferred method for diagnosing ICU-AW. It measures voluntary muscle strength in six different muscle groups on both sides of the body, including shoulder abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, and ankle dorsiflexors. The MRC scale is simple to use and has a strong ability to predict ICU-AW, with good inter-investigator agreement in ICU patients [16]. MRC assessment is performed 24 hours after intubation and sedation administration. Several factors contributing to ICU-AW in this study include the use of neuromuscular blocking agents, antibiotics, and electrolyte imbalances such as hypermagnesemia, hypokalemia, hypocalcemia, and hypophosphatemia, as well as prolonged immobilization. The diagnosis of ICU-AW is established through manual muscle strength testing using the MRC scale [17]. This study found that the median MRC sum score (MRC-SS) upon ICU admission was 40 (range: 20–48). Muscle strength assessment using the MRC-SS is conducted on 12 muscle groups, with a total score below 48 out of 60 indicating ICU-AW or significant weakness. An MRC score between 36 and 48 suggests moderate weakness, while a score below 36 indicates severe weakness. The MRC assessment performed upon ICU admission revealed scores below 48, indicating that ICU patients in this study experienced ICU-AW [18], [19].

The muscles of patients with ICU-AW exhibit various changes, as muscle strength depends on both force-generating capacity and muscle mass, both of which are believed to be affected in ICU-AW. Clinically, this condition manifests as muscle atrophy, preceded by abnormal muscle electrophysiology. A key characteristic is the loss of thick myosin filaments, resulting in an altered actin-to-myosin ratio and disrupted myofilament organization within the tissue. Normally, skeletal muscle exhibits a well-organized striated pattern formed by the arrangement of myofilaments, which is essential for generating force in a coordinated manner. However, in ICU-AW patients, significant disruptions in this organization are observed, likely contributing to a reduced force-generating potential [20]. Muscle mass is regulated by the equilibrium between muscle protein synthesis and breakdown. During hypertrophy, both processes increase, but protein synthesis surpasses degradation. In contrast, atrophy occurs when protein breakdown exceeds synthesis. In cases of critical illness, this balance is disturbed, resulting in a predominantly catabolic state due to the heightened activity of atrophy pathways [21].

This study uncovers that subjects with reduced diaphragm thickness also exhibit weak excursion. Diaphragm strength is essential for successfully weaning patients from mechanical ventilation (MV)

and facilitating their transition to long-term care facilities. Furthermore, diaphragm strength is a key determinant of ICU mortality. A recent study found that around 80% of ICU patients on mechanical ventilation experience some degree of ICU-acquired diaphragm weakness after initial MV use. Moreover, diaphragm inactivity occurs twice as often as limb inactivity in critically ill patients. Multimodal assessments, including phrenic nerve magnetic stimulation, ultrasound-based diaphragm movement and thickening measurements, and maximal inspiratory pressure tests, have shown that diaphragmatic dysfunction is prevalent in ICU-acquired inactivity. This condition is linked to higher rates of weaning failure and increased ICU mortality [22].

Measurements of diaphragm excursion and thickness were conducted during a T-piece trial/spontaneous breathing trial (SBT), with statistical analysis performed using a T-test for excursion due to its normal distribution, while Mann-Whitney was used for thickness due to the presence of non-normally distributed data. The results indicated a significant association between both diaphragm assessments and the incidence of reintubation, with three patients (13%) requiring reintubation within 48 hours post-extubation due to increased work of breathing during the observation period. The analysis further revealed a significant relationship between MRC scores and both diaphragm thickness and excursion, as determined by Fisher's Exact Test (Tables 5 and 6). The correlation between ICU-AW and diaphragmatic dysfunction is often overlapping. Although both the diaphragm and limb muscles are skeletal muscles and share similar cellular mechanisms, they exhibit different vulnerabilities to mechanical ventilation and bed rest. Immobilization remains the primary factor contributing to muscle weakness. While limb muscle activity can be drastically reduced, the diaphragm possesses continuous activity throughout life, making it particularly susceptible to even short periods of immobilization [23].

Weakness in limb muscles and respiratory muscles (in this case, the diaphragm) is often assumed to be part of a similar disease mechanism. Nevertheless, there are multiple factors indicating that these should be seen as distinct occurrences. To start with, the timing of alterations in muscle structure varies greatly among the two categories. The size of the quadriceps muscle decreases around 10% after a week on a ventilator, while diaphragm atrophy happens even quicker. About half of patients see a 20% reduction in diaphragm size within 3 or 4 days of being put on a ventilator. Diaphragmatic atrophy develops earlier and more severely than limb muscle atrophy. Additionally, in the initial phase of weaning, respiratory muscle weakness shows only a weak correlation with limb muscle weakness. Research has indicated that diaphragmatic weakness is significantly more prevalent than peripheral or limb muscle weakness. At that stage, only 21% of patients exhibited concurrent weakness in both the diaphragm and limb muscles. This lack of correlation, along with the notable difference in prevalence, suggests that the underlying mechanisms or pathophysiology of diaphragmatic and limb muscle dysfunction differ [6].

In the ICU, mechanical ventilation (MV) has the ability to rescue critically ill patients, although it can lead to weaning difficulties for around 20% of patients. This is mainly due to the quick deterioration of diaphragm strength and endurance, resulting in a condition referred to as Ventilator-Induced Diaphragmatic Dysfunction (VIDD). Diaphragmatic dysfunction or VIDD is common in critically ill patients and is associated with poor outcomes, including the need for mechanical ventilation and increased mortality rates. In the majority of ICU patients (80%), diaphragmatic dysfunction can occur

upon admission or during subsequent hospitalization. Clinical evidence has shown that VIDD worsens ventilator-associated pneumonia (VAP), increases the risk of extubation failure, raises in-hospital mortality, prolongs ventilator dependency, and escalates healthcare costs. VIDD shares a comparable pathophysiology with Ventilator-Induced Lung Injury (VILI), marked by widespread inflammation and heightened oxidative stress, which ultimately compromise gas exchange. The mechanisms underlying VIDD are thought to be multifactorial, involving oxidative stress, muscle weakness (mediated by caspase-3, calpain, activation of the ubiquitin-proteasome system (UPS), and the autophagy-lysosomal pathway (ALP)), as well as structural damage and myofiber remodeling. Further research is needed to fully elucidate these processes. Hence, it is essential to have an in-depth comprehension of the molecular processes that cause VIDD in order to devise effective methods to lower the duration of mechanical ventilation, ICU stay, and ICU fatality rates [22], [24].

6. Conclusion

Ultrasonography (USG) can be utilized as a diagnostic tool to assess diaphragm capacity and serve as a predictor of ventilator weaning success. A decline in diaphragm capacity may occur in ICU-AW patients, increasing the risk of ventilator weaning failure.

Limitation

This research exhibits heterogeneity in sample selection, which may impact the accuracy and reliability of data analysis results. Additionally, the study population was limited to a single hospital, restricting its generalizability to the broader population.

Ethical Approval

This study received approval from the Ethics Committee of Dr. Soetomo Surabaya Hospital (0999/KEPK/V/2024). Written informed consent was obtained from all patients and/or their families before participation.

Conflicts of Interest

The author declares no conflicts of interest, financial or otherwise.

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