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Role of cumulative fluid balance, intraabdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio on the difficulty of the weaning process from mechanical ventilation in critically ill patients

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Abstract

***Objective*: The weaning process of mechanical ventilation in critically ill patients could face resistance from multifactorial causes and about 30% become difficult in the weaning process, which lead to many other complications. As the consequences of Surviving Sepsis Campaign Guidelines for septic shock patients, there would be fluid accumulation in intensive care unit (ICU) patients resulting in positive cumulative fluid balance. Movement of the diaphragm muscle as the main respiratory muscle could be restricted by high intraabdominal pressure. The measurement of intraabdominal pressure has not been a routine examination in ICU and so diaphragm movement and excursion. Ongoing infection also contributed to the difficulty in the weaning process of mechanical ventilation. The aim of this study was to find whether the weaning process of mechanical ventilation was influenced by cumulative fluid balance, intraabdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio.**

***Design*: This study was an analytic observational study with a prospective cohort design.**

***Setting*: Intensive Care Unit of Cipto Mangunkusumo National General Hospital Jakarta, Indonesia.**

***Patients and participants*: The subjects of this study were 30 mechanically ventilated patients in the ICU from November to December 2020.**

***Interventions*: Cumulative fluid balance, intra-abdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio were initially documented on the first 24 hours on mechanical ventilation and be compared when the ventilator mode was pressure support ≤8 or using T-piece until 7 days maximum or until day 7 if the patients could not be weaned.**

***Measurements and results*: Demographics and clinical characteristics were evaluated. The relationship between cumulative fluid balance and the weaning process from mechanical ventilation was not significant (p=0.243; odds ratio [OR] 1.257; confidence interval [CI] 95% 0.787-2.007). The relationship between intraabdominal pressure and the weaning process from mechanical ventilation was not significant (p=0.550; OR 1.14; CI 95% 0.691-1.891). The relationship between diaphragm excursion and the weaning process from mechanical ventilation was not significant (p=0.053; OR 1.4; CI 95% 0.321-6.109). The relationship between neutrophil-lymphocyte ratio and the weaning process from mechanical ventilation was not significant (p=0.259; OR 1.33; CI 95% 0.586-3.03).**

***Conclusion*: Cumulative fluid balance, intraabdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio did not affect the difficulty in the weaning process from mechanical ventilation in critically ill patients in this study.**

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Key words: Cumulative fluid balance, intraabdominal pressure, diaphragm excursion, neutrophil-lymphocyte ratio, weaning, mechanical ventilation.

Introduction

The weaning process from mechanical ventilation is a shifting process from mechanical ventilation support to spontaneous breathing that is done quickly or gradually. (1) Reduction of mechanical ventilation usually does not need a special technique or strategy, however, 20-30% of patients can experience difficulty in the weaning process of mechanical ventilation. (2) Difficult in weaning is defined if patients can not be weaned in 7 days or patients need 3 times spontaneous breathing trial (SBT). Weaning failure is defined if in 48 hours after extubation there is a need for reintubation. There are around 20-30% of post-extubated patients will need reintubation. (3) Delayed weaning will lead to complications such as ventilator-induced lung injury (VILI), ventilator-associated pneumonia (VAP), and ventilator-induced diaphragm dysfunction (VIDD). (4)

One of the sepsis treatments in the Surviving Sepsis Campaign Guidelines is rapid fluid resuscitation with 30 ml/kg body weight (BW) crystalloid in 1 hour for septic shock cases or if blood lactate ≥4 mmol/l. This will lead to fluid overload in patients. In the study by Ghosh, it was found that positive fluid balance was a significant factor in group subject with difficulty in weaning from mechanical ventilation. (5)

As the main respiratory muscle, diaphragm movement can be affected by the increase in intrabdominal pressure. The increase in intraabdominal pressure restricts the movement of the diaphragm and lung function in the respiratory system. High intraabdominal pressure would push the diaphragm into the thoracal space and will compress the lung that results in difficulty in the breathing process.

From a previous study, the main cause of difficulty in the weaning process was diaphragm dysfunction. The diaphragm is the main inspiration respiratory muscle of the spontaneous breathing process. The movement of the diaphragm can be evaluated by several techniques. The easy one is by using ultrasonography because it is safe, non-invasive, has no radiation, and can be done bedside.

Bacteremia is related to 30% of inpatient mortality. Early diagnosis of bacteremia is important for specific therapy and increases the prognosis of patients, especially in emergency cases. (6) Neutrophil-lymphocyte ratio (NLR) from blood samples is related and can predict the process of systemic inflammation and stress. It is also cheap and accessible that made it a routine examination in severely ill patients. NLR is a significant factor in the severity and mortality of illness.

Researchers found that there were several factors that contributed to the difficulty in the weaning process from mechanical ventilation and it is important to evaluate some of them such as cumulative fluid balance, intraabdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio.

Materials and methods

This analytical observational study is using a cohort prospective study design. The subjects were adult mechanically ventilated intensive care unit (ICU) patients. Cumulative fluid balance, intraabdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio were initially documented on the first 24 hours on mechanical ventilation and then compared with ones when ventilator mode was pressure support ≤8 or using T-piece until maximum 7 days or until day 7 if the patients could not be weaned. The study protocol was approved by the institutional review board and all participants were provided the written informed consent. The aim of this study was to find whether the weaning process of mechanical ventilation was influenced by cumulative fluid balance, intraabdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio.

Patient population

The subjects of this study were critically ill patients in the ICU who were mechanically ventilated from November to December 2020. The inclusion criteria were age >18 years old, partial pressure of oxygen (PaO_2)/the fraction of inspired oxygen (FiO_2) 250-350, subjects and the family/guardian of the subjects agreed in participating in this study, and the time patients participated was when they were still in the first 24 hours in the ICU. The exclusion criteria were pregnant, had stoma in the abdomen, had tracheostomy procedure since the beginning of admission, >24 hours intubated patients outside the ICU, history of neuromuscular disease, cervical and thoracal trauma patients, has been >24 hours extubated, had a water-sealed drainage tube, and patients with chronic renal failure. The total number of subjects in this study who met inclusion criteria was 30 subjects.

Definitions

Weaning is a process of discontinuation usage of mechanical ventilation breathing to spontaneous breathing. Weaning starts when a spontaneous breathing trial was done, by T-piece or by low-level pressure support. The weaning process is classified into 3 groups, which are: (7)

1. Easy cases are when the patient has successful extubation and does not have difficulty since the beginning of the weaning process until the extubation.
2. Difficult cases are when the patients fail to wean from mechanical ventilation and need 3 spontaneous breathing trials or need 7 days from the first spontaneous breathing trial until they succeed weaning from mechanical ventilation.
3. Prolonged cases are when patients fail more than 3 times in weaning from mechanical ventilation or need more than 7 days from the first spontaneous breathing trial to succeed.

Methods

Data of cumulative fluid balance, intraabdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio were collected twice from 30 subjects who were supported by mechanical ventilation. Cumulative fluid balance, intraabdominal pressure, diaphragm excursion, and neutrophil-lymphocyte ratio were initially documented at the first 24 hours on mechanical ventilation and then when the ventilator mode was pressure support ≤8 or using T-piece until a maximum of 7 days or until day 7 if they could not be weaned.

Cumulative fluid balance (in milliliters) was achieved by calculating the accumulation of 24 hours daily fluid balance. The equation for cumulative fluid balance is the difference between intake fluid (intravenous fluid, intravenous drugs, diet per nasogastric tube) and the output (urine, fluid from nasogastric tube, insensible water loss, fever) in 24 hours.

Intraabdominal pressure data was achieved by calculating the pressure of intravesical from urine catheter using Kron method: (8)

1. Make zero point for examination based on pubic symphysis using water transducer on central venous pressure (CVP) device
2. Urinary catheter and urine bag tube was cleaned using chlorhexidine 2.5% and then detached
3. Empty the urinary bladder using a 50 ml syringe
4. Fill the urinary bladder with 50 ml sterile NaCl 0.9% using a 50 ml sterile syringe with sterile gloves
5. Connect urinary catheter with new intravenous (IV)-line tube that has been connected to CVP device
6. Wait for 1 minute to get the balance
7. Watch for urine undulation on IV-line tube
8. Record the height of undulation (in centimeters) at the end of expiration vertically from zero point using CVP device
9. Convert the results into mmHg (1 mmHg=1.36 cmH2O)

Diaphragm excursion is a movement of diaphragm muscle during the breathing process and can be examined by ultrasonography in M-mode by only one examiner. The steps in examining the excursion diaphragms are: (9)

1. Lay down the patients
2. Use 3.5-5 MHz probe for ultrasonography
3. Apply gel to clear the air distance between the transducer and the patients' skin so all the sound waves from the transducer are transmitted well and made the movement of the transducer easier during the examination
4. Place probe below the lowest right costa that lined with axillary anterior line
5. Aim transducer to the medial, cranial, and dorsal in visualizing 1/3 posterior right diaphragm, approaching 5 cm lateral to the for a-men of the inferior cava vein
6. Record the excursion of the diaphragm in millimeters

The neutrophil-lymphocyte ratio is calculated by dividing neutrophil counts with lymphocyte counts from the results of complete blood cell counts. (10)

Statistical analysis

Data were calculated and processed with SPSS (Statistical Package for the Social Sciences) software.

All data were recorded and saved in electronic storage to be coded before being analyzed. A normality test was performed to decide the statistical test that fit the data. Descriptive analyses were performed, and the results were presented in narration, table, or picture. For numeric data, the result was presented in mean±standard deviation (SD) or median (minimum-maximum) depending on the data.

The changes in cumulative balance fluid, intraabdominal pressure, excursion diaphragm, the neutrophil-lymphocyte ratio were presented as mean and ratio based on the first examination on the first day.

In order to know the relationship between independent variables and dependent variables, a comparative bivariate analysis was performed. Analysis for comparative categorical data was by the chi-square test or the alternative test. Analysis for comparative unpaired numeric data was unpaired t-test if the data variation was normal or Mann-Whitney test if the data variation was abnormal.

Categorical bivariate analysis (logistic regression test) was performed to know the relationship between all independent variables (cumulative fluid balance, intraabdominal pressure, excursion diaphragm, neutrophil-lymphocyte ratio) and dependent variable (weaning from mechanical ventilation).

Results

Of 30 subjects, there were 14 who were easily weaned from mechanical ventilation and 16 others were difficult to be weaned from mechanical ventilation.

Based on patients' characteristics, only age that had significant results with the mean of patients who easily weaned was 37 years old and the mean of the difficult one was 50 ($p<0.05$).

Cumulative fluid balance from subjects who were easily weaned was 733.39 ml. On the other hand, the subjects with difficulty in weaning from mechanical ventilation had 649.3 ml as the mean in cumulative fluid balance.

The mean of intraabdominal pressure in the easy weaning group was 8.32 mmHg, while the difficult weaning one was 9.61 mmHg.

Subjects who were easily weaned had 13.19 mm for the mean of the diaphragm excursion test and the other group had smaller results which were 12.35 mm.

The mean neutrophil-lymphocyte ratio for the easy weaning group was 11.12%, meanwhile, the difficult weaning group had 18.63%.

Discussion

Invasive mechanical ventilation could lead to hypotension due to a decrease in venous return which is treated by fluid resuscitation. Fluid balance is one of the treatments in critically ill patients which has a role in the weaning process of mechanical ventilation. (11) In this study, the subjects in the group who were easily to wean from the ventilator had a mean cumulative fluid balance of 733.39 ml, while the difficult weaned group had 649.3 ml. The study by Ghosh (5) with 201 samples has shown that the group who was difficult to wean had a higher cumulative fluid balance compared to the easy one (median 4336.5 ml vs 2752 ml). In our study, the number of samples was 30. The smaller samples could interfere with the result of the cumulative fluid balance mean in the study. During the ICU hospitalization, there were efforts to avoid the cumulative fluid balance being highly positive. There was also no available fluid balance recording before the patients went to the ICU which could make bias in this study.

The cumulative fluid balance and the weaning process of mechanical ventilation has shown insignificant results statistically ($p=0.243$; OR 1.25). Antonio (12) in his study showed there was no statistical difference ($p=0.52$) in 48 hours cumulative fluid balance before spontaneous breathing trial both in the succeeding group and failed group with a total of 250 subjects. Statistically insignificant results in our study do not mean that fluid balance is not an important factor because the weaning process of mechanical ventilation is a multifactorial process.

In our study, the difficult weaned group had a higher mean of intraabdominal pressure (9.61±3.29 mmHg) compared to the easy weaned one (8.32 mmHg), but when it was analyzed with bivariate analysis, the difference was not statistically significant ($p=0.55$; OR 1,14). Analysis with multivariate also had the same insignificant results ($p=0.170$). This was similar to a study by Elghonemi (13) with 124 samples. Elghonemi examined the intraabdominal pressure 5 times in 1 hour before the weaning. The result was similar in the first four examinations until the fifth one that the difficult weaned group (6.79, 11.28, 10.92, 15.33, 14.55 mmHg, respectively) had higher intraabdominal pressure than the easy weaned one (5.97, 7.27, 7.68, 7.69, 7.65 mmHg, respectively). It was because the increase in intraabdominal pressure was related to the respiratory function by decreasing the lung volume and compliance. Therefore, critically ill patients in ICU with high intraabdominal pressure should be treated carefully, especially in intraabdominal hypertension cases. Intraabdominal hypertension is a condition when the intraabdominal pressure is >20 mmHg. The intraabdominal hypertension leads to multiorgan failure and higher morbidity in ICU patients. (14) A study by Murtaza (15), who studied intraabdominal hypertension and its relation with weaning outcome of ICU patients, revealed that weaning from mechanical ventilation was more difficult in the intraabdominal hypertension cases (37.9%) when compared to the normal ones (25.9%) and that was statistically significant ($p=0.008$). The difference in statistic results in ours and Murtaza's could be related to subjects' numbers. Murtaza's study had 83 subjects while we only got 30 samples which made the results insignificant statistically.

Our study also showed that the mean of diaphragm excursion in the easy weaned group was 13.19 mm. This number was higher when compared to the difficult weaned one (12.35 mm). As we know diaphragm excursion is calculated by the distance between the highest point to the lowest point of diaphragm movement. A low diaphragm excursion score means less movement of the diaphragm that contributes to respiratory function. (16) The bivariate analysis showed that diaphragm excursion was statistically significant related to the weaning process of mechanical ventilation (p=0.013; OR=1.4). The data was then analyzed with multivariate analysis to know the influence of diaphragm excursion without any other independent variables in the study. The results from the multivariate analysis showed that diaphragm excursion was not related statistically with the difficulty in weaning from mechanical ventilation (p=0.053). The results were similar to the study by Xue (17) who got the mean diaphragm excursion in the easy weaned group (0.74±0.75 mm) higher than the difficult weaned one (0.45±0.32 mm). The study by Xue also got that statistically diaphragm excursion was not related significantly to the weaning process (p=0.23). A study by Theerawit (18) on 62 subjects also got similar results that diaphragm excursion was not statistically significant with weaning from mechanical ventilation (p=0.87). Although not statistically significant, Theerawit's study found that mean diaphragm excursion was higher both in left and right diaphragm of the easy weaned subjects (right 13.7±5.6 mm, left 13.5±5.3 mm) compared to the difficult weaned one (right 12.4±10 mm, left 12.8±9.6 mm). Insignificant results in Xue, Theerawit, and our studies came from a small sample size. One examiner was recruited in the study to overcome bias such as examiner bias in recording the diaphragm excursion data. Small sample size becomes a problem because in a small sample size study it is hard to homogenize the subjects and make the bias factor from different subject characteristics will influence the results including the insignificant results.

The result for mean NLR for the easy weaned group in this study was 11.12%. This was lower compared to mean NLR in the difficult weaned group (18.63%). NLR represents the inflammation process in the body. Therefore, a high NLR can give information about high inflammation in the body and lead to difficulty in the weaning process. Bivariate and multivariate analyses were done and the results were statistically insignificant both in bivariate (p=0.259; OR=1.33) and multivariate (p=0.262). A study by Luo (10) had a result that median NLR in the weaning failure group (median 15%, range 10-31%) was higher compared to the easy weaned one (median 10%, range 6-18%), and this was statistically significant (p<0.001). Savluk (19) got a similar result that mean NLR in the group who had to succeed in weaning was lower (2.08±0.77%) compared to the failed one (4.79±2.83%), and the result was statistically significant (p=0.001). The difference between our study and the other two studies was that we had a small sample size. With only 30 subjects, it was more difficult for us to homogenize the subjects. The difference in sample size would make bias some factors that led the results statistically insignificant. The study by Luo used 269 subjects and in Savluk's study, there were 99 subjects. Compared to our study with only 30 subjects, it would make different results.

Study limitations

The sampling period in this study happened during the COVID-19 pandemic that made limitations in the sample size numbers and could not meet the equation for study sample size. The limitation was also due to the study needing to be done carefully with social distancing in the pandemic era. The subjects in this study also were not having the same severity in their illness which made them not homogeny.

Conflict of interest

All authors declare that there is no conflict of interest.

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None.

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