Original article

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The accuracy of diaphragm thickening fraction, C-reactive protein, cumulative fluid balance, and rapid shallow breathing index in predicting the ease of weaning from mechanical ventilation in critical patients in the ICU

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Abstract

***Background*: Weaning from mechanical ventilation is essential for critically ill patients and obtaining mechanical ventilation. Several parameters were used to assess the patient's ability to predict the success of weaning.**

***Objective*: The purpose of this study was to determine the accuracy of diaphragm thickening fraction, C-reactive protein, cumulative fluid balance, and rapid shallow breathing index in predicting the ease of weaning mechanical ventilation in critical patients in the intensive care unit (ICU).**

***Method*: This was a prospective cohort study in which the subjects were adult patients who were treated using mechanical ventilation. Diaphragm thickening fraction, C-reactive protein, cumulative fluid balance, and rapid shallow breathing index were examined during the first 24 hours in the ICU and during mechanical ventilation in pressure support (PS)<8 or T-piece mode until a maximum of the seventh day of the treatment in the ICU or on the seventh day if have not been successfully weaned.**

***Result*: We found that there was no statistical significance between the diaphragm thickening fraction and the ease of weaning from mechanical ventilation (p=0.071). The effect of C-reactive protein on the ease of weaning on mechanical ventilation was not statistically significant (p=0.724). The cumulative balance and rapid shallow breathing index values were also not statistically significant to predict the ease of mechanical ventilation weaning (p=0.510 and p=0.116)**

***Conclusion*: Diaphragm thickening fraction, C-reactive protein, cumulative fluid balance, and rapid shallow breathing index statistically cannot predict the ease of weaning mechanical ventilation in critical patients in the ICU.**

Key words: Diaphragm thickening fraction, C-reactive protein, fluid balance, rapid shallow breathing index, weaning mechanical ventilation.

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Introduction

Weaning from mechanical ventilation is essential in treating critically intubated patients and receiving mechanical ventilation. Weaning from mechanical ventilation accounts for about 40% of the duration of mechanical ventilation. (1) Although most of the weaning process is easy, there are 20-25% who have difficulty weaning from mechanical ventilation. (2) Several parameters were used to assess the patient's ability to predict the success of weaning. Variables such as minute ventilation, maximal inspiratory pressure, respiratory rate, rapid shallow breathing index (RSBI), tracheal airway occlusion pressure 0.1s have been frequently used in clinical practice.

RSBI can be regarded as one of the accurate predictors of weaning success. However, the values of sensitivity, specificity, positive predictive value, and negative predictive value for the recommended threshold differ in many studies. (3) Yang and Tobin in their study said that RSBI values below 105 can predict the success of mechanical ventilation weaning with sensitivity, specificity, positive predictive value, and negative predictive value of 0.97, 0.64, 0.78, and 0.95. The low specificity and positive predictive value can lead to errors when assessing mechanical ventilation weaning. (4)

Ultrasonography can be used to assess diaphragmatic muscle dysfunction so that it can be used to predict failure in the mechanical ventilation weaning process, assess respiratory workload, and assess the progression of diaphragmatic muscle atrophy. Decreased diaphragmatic muscle mass thickness is an important component of diaphragmatic dysfunction resulting in difficulty in weaning mechanical ventilation. (5) Diaphragm thickening fraction (DTF) is assessed by measuring the thickness of the diaphragm muscle during inspiration minus the thickness of the diaphragm muscle during expiration, divided by the thickness of the diaphragm muscle during expiration and multiplied by 100%. Several studies have provided the best minimal diaphragmatic thickening fraction for predicting successful extubation. (3,4,6)

Inflammatory marker C-reactive protein (CRP) is an acute-phase protein produced by the liver in response to tissue damage or infection. CRP is a clinical marker that is often used as an indicator of the occurrence of sepsis in patients admitted to the intensive care unit (ICU). Sierros et al found a CRP threshold of 2 mg/dl to have a sensitivity of 100% and specificity of 20% to predict mortality within 60 days of patients on long-term mechanical ventilation. (7) Hsiao et al showed high CRP values associated with respiratory failure and prolonged use of mechanical ventilation. (8)

A positive cumulative fluid balance has been shown to be associated with increased mortality in critically ill patients. Ghosh et al showed that cumulative fluid balance was significantly higher in patients who failed to extubate (median 4336.5 ml vs 2752 ml, p=0.036). (9) Frutos-Vivar et al reported that a positive cumulative fluid balance 24 hours before extubation was a risk factor for spontaneous breathing trial (SBT) failure (OR 1.70; 95%CI=1.15-2.53). (10) Therefore, we hypothesized that DTF, CRP value, cumulative fluid balance, and assessment of RSBI can predict the ease of weaning mechanical ventilation in critically ill patients admitted to the ICU.

Materials and methods

This was a prospective cohort study in which the subjects were adult patients who were treated using mechanical ventilation. The study protocol was approved by the institutional review board and all participants provided written informed consent. The primary objective of this study was to determine the accuracy of DTF, CRP, cumulative fluid balance, and RSBI in predicting the ease of weaning mechanical ventilation in critical patients in the ICU.

Patient population

Critically ill patients who were treated using mechanical ventilation in the ICU between November 2020 and December 2020 were enrolled in this study. Inclusion criteria were adult patients aged 18 to 65 years old who were treated in ICU with a P/F ratio from blood gas analysis between 250 to 350 and agreed to become a participant in the study with written consent from a family member. Exclusion criteria were patients who were pregnant, predicted to be extubated within 24 hours, had neuromuscular disorders, and had a tracheostomy.

The sample size needed for this study was 30 samples.

Definitions

A weaning ventilator is defined as a condition where the patient can breathe spontaneously with mechanical ventilation mode pressure support 8 or T-piece for 2 hours without problems. Simple weaning is defined as where weaning can be done less than 7 days of ICU treatment, whereas difficult weaning is defined as failure to do weaning within 7 days of ICU treatment.

Methods

This study recruited 30 patients who were treated using mechanical ventilation and met the study criteria. We collected measurements of DTF, cumulative fluid balance, CRP value, and RSBI in the first 24 hours of hospitalization in the ICU using mechanical ventilation. When the patient starts the weaning process, we collected measurements of DTF, cumulative fluid balance, CRP value, and RSBI when mechanical ventilation mode PS 8 or T-piece until the maximum of the seventh day of treatment in the ICU or on the seventh day if it has not been successfully weaned. The mechanical ventilation weaning process was recorded and classified as simple weaning or difficult weaning. Baseline characteristics, including age, Sequential Organ Failure Assessment (SOFA) score, diagnosis, were also recorded.

Statistical analysis

SPSS software (version 21.0; IBM) was used for statistical analysis. Patients' demographic and clinical characteristics were reported using mean (standard deviation [SD]) or median (interquartile range [IQR]) or number (percent). Changes in DTF, CRP levels, cumulative fluid balance, and RSBI values would be calculated as the average value and the ratio value between the measurement value and the first-day baseline value. The comparison of data between an independent variable and the dependent variable was analyzed using chi-square or Fisher's exact test for categorical data. Logistic regressions were performed to measure the association between clinical variables. A p-value of less than 0.05 was considered statistically significant.

Results

Thirty patients were recorded during our study. There were 14 subjects with easy weaning and 16 subjects with difficult weaning. The mean age of the research subjects was 44.46±19.64 years. In this study, age was found to have a statistical effect on the ease of weaning on mechanical ventilation (p=0.044; OR 5.17 [0.455-6.198]). Furthermore, for the characteristics of the research subjects, namely gender (p=0.073; OR 2.286 [0.873-5.983]), height (p=0.07; OR 2 [0.972-4.117]), and patient's weight (p=0.282; 1.524 [0.7-3.319]) had no statistical effect on the ease of weaning on mechanical ventilation. The SOFA value of the patients at the time of admission to this study was 5.867±3.21. The SOFA value for the research subjects in this study was statistically significant for the ease of weaning from mechanical ventilation with a p-value=0.003 and an OR value of 4.588; 95%CI 1.236-17.026. The most common diagnoses in the study subjects were sepsis, postoperative, and ARDS, although statistically the diagnosis of the study subjects did not affect the ease of mechanical ventilation (p=0.063; OR 2.188 [0.88-5.44]).

A non-significant difference between DTF and ease of weaning mechanical ventilation was reported (p=0.071). The mean DTF for the easy weaning from mechanical ventilation was 23.13±13.47 %, while the average DTF for the difficult weaning from mechanical ventilation was 22.7±17.67%. A non-significant difference between CRP value and ease of weaning from mechanical ventilation was also reported (p=0.724). The mean CRP value for the easy weaning from mechanical ventilation was 99.91±87.98 mg/dl. Meanwhile, the average CRP value for the difficult weaning from mechanical ventilation was 139.81±115.67 mg/dl.

There was no significant difference between cumulative fluid balance and ease of weaning from mechanical ventilation (p=0.510). The mean cumulative fluid balance for cases of easy weaning from mechanical ventilation was 733.39±680.42 ml. Meanwhile, the average cumulative fluid balance for cases of difficult weaning from mechanical ventilation was 649.3±1205.19 ml. There was no significant difference between RSBI values with ease of weaning mechanical ventilation (p=0.116). The mean RSBI value for cases of easy weaning from mechanical ventilation was 75.43±25.82 breaths/minute/l. Meanwhile, the mean RSBI value for cases of difficult weaning from mechanical ventilation was 98.23±40.99 breaths/minute/l.

A logistic regression test was performed to analyze the difference between those variables with ease of weaning mechanical ventilation. We found there was no significant difference between DTF, CRP value, cumulative fluid balance, and RSBI value with ease of weaning mechanical ventilation.

Discussion

Weaning from mechanical ventilation presents its challenges for the clinician. Too fast and too late weaning has a bad impact on patients in the ICU. (2) Factors that influence the difficulty of weaning mechanical ventilation include airway obstruction, decreased lung compliance, brain disorders such as delirium and anxiety, impaired cardiac function, weakness of the diaphragm and other respiratory muscles, as well as metabolic and endocrine disorders such as adrenal insufficiency, hypothyroidism, and malnutrition. (11)

Respiratory muscle weakness in critically ill patients is associated with increased duration of ventilator use and increased patient return to the ICU. (12) In this study, the average DTF that is easy to wean off was 23.13±13.47% and for difficult cases, it was 22.7±17.67%. This was similar to the study of Samantha et al who found that the easy group had a higher DTF (DTF=29%) than the difficult group (DTF=21%). (2) Based on a study conducted by Pirompanich et al, it was found that the higher the DTF, the easier it was to wean mechanical ventilation. (4) In this study, 8 samples had DTF values with a limit of 30%, 6 of which were easy for ventilation weaning. In addition, in 22 samples with lower DTF, the majority (n=14) found it was difficult to do mechanical ventilation weaning.

Furthermore, data analysis was carried out and it was found that there was no statistical significance between the factor of the DTF and the ease of weaning of mechanical ventilation. It could be caused by various factors, ranging from the small number of samples (n=30) and other bias factors. Different re-

sults were obtained in a study conducted by Samanta et al who found that the DTF could be a statistically significant predictor of ease of weaning from mechanical ventilation ($p<0.001$). In the study conducted by Samanta et al, which obtained statistically significant results, the study used a sample of 64 subjects. (2)

CRP is an inflammatory marker that is known to increase when the body is under stress. (13) In this study, the average CRP value for cases of weaning from easy mechanical ventilation was 99.91±87.98 mg/dl, and the average CRP value for cases of difficult weaning from mechanical ventilation was 139.81±115.67 mg/dl. In bivariate and multivariate analysis, the effect of CRP on the ease of weaning from mechanical ventilation, the results were not statistically significant ($p=0.724$ and $p=0.874$). This result is different from the study of Luo et al which showed that the effect of CRP value on the ease of weaning from mechanical ventilation was statistically significant with $p=0.027$. This difference might be due to the larger sample of Luo's study ($n=269$). (14) However, our study was in line with the study of Forgriani et al that found the effect of CRP values on the ease of weaning from mechanical ventilation was not statistically significant ($p=0.12$). (15)

Positive cumulative fluid balance is associated with increased mortality in critically ill patients. (9) In this study, the mean cumulative fluid balance for easy weaning from mechanical ventilation was 733.39±680.42 ml and 649.3±1205.19 ml in difficult weaning from mechanical ventilation. The study of Upadya et al found a negative cumulative fluid balance in patients with successful mechanical ventilation weaning (median -633 vs +920 ml). (16) In this study, as many as 46.6% were postoperative patients who were likely to receive more fluid therapy in the operating room and the first day of ICU treatment. As many as 23.3% of patients were postoperative patients who had good clinical preoperative and short ICU length of stay, but the fluids were given in the operating room and the first day of ICU treatment had not been removed, so that the cumulative fluid balance was still positive. Nevertheless, the patient could be weaned from mechanical ventilation. In contrast to the study of Upadya et al, where the patient sample was more homogeneous with a total of 87 patients where the most samples were mechanically ventilated patients requiring airway protection (37%) and pneumonia patients (31%), (16) in our study, the number of research samples was limited so that heterogeneous results were obtained with a large standard deviation.

The mean RSBI value for cases of easy weaning from mechanical ventilation was 75.43±25.82 breaths/minute/l and the average RSBI value for cases of difficult weaning from mechanical ventilation was 98.23±40.99 breaths/minute/l. The mean value in cases of difficult weaning form mechanical ventilation was close to the cutoff value of 105, which was a predictor of weaning failure. (17) The study of Abbas et al in chronic obstructive pulmonary disease (COPD) patients obtained a mean RSBI value of 68.43±13.59 breaths/min/l in easy mechanical ventilation weaning and 76.15±13.10 breaths/minute/l in difficult weaning cases. (18) In our study, the p-value was 0.116 so it is not statistically significant. This was also found in the study of Abbas et al, which showed that the RSBI difference was not statistically significant ($p=0.082$). (18) The predictive value of the RSBI is not a good predictor in patients with major problems related to increased secretions and impaired airway protection. In addition, the initial RSBI measurement is not accurate in predicting the success of weaning in patients with COPD. (19)

Study limitations

This study has limitations, including the number of sample populations that were limited and varied. Another limitation is that the study was conducted during the COVID-19 pandemic, where this new disease might cause physical changes in the lungs. The short length of observation time may also explain why we found insignificant results in some study variables. Further studies with larger samples and research centers are still needed to analyze the accuracy of DTF, CRP, cumulative fluid balance, and RSBI in predicting the ease of weaning from mechanical ventilation in critical patients in the ICU.

Conclusions

DTF, CRP value, cumulative fluid balance, and RSBI cannot be used together to predict the ease of weaning from mechanical ventilation in this study.

Conflict of interest

All authors declare that there is no conflict of interest.

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None.

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