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Ultrasound assessment of diaphragm thickness in mechanically ventilated patients suffering from obstructive pulmonary disease and its relationship with outcomes of mechanical ventilation and mechanical parameters of lungs

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***Abstract*---**Introduction: Successful weaning from the ventilator depends on several factors including muscular, cardiac, respiratory, and metabolic strength. Acquired weakness of diaphragm muscle caused by mechanical ventilation is one of the reasons for failure to wean patients from ventilators. Meanwhile, it has been shown that the thickening fraction (TF) and ultrasound of the diaphragm are proper non-invasive indicators for making decisions on weaning patients from the ventilator. Methodology: Mechanically ventilated patients with chronic obstructive pulmonary disease who had been admitted to pulmonary intensive care units during a period of one year were selected for this study. Through statistical consultation, sixty patients were examined for the study. There was no gender difference in the number of patients. After selecting the patients, all of them underwent

a B-mode ultrasound with a linear probe of 9 to 12 megahertz on the second day after intubation in the supine position. The thickness of the diaphragm in all patients was measured at the end of exhalation and in the space between the 9th and 10th ribs, between the anterior and middle axillary lines, and the results were compared between the individuals in two ways: successful and unsuccessful weaning. Findings: The difference in diaphragmatic thickness fraction (DTF) between the successful and unsuccessful weaning groups indicated the median of 32.65% and the interquartile range of 24.50% to 34.25% in the successful weaning group and the median of 17.50% and the interquartile range of 13% to 25% in the unsuccessful weaning group. Also, based on the analysis of the results, it was found that the patients with successful weaning had significantly better condition in the duration of ventilation (P=0.001), tidal volume (P=0.049), Cdyn (P=0.005), Cstat (P=0.019), and APACHE II (P=0.009). Conclusion: Diaphragm ultrasound is an appropriate method for predicting weaning time and weaning success in patients under mechanical ventilation.

***Keywords*---**ultrasound, weaning, intubation, extubation.

Introduction

Mechanical ventilation is one of the most basic support measures in providing treatments and special care to patients in ICU. Prolonging the duration of mechanical ventilation increases the length of the hospitalization of the patient in ICU, which can lead to a shortage of ICU beds and an increase in health care costs. Accordingly, the process of weaning the eligible patient from the mechanical ventilator should be started as soon as possible (1).

According to the results of a study, weaning the patient from mechanical ventilator is one of the most important stages of treating mechanically ventilated patients (2). Determining the time to start weaning the patients from the mechanical ventilator is of particular importance. Hence, there are several indicators to predict the appropriate time for weaning (3). These indicators cause a more accurate prognosis and better monitoring of the patient, and can also be effective in preventing disabilities, reducing the length of stay in the ICU, and improving the efficiency of health care systems. Rapid and Shallow Breathing Index (RSBI), Integrated Weaning Index (IWI), Obstructive Pressure Index, Negative Inspiratory Force (NIF), CROP Index, as well as other uncommon indexes such as Jabour weaning index, Huaringa weaning index, DTF, Time Inspiratory Effort (TIE), CORE index, Epstein weaning index, non-pulmonary weaning index, albumin and blood protein composition and Date - Time Constant (DTC) are among the common indicators that are used for weaning patients from mechanical ventilator (4). Determining reliable indicators in predicting the appropriate time and consequences of weaning the patient from mechanical ventilator has always been one of the challenges of ICU medical staff (5). Furthermore, lack of knowledge about predictive indicators of successful weaning is one of the reasons for the delay in the weaning process or its failure. Therefore,

it is necessary to provide reliable predictive indicators for evaluating the patient's readiness and determining the exact time to start the process of weaning the patient (6).

B-mode and M-mode Ultrasounds are the most chosen methods to evaluate the amount of movement and thickness, and their normal values are determined in a standardized way (15). This measurement method had initially been used in premature neonates and then in ICU. Chronic obstructive pulmonary disease (COPD) is mainly defined on the basis of air trapping and airway obstruction (7). Studies on inspiratory muscle weakness in these patients are mainly focused on the diaphragm because it is the only main muscle of the inhalation (8). In this study, the thickness of the diaphragm muscle was measured by ultrasound in COPD patients, and then its relationship with the functional, clinical, and mechanical parameters of the ventilator was investigated. The purpose of this investigation includes the following: 1. The relationship between diaphragm thickness (Tdi) and disease progression. 2. The relationship between the thickness of the diaphragm and the minimum expiratory volume in the first second to start weaning. 3- The outcome of weaning is based on the Tdi (9).

Recently, pulmonary and diaphragmatic ultrasound methods have been introduced which assess pulmonary airway patterns and diaphragm function. A systematic study was conducted to measure the effects of diaphragmatic ultrasound on the weaning time of patients from a mechanical ventilator. In this study, the results of 17 case-control studies were conducted through the participation of 1250 patients. All studies were extracted from the PubMed database and had good quality according to STROBE. Finally, the results indicated that pulmonary and diaphragmatic ultrasound might help predict the outcome of weaning patients from ventilators, yet its accuracy may vary depending on the condition of the underlying diseases and the duration of the patient's ventilation. Namely, this index should be applied in the first days of setting up the patients to the ventilator, thus the best results can be achieved in determining the proper time for weaning the patients (10). A study was conducted to evaluate the diaphragm function (thickness and excursion) which was measured by ultrasound as a predictor of the outcome of intubation and weaning of ventilated patients. The results indicated that diaphragmatic ultrasound is a promising tool for predicting the outcome of weaning mechanically ventilated patients. According to the results of this study, the researchers suggested using this method for the early weaning of patients (11). It seems that using ultrasound to check the condition of the diaphragm has been successful in recent studies. According to the results of several studies, diaphragmatic ultrasound is a reliable, non-invasive, and convenient method for predicting the success of weaning patients from a mechanical ventilator. Incorporating diaphragmatic ultrasound into current weaning protocols for ventilated patients improves the decisions on the optimal weaning time and has led to promising results, avoiding the harmful effects of prolonged or premature intubation. Therefore, it seems that using diaphragmatic ultrasound can be effective in weaning diseases, which we discuss in this study.

Materials and Method

The population of this cross-sectional descriptive study was the patients suffering from COPD who had been admitted to the pulmonary ICU of Imam Reza Hospital (affiliated with Tabriz University of Medical Sciences) in 2021.
According to the available sampling method, based on previous studies, using the Power and Sample Size software, and considering the alpha error of 5% and the power of 80%, a total number of 60 patients were determined as the sample size. In this study, the gender difference of patients was remarkably not observed in the number of patients. The inclusion and exclusion criteria were applied as follows:

Inclusion criteria of the study

1. Patients suffering from obstructive pulmonary disease
2. Patients who use a mechanical ventilator
3. Patients whose duration of mechanical ventilation was longer than 48 hours
4. Patients with stable hemodynamic status
5. Hemoglobin more than 7

Exclusion criteria of the study

1. Having a record of cerebrovascular accidents
2. Cardiothoracic surgery or chest deformity
3. BMI greater than 45

This study was approved by the Research Council of Tabriz University of Medical Sciences and Faculty of Medicine under the ethical code (IR.TBZMED.REC.1400.181). The process of confirming the COPD diagnosis included a medical history and clinical examination, the previous medical record including spirometry (values of FEV1, FVC, FEV1/FVC), CO_2 retention, and a history of risk factors of this disease. Finally, all these cases were recorded by the underlying factor aggravating the disease or causing respiratory failure. After selecting the patients on the first day, all of them were subjected to B-mode ultrasound with a linear probe of 9 to 12 megahertz in the supine position. The Tdi of all patients was measured at the end of exhalation and in the space between the 9^{th} and 10^{th} ribs between the anterior and middle axillary lines. In this study, a thickness below 2 mm in males and 1.9 mm in females was considered abnormal. The ultrasound of all patients was performed immediately two days after admission to the ICU and the start of intubation, and no fees were charged to the patients.

The statistical analysis was performed with SPSS V. 21 after data collection. The Kolmogorov-Smirnov method was used to examine the normal distribution of descriptive statistics. The Demographic variables were analyzed by descriptive statistical methods and the results were presented as mean ± standard deviation and percentage (frequency). Pearson chi-square and non-independent t-test were used to compare qualitative data and quantitative variables, respectively. The p-value was considered to be less than 0.05 to evaluate the statistically significant relationship between the variables.

Results

Among all the participants, 28 were men and the rest were women. The mean ± standard deviation of the age of the participants in the study was 59.61 ± 5.26 years. The (controlled) hypertension was the most common co-morbidity in these patients with a number of 33 individuals. During the study, the weaning of 35 individuals was successful and 25 individuals failed in weaning. Based on the success and failure of the weaning, the patients were divided into two groups and the measured parameters were compared between them.

The difference in diaphragmatic thickness fraction between the successful and unsuccessful weaning groups indicates the median of 32.65% and the interquartile range of 24.50% to 34.25% in the successful weaning group and the median of 17.50% and the interquartile range of 13% to 25% in the unsuccessful weaning group. According to the results, the Tdi of the patients of the successful weaning group was significantly higher than that of the unsuccessful weaning group (Figure 1).

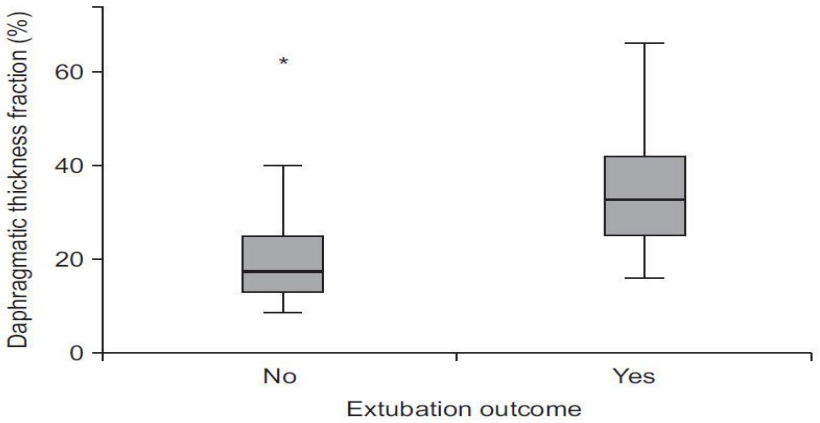

Figure 1: Difference in Tdi of patients with successful and unsuccessful weaning

The information on the two groups based on success in weaning patients is presented in the below table. According to the results, the duration of ventilation (P=0.001), tidal volume (P=0.049), Cdyn (P=0.005), Cstat (P=0.019), and APACHE II (P=0.009) in patients with successful weaning had significantly better condition. The results of the variables of basic parameters and pulmonary function status are presented in Table No. 1.

Table 1. Comparison of basic parameters and pulmonary function status between the two groups of the study

Variables	Study groups (60 Patients)		P value
	Successful weaning	Unsuccessful weaning	
Age (Year)	61.19±6.03	55.59±5.44	0.325
Duration of ventilation (Day)	5.24±1.11	9.14±1.39	0.001

Breathing rate (per minute)	19.02±3.26	23.42±49.36	0.125
Tidal current (cc)	457.96±54.96	395.75±4.34	0.049
RSBI (liters per minute)	42.59±6.65	47.11±7.26	0.054
P/F ratio	179.22±12.36	175.15±11.95	0.362
Cdyn	20.02±3.19	14.51±2.59	0.005
Cstat	33.85±6.19	24.75±3.89	0.019
APACHE II	10.33±1.86	19.86±2.03	0.009

Examining the results of diaphragmatic ultrasound between the two groups of patients with successful and unsuccessful weaning showed that in all the investigated indicators, the status of the diaphragm in patients with successful weaning had significantly better results. The results of the ultrasound status of the diaphragm muscle are presented in Table 4-2.

Table 2. Ultrasound comparison of the diaphragm muscle between the two groups of the study

Variables	Study groups (60 Patients)		P value
	Successful weaning	Unsuccessful weaning	
Insp DT (cm)	0.41±0.14	0.02±0.08	0.002
Exp DT (cm)	0.24±0.09	0.30±0.11	0.003
DE (cm)	2.02±0.19	1.29±0.09	0.001
DTF(%)	35.75±2.59	24.81±1.89	0.008

The ROC curve was used to evaluate the accuracy of diaphragm movement and DTF in predicting the weaning result. A diaphragmatic cut-off value of more than 1.25 cm was associated with successful extubation (97% sensitivity and 82% specificity). This curve predicts a DTF of more than 21.5% in successful extubation with a sensitivity of 91.2% and a specificity of 60.7%. The results of the ROC curve are presented in Figure 2.

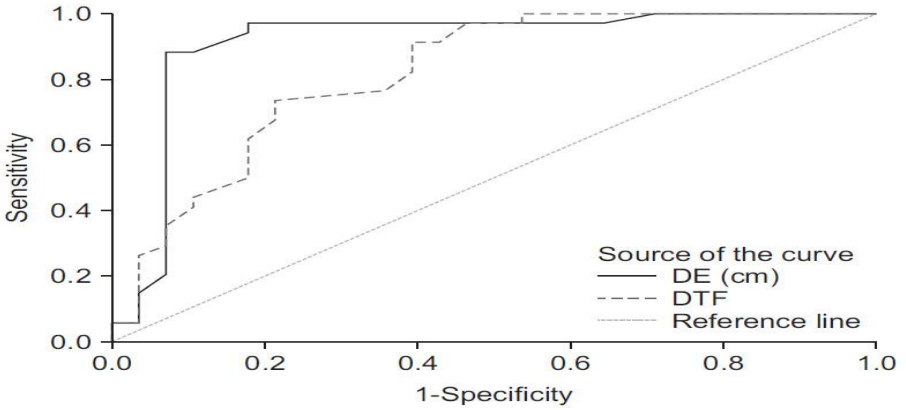

Figure 2: ROC curve results for predicting patients' weaning

Discussion

The results of this study indicated that:

1. Diaphragmatic ultrasound can be a useful index in predicting the success of weaning patients from mechanical ventilator.
2. The Tdi has a direct and significant relationship with successful weaning, i.e., the greater the thickness of the diaphragm, the more likely the patients will be weaned from the ventilator.
3. An increase in the Tdi leads to an increase in the state of pulmonary function in mechanically ventilated patients.
4. By knowing the thickness of the diaphragm through ultrasound, it will be possible to implement the planning of weaning patients.
5. The high thickness of the diaphragm leads to the improvement of the pulmonary function of mechanically ventilated patients.
6. The sensitivity of diaphragmatic ultrasound in predicting successful weaning of patients from mechanical ventilator is 97%.
7. The increase in the thickness of the diaphragm has an opposite relationship with the progression of the disease.

Accordingly, using ultrasound as a practical tool is well established when performed by a radiologist for the evaluation of cardiopulmonary failure. Considering that ultrasound is an evolving part of critical care medicine, we managed to achieve the positive effects of it in this study. One of them is its potential application in the process of weaning the patient from mechanical ventilator (12). Since the protocol for using this tool is not yet well defined, this article reviews some of the uses of ultrasound that may be relevant to the process of weaning patients. In reviewing studies on this topic, it is important to define what leads to successful weaning of patients. Most researchers define success as when the patient is extubated within 48 hours of intubation (13). In other words, successful weaning will be achieved if the patient is completely weaned from the ventilator for 48 hours. Yet this is a bit different in patients suffering from pulmonary problems. It is very difficult to predict the weaning of these patients, and there is no proper criterion for diagnosing the appropriate weaning time because various factors play role in the successful weaning of these patients (14).
Diaphragm ultrasound allows easy visualization of hemi-diaphragm and its motions during respiratory cycles. Two different ultrasound parameters have been described to evaluate diaphragm function. The first parameter refers to the measurement of diaphragmatic motion (E) during inhalation (15). The diaphragmatic motion can be easily measured with a 3- to 5-MHz probe in either B- or M-mode or the so-called anatomical M-mode which allows the placement of the M-mode line parallel to the diaphragmatic path. The second parameter describes the Tdi during inspiration in the region of the diaphragm to the chest with at least one probe of 10 MHz using B- or M-mode (16).

In patients with spontaneous breathing, diaphragmatic motions are the result of a certain diaphragmatic contraction for a certain mechanical load (i.e. compliance of the respiratory system including abdominal compliance) (28). In patients receiving mechanical support, diaphragmatic circulation also depends on the amount of support and the level of PEEP. Actually, PEEP increases EELV. A

corresponding increase in lung volume reduces the dome of the diaphragm, which can lead to a decrease in diaphragmatic motion. Measuring the Tdi can be used as a direct indicator of diaphragm efficiency as a pressure generator, although the thickness may also be affected by lung volume in a non-linear relationship (17). Both E and TF have been shown to correlate with functional measures of diaphragmatic function (typically trans-diaphragmatic pressure measurements) in spontaneously breathing patients (18). Therefore, by knowing the thickness of the diaphragm, it is possible to help the rate of success in weaning patients from mechanical ventilator (19).

Meanwhile, the diaphragmatic dysfunction in mechanically ventilated patients is often secondary to neuromuscular disorders or non-myopathic diseases such as COPD, ICU-acquired-neuromyopathy, and/or diaphragmatic dysfunction due to the ventilator. Accordingly, most studies performed in non-cardiac surgery patients recorded E or TF on only one hemi-diaphragm (usually on the right side), which is considered as a proxy for the entire diaphragm function (20). In cardiac surgery patients, phrenic nerve injury may result in complete paralysis of one hemi-diaphragm while the other nerve is not affected. This generally does not lead to diaphragmatic dysfunction. According to the results of this study, patients who are exposed to a certain type of phrenic nerve injury need a bilateral diaphragm examination (21). Although in other settings, unilateral measurements may work well in assessing overall diaphragmatic function, initial screening for asymmetric diaphragmatic dysfunction may be appropriate (22).

Conclusion

Successful and early weaning of mechanically ventilated patients is one of the essential actions of specialist doctors in ICU. The shorter the duration of intubation and mechanical ventilation in these patients, the fewer side effects of intubation and mechanical ventilation will be. So far, no criterion has been effective for 100% of the patients. The thickness of the diaphragm muscle and its relationship with successful weaning were evaluated in this study and it was found that the diaphragmatic ultrasound and knowing the thickness of this muscle can be used as an appropriate predictor for weaning the patients from mechanical ventilator. Finally, it is noteworthy that the limitations of our research included the low sample size and the single-center nature of this study. Also, it seems that the involvement of relaxing medications was a confounding factor which was not considered in this study. It is recommended to overcome these limitations in future studies.

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