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PREDICTORS OF VENTILATOR WEANING FAILURE IN SEPSIS PATIENTS IN INTENSIVE CARE UNIT

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ABSTRACT
Sepsis is one of the most common infection complications in intensive care units (ICU). Sepsis causes organ dysfunction, including respiratory failure, that requires ventilator breath support. However, patients often experience ventilator weaning failure. We analyse the relation of predictor ventilator weaning failure in sepsis patients in ICU. This study was a cross-sectional study with study population consisting of sepsis patients who used ventilators in the ICU of Sulianti Saroso Hospital, and there were as many as 58 patients. We studied age, gender, body mass index (BMI), PCO2 value, prolonged ventilator use, pneumonia, malnutrition, vasopressor use and ventilator weaning with secondary data. The data collection instruments used were case report formulas. Descriptive statistical analysis in the form of frequency distribution (n) and proportion (%) and further analysis with binomial logistic regression ($\alpha<0.05$). Three factors significantly influenced weaning failure were vasopressor use, malnutrition, and BMI ($p<0.05$). There is a significant influence of vasopressor use, malnutrition, and BMI with ventilator weaning failure.

Keywords: weaning failure; sepsis; ventilator

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INTRODUCTION

Sepsis is one of the most common cases in the ICU, causing patients to experience organ dysfunction, including respiratory failure. This condition poses a threat to the survival of patients (Kyriakoudi et al., 2021). World Health Organization (WHO) reported that in 2020, there were 48.9 million cases of sepsis, and around 11 million deaths were attributed to it. In the United States, sepsis was the leading cause of death in 2017 (Prest et al., 2022). A prevalence study conducted in 22 Asian countries in 2019 over a period of 4 days involving 386 adult ICU patients gathered extensive data on the processes and outcomes of sepsis patient care. The overall prevalence of sepsis, defined using the Sepsis-3 criteria (Third International Consensus Definitions for Sepsis and Septic Shock), was 22.4%, ranging from 20.9% in low- and lower-middle-income countries (LIC/LMIC) to 24.5% in upper-middle-income countries.

Meanwhile, the prevalence of sepsis in Indonesia remains very limited. According to a retrospective observational study, there were 14,076 sepsis cases in Indonesia from 2013 to 2016, with 41.7% of patients recovering and 58.3% not surviving. The case fatality rate

(CFR) for sepsis patients treated in the ICU was 69%. Approximately 31% of sepsis cases were due to multifocal infections. The average age of sepsis patients was 49.4 years (Purba et al., 2020).In severe sepsis, the patient sometimes requires mechanical ventilation support as respiratory failure occurs. Sepsis patients typically have more difficulty weaning off of artificial breathing and require it for a longer duration of time than non-septic patients. According to reports, critically sick patients with sepsis require more days (3.8 days) for weaning compared to critically ill patients without sepsis (2.5 days), and they are 2.4 times more likely to fail spontaneous breathing trials (Kyriakoudi et al., 2021)

Weaning is undertaken once the underlying cause of respiratory failure has been resolved (Özsancak U¿urlu & Ergan, 2023; Zein et al., 2016), the results of the Arterial Blood Gas (ABG) analysis are within normal limits (Hazarika et al., 2023), spontaneous breathing is adequate (Zein et al., 2016), and mechanical ventilation support has been minimised (Shelledy & Peters, 2020). The failure to pass a spontaneous breathing trial or the need for reintubation within 48 hours after extubation is ventilator weaning failure (Yan et al., 2022). The study conducted by several researchers identified the following risk factors for ventilator weaning failure: age, sex, BMI, PCO2 levels, prolonged use of mechanical ventilation, bronchospasm, pneumonia, malnutrition, and duration of vasopressor use (Trudzinski et al., 2022). The objective of the study is to analyse factors influencing ventilator weaning failure in sepsis patients in the ICU of Sulianti Saroso Infectious Disease Hospital.

METHOD

This retrospective cohort study analysed secondary data from the electronic medical records of patients treated for sepsis in the intensive care unit at Sulianti Saroso Hospital.The study included patients ≥18 years old with a diagnosis of sepsis who were treated in the ICU and required mechanical ventilation. Patients with tracheostomy were excluded from the study. The research was conducted from January to June 2023. Sampling was performed using purposive sampling. Sample size calculation was done using G-power version 3.1.9.4 with a medium effect size of 0.5, a standard error of 0.05, and a power of 0.80, resulting in a sample size of 58 patients. Data collection instruments included case report forms and patient observation sheets.The diagnosis of sepsis is based on the patient's clinical presentation, hemodynamics, and other supplementary examinations, with the physician's final diagnosis. PCO2 levels were obtained from clinical pathology laboratory examinations of sepsis patients and recorded in their medical records. Samples were taken upon patient admission to the emergency room and at the same time. The computation of the Body Mass Index (BMI) was done using the weight and height data. The formula: BMI = weight / height². Malnutrition is defined as an imbalance, deficiency, or excess of nutrients in the body, as diagnosed by a clinical nutrition specialist. Data analysis was performed using the Jamovi statistical software package. The statistical methods used included descriptive statistics, frequency distribution, and logistic regression analysis to assess the relationship between predictors and weaning failure ($p<0.05$). Research permission was obtained from the Research Ethics Committee of the Faculty of Nursing, Muhammadiyah University of Jakarta, with the reference number: 0465/F.9-UMJ/IV/2023.

RESULTS

The total number of sepsis patients who met the inclusion and exclusion criteria was 58. Descriptive analysis revealed that the average age of the subjects was 56.2 years. The majority were male, had nutritional issues, and experienced pneumonia. However, PCO2 levels were normal, despite the fact that mechanical ventilation had been used for a considerable duration (≥ 7 days) and vasopressors were employed (Table 1).

Table 1.
Characteristics of Sepsis Patients on Mechanical Ventilation in the ICU (n=58)

Characteristic	Mean(SD)/ f(%)
Age (year), mean (SD)	56.2 (9.47)
Gender, n (%)	
Male	39 (67.2)
Female	19 (32.8)
IMT, n (%)	
Normal	24 (41.4)
Abnormal	34 (58.6)
Malnutrition, n (%)	
No	30 (51.7)
Yes	28 (48.3)
Pneumonia, n (%)	
No	7 (12.1)
Yes	51 (89.9)
PCO_2, n (%)	
Normal	36 (62.1)
Abnormal	22 (37.9)
Duration of Mechanical Ventilation, n (%)	
1-7 days	13 (22.4)
≥7 days	45 (77.6)
Vasopressor Use, n (%)	
No	11 (19.0)
Yes	47 (81.0)

Note: Standard Deviation (SD), Body Mass Index (BMI), *Partial Pressure of Carbon Dioxide* (PCO_2)

Table 2 showed that there is a significant relationship between pneumonia status, duration of mechanical ventilation, BMI, malnutrition, and use of vasopressors with weaning failure ($p<0.05$).

Table 2.
Impact of Predictors on Ventilator Weaning Failure in Sepsis Patients in the ICU (n=58)

Predictor	p-value	OR (95% CI)
Intercept	0.316	0.02 (1.02-40.95)
Age	0.369	0.94 (0.83-1.07)
Pneumonia	0.581	2.28 (0.12-42.89)
Duration of Mechanical Ventilation	0.334	3.64 (0.27-49.85)
BMI	0.046	16.29 (1.05-253.45)
Vasopressor Use	0.005	53.40 (3.33-857.52)
PCO2	0.186	5.51 (0.44-69.18)
Malnutrition	0.022	31.95 (1.64-623.89)
Gender	0.225	4.94 (0.37-65.29)

Note: Standard Deviation (SD), Body Mass Index (BMI), *Partial Pressure of Carbon Dioxide* (PCO_2), α=0.05, 95% *Confidence Interval* (CI)

DISCUSSION

This study is the first to use secondary data to evaluate variables related to ventilator weaning failure in sepsis patients in the ICU of Sulianti Saroso Hospital. The research focused on several predictors, including age, sex, BMI, malnutrition, pneumonia, PCO2 levels, duration of mechanical ventilation, and use of vasopressors, about weaning failure in sepsis patients. From January to June 2023, 390 patients were treated in the ICU of Sulianti Saroso Infectious

Disease Hospital, of whom 204 required mechanical ventilation. This large sample size provided a comprehensive view of the factors influencing ventilator weaning outcomes.

The use of mechanical ventilation and its associated complications, such as infections and pneumonia (Kohbodi et al., 2023; Wittler, 2023), have been identified as predictors of mortality in the ICU (Kondili et al., 2019; Papazian et al., 2020). The study found that prolonged use of mechanical ventilation is linked to a decreased rate of successful weaning and an increased mortality rate (Noviyanti et al., 2022). Mechanical ventilation frequently results in ventilator-associated pneumonia, a severe side effect with high morbidity and mortality. The SOFA (Sequential Organ Failure Assessment) score, introduced in 1994, is a reliable predictive factor for mortality during an ICU stay (Ferreira et al., 2001; Lambden et al., 2019; Velho et al., 2022). Prognosis is indicated by a sequential assessment of organ dysfunction in the initial days after ICU admission. The highest and mean SOFA scores are both excellent indicators of success. An increase in SOFA score within the first 48 hours in the intensive care unit (ICU) indicates a minimum 50% mortality rate, regardless of the beginning score. The SOFA score assesses the extent of a patient's organ dysfunction by evaluating six different organ systems, which helps estimate the likelihood of mortality and guide clinical decision-making (Gnanapandithan et al., 2011). The SOFA score, which is used to assess a patient's condition or the degree of organ failure and malfunction in intensive care units (ICUs), is based on six distinct, independent scores, including those for the respiratory, cardiovascular, hepatic, renal, coagulation, and neurological systems (Arina & Singer, 2023; Vincent, 2009). Generally, its purpose is to forecast death rather than the success or failure of medical interventions. In addition, Tseng et al. reported that a higher SOFA score is associated with the more extended use of ventilators in VAP (Tseng et al., 2012).

Our study did not measure the SOFA score, so we could not correlate it with weaning failure in patients requiring prolonged mechanical ventilation (PMV). Patients who require PMV have complex clinical predictive variables. The SOFA score could be a valuable predictor for both weaning failure and mortality in the ICU (Dehghani et al., 2016; Moreno et al., 2023; Shin et al., 2017). However, the SOFA score does not predict weaning failure specifically for survival patients. Further prospective multicenter studies are needed to validate the usefulness of assessing the SOFA score on day 21 about weaning failure.In this study, most patients (77.6%) were on mechanical ventilation for more than seven days, with only 22.4% successfully weaning. An observational study in 2018 found that complications in ventilator weaning were particularly challenging for patients with acute respiratory distress syndrome (ARDS) due to lung contusion and pneumonia (Prasetya & Indriasari, 2018). Other studies have also explained that the reason for respiratory failure, such as a high SOFA score on day 21, has been shown to affect weaning failure significantly (Cho et al., 2016).

Impact of BMI on Ventilator Weaning Failure in Sepsis Patients

The results of this study indicate that Body Mass Index (BMI) is a predictor of ventilator weaning failure in sepsis patients in the ICU. Weaning from the ventilator should begin as soon as possible, and a number of characteristics can be used to predict the weaning outcomes of patients receiving short-term mechanical ventilation. These results are in line with an observational study carried out in a referral hospital in Taiwan (Huang, 2022). The rapid shallow breathing index is the most frequently studied and is essential in deciding whether to start weaning a patient. Additionally, a BMI > 30 is identified as one of the predictors of prolonged weaning. Obese patients suffer from increased respiratory workload and impaired gas exchange. These disturbances reduce physical capacity and health margin when exposed to respiratory stress. The underlying trigger factor is diminished lung volume, caused by

increased abdomen tissue mass and chest wall tissue. These factors can lead to complications during ventilator weaning (Zaidi & Saleem, 2021).

The Impact of Vasopressor Use on Ventilator Weaning Failure in Sepsis Patients

In this study, vasopressor use is a predictor of weaning failure in sepsis patients in the ICU. Vasopressors are medications required to maintain heart function and perfusion pressure in severe hypotension and achieve desired hemodynamic parameters such as central venous pressure, MAP, urine output, and oxygenation. The indications for starting weaning are stable heart function: HR < 140/min, absence of myocardial ischemia, and either no vasopressor use or only low-dose inotropic medications (Kusuma & Atmajaya, 2015). Heart function significantly impacts the process of ventilator weaning (Wang et al., 2018). During the weaning trial, the patient's hemodynamics are already stable, and if necessary, small doses of vasopressors are maintained to ensure hemodynamic stability during the weaning process. Although initial practice indicated that using vasopressors during weaning trials might prevent successful extubation, later research found no negative impact on this outcome. It's unclear whether using vasopressors during extubating has risks. This study aims to determine whether worse outcomes are linked to extubation when taking vasopressors.

The Impact of Malnutrition on Ventilator Weaning Failure in Sepsis Patients

In this study, malnutrition predicts weaning failure in sepsis patients in the ICU. Malnutrition can result in hypophosphatemia, hypomagnesemia, hypocalcemia, and hypokalemia, which can cause weakness in the respiratory muscles. This can lead to respiratory failure and delay the ventilator weaning process (Deli et al., 2018). The results of the prospective cohort study conducted in Thailand indicate that the length of time critical patients spend on mechanical ventilation is correlated with their nutritional status, the time to start enteral feeding, and the number of calories they must meet within seven days of admission (Koontalay et al., 2021). When they are in severe conditions, their bodies react to systems that stimulate inflammation because they are hypermetabolic and hypercatabolic, which helps them identify starvation. Due to severe hypercatabolism, which causes infection problems, delayed recovery, ongoing hospitalisation, or the need for artificial breathing, their protein and energy levels have dropped. In 40% to 60% of patients, malnutrition is linked to changes in systematic functions(O'Leary-Kelley & Bawel-Brinkley, 2017), such as loss of body mass, impaired respiratory function, weakness in the diaphragm muscle, depletion of fat or protein, and length of hospital stay, which increases morbidity and mortality.

There are several limitations to this study. First, the number of patients included in this study is small because it is a single referral hospital study. Additionally, there is a risk of potential overfitting due to the small number of enrolled patients and the presence of interdependent covariates, which may have limited the statistical power of this study. Second, although various factors are associated with ventilator weaning failure, we could not thoroughly investigate factors such as respiratory physiological parameters, MV modes, endocrine and metabolic dysfunction, ICU-acquired weakness, or diaphragm dysfunction because this study was conducted retrospectively. Therefore, future prospective multi-centre studies on patients requiring PMV are essential.

CONCLUSION

Our study shows a significant relationship between pneumonia status, prolonged use of the ventilator, BMI, malnutrition, and vasopressor use, significantly affecting weaning failure ($p<0.05$). The presence of these predictors increases the risk of ventilator weaning failure in sepsis patients.

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