ORIGINAL ARTICLE

# Evaluation of Diaphragm dysfunction to Predict Extubation Time of Critically Ill Patients in ICU with Ultrasonography

MOHAMMAD GHASEM HANAFI[1], HASAN KIANI[2] , MAHBOOBEH RASHIDI[3]
[1]*Department of Radiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.*
[2]*Department of Radiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*
[3]*Department of Anesthesiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*
*Correspondence to Dr. Hasan Kiani, E-mail: dr.hsn.kiani@gmail.com Tel: 09131849193*

## ABSTRACT

**Background**: Diaphragm dysfunction (DD) is highly prevalent in critically ill patients and is one of the major causes of respiratory failure and prolonged time of removing patients from the mechanical ventilation. Among the various methods of evaluating diaphragm dysfunction, ultrasonography (US) is a noninvasive, rapid and accessible method in the patient's bedside.
**Aim:** To evaluate diaphragm dysfunction for predicting extubation time in critically ill patients in ICU with ultrasonography.
**Methods:** This prospective observational study was performed on critically ill patients admitted to intensive care unit under mechanical ventilation for at least 48 hours. All patients were evaluated by ultrasonography for evaluation of diaphragm dysfunction. Ultrasonography was performed using M-mode to measure diaphragm thickness and excursion 24 hours before extubation. The area under curve (AUC) of ROC was calculated to determine the ability of diaphragm ultrasonography to predict the success of extubation.
**Results:** In this study, there were 3 cases (2.83%) of extubation failure and in other cases, extubation was successful (97.17%).There was a significant positive correlation between excursion and diaphragm thickness (P <0.0001). The area under the ROC for the right and left thickness was 0.898 (95% CI: 0.824-0.948; P <0.001) and 0.975 (95% CI: 0.930-0.997; P <0.0001) and for right and left excursions was 0.841 (95% CI: 0.758-0.905; P <0.002) and 0.989 (95% CI: 0.945-1.000; P<0.0001) respectively.
**Conclusion:** The results of this study showed that both ultrasound thickness and diaphragm excursion indices are useful in evaluating diaphragm function to predict extubation success. In addition, it seems that the diaphragm excursion rate is a better indicator for predicting extubation than the diaphragm thickness in critically ill patients.
**Keywords:** Extubation, Diaphragm Dysfunction, Ultrasonography, Excursion, Thickness

## INTRODUCTION

About 40% of patients admitted to intensive care units require mechanical ventilation during their treatment[1]. Extubation is an important process in critically ill patients undergoing mechanical ventilation, and determining the appropriate timing of respiratory tract removal in critically ill patients has a specific importance[2]. Early extubation could cause respiratory failure after extubation resulting in re-intubation, and delayed implementation of this task causes respiratory blockage, tracheal stenosis or pneumonia, all of which cause poor prognosis in patients[2]. In addition, long-term mechanical ventilation impairs respiratory muscle contraction, especially the diaphragm[1].

Extubation failure is defined as requiring the mechanical ventilation within 48 hours after Extubation[3] and occurs in 10 to 30% of patients that is associated with poor prognosis and clinical outcome[4]. Therefore, appropriate extubation and attention to the factors that influence and predict the success of ventilator separation are critical for improving outcomes in critically ill patients[5].

One of the main causes of failure in Extubation is the diaphragm dysfunction[5]. The diaphragm is the primary respiratory muscle that plays a role in spontaneous respiration. Therefore, assessment of its dysfunction may play a central role in the attempt for Extubation[2]. Diaphragm dysfunction is common and usually severe in critically ill patients undergoing mechanical ventilation in the ICU[6]. This disorder causes increased ICU days, delayed ventilator removal time, increased treatment costs, and increased morbidity and mortality[3,7]. Therefore, evaluation of diaphragm dysfunction is essential in the management of critically ill patients and can help to predict Extubation time.

There are several ways to evaluate diaphragm dysfunction, including fluoroscopy, electrical or magnetic stimulation of the phrenic nerve, and trans-diaphragmatic pressure measurement. All of these methods have serious limitations, for example, radiation, high cost, difficulty in performing, being aggressive and uncomfortable; and most importantly, they are difficult to perform on the patient's bedside[8,9].

Ultrasonography is currently considered for its non-invasive nature, lack of radiation, feasibility in the patient's bedside repeatability and accuracy for evaluating diaphragm function[2,3]. However, ultrasonography is not routinely used in the diaphragm evaluation[8]. There are two ultrasound techniques to evaluate diaphragm function: one is to assess diaphragm excursion and the other is to evaluate diaphragm muscle thickness during spontaneous breathing[2,10,11], and by evaluating these parameters, the extubation success can be predicted[2,12,13]. Diaphragm excursion measures the distance the diaphragm is able to move during the respiratory cycle[12,14]. The diaphragm thickness measured at the end of inhalation is associated with maximal respiratory pressure[11]. Therefore, the use of diaphragm ultrasound in critically ill patients admitted to intensive care units can be of great value for evaluating diaphragm dysfunction[8,10,15].

In the past decade, most studies have focused on evaluating the cause of diaphragm dysfunction and the underlying mechanisms of dysfunction and respiratory muscle atrophy in critically ill patients. However, the methods for evaluating and monitoring this disorder remain controversial. Few studies have also reported the use of M-mode ultrasound to diagnose diaphragm dysfunction and predict extubation time in patients undergoing mechanical ventilation. The aim of this study was to evaluate diaphragm dysfunction for predicting extubation time in critically ill patients in ICU using ultrasonography.

## METHOD

The present study is a prospective observational study that was performed between January and May 2019 on critically ill patients admitted to intensive care unit of Imam Khomeini and Golestan hospitals in Ahvaz. After obtaining permission from Ahvaz Jundishapur University of Medical Sciences -School of Medicine and the Code of Medical Ethics (IR.AJUMS.REC.1398.168), 122 patients with above 18 years of age admitted to the ICU who underwent mechanical ventilation for at least 48 hours were included in the study consecutively by non-random sampling. Prior to entering the study, patients' family informed consent was obtained and written consent was obtained for ultrasound and participation in the study. Patients with neuromuscular disease (myasthenia gravis, Guillain-Barre syndrome and amyotrophic lateral sclerosis (ALS), previous diaphragmatic paralysis, cervical injury, pregnant patients, pneumothorax or mediastinal emphysema, as well as poor echogenitia in the ultrasound) or those who could not withstand ultrasonography were excluded[2,5]. Finally, 16 patients due to poor image quality due to edema, hemiplegia, or diaphragm paralysis were excluded and the final sample size was 106.

**Patient evaluation:** Initially, baseline information of eligible patients, including age, gender and number of days they underwent ventilation were recorded in the data collection checklist. The following conditions were considered for extubation: 30 to 120 minutes spontaneous breathing, spontaneous breathing tolerance, respiratory rate less than 35, heart rate less than 140, heart rate variations below 20%, oxygen saturation above 90%, blood pressure between 80 and 180mmHg[2].

All patients underwent diaphragm ultrasonography 24 hours prior to extubation.

In this study, the success of extubation was defined as the need for no mechanical ventilation or non-invasive ventilation over 48 hours. Extubation failure was also defined as the need for mechanical or noninvasive ventilation within 48 hours after extubation or the need for tracheostomy[2].

**Diaphragm ultrasonography:** Av experienced radiologist performed ultrasonography by a…device to determine the thickness and motion of the diaphragm. Two acoustic windows were used in the ultrasonography to examine the diaphragm: 1- Between 8 and 10 intercostal space in the middle or anterior axillary line and half to 2 cm below the costofrenic sinus using a high frequency linear probe (≥ 10 MHz). In this method the thickness of the diaphragm was measured at the rest and deep inhalation states with M mode. Using the subcostal space between the anterior axillary and midclavicular lines, using a cardiac or ventricular probe (2 - 5 MHz) and using the liver and spleen as the acoustic window. In this method, the respiratory excursion was measured with M mode[8].

**Statistical analysis:** SPSS version 22 and Medcalc software programs were used for statistical analysis. Data normality was analyzed using Kolmogorov-Smirnov test. Non-parametric tests were used for data analysis due to lack of normal distribution of data. Mann-Whitney, Chi-square and Spearman correlation coefficients were used for data analysis. The P-value of less than 0.05 was considered as the level of significance in the tests. The ROC and the area under curve (AUC) were used to investigate the predictive power of the variables. Moreover, the appropriate cut-off point for the variables was calculated based on sensitivity and specificity.

## RESULTS

In this study, 66 males (62.3%) and 40 females (37.7%) with mean age of 51.47±21.6131 years (range 18-94 years) were included. The mean duration of mechanical ventilation was 4.8±3.1 (3-9 days). In this study, three cases (2.83%) had extubation failure and in other cases, extubation was successful (97.17%). All three cases of extubation failure were due to respiratory failure. The results of ultrasound thickness measurement and diaphragm excursion are presented in Table 1. Diaphragm thickness and excursion in patients with successful and failed extubation are presented in Table 2. The results showed that the mean thickness of the diaphragm in the successful extubation group was significantly higher than the one with extubation failure ($P < 0.05$). Moreover, the mean diaphragm excursion in the successful extubation group was significantly higher than the one with the extubation failure ($p < 0.05$).

Diaphragm thickness in male patients was significantly higher (right and left $p = 0.024$ and $P = 0.049$). However, there was no significant difference in diaphragm excursion between men and women (right and left $P = 0.709$ and $P = 0.725$, respectively). There was an inverse and significant difference between the thickness and excursion of the diaphragm and age ($P < 0.001$).

Spearman correlation results showed a significant positive correlation between excursion and diaphragm thickness (right: $P < 0.0001$, $r = 0.485$, and left: $P < 0.0001$, $r = 0.552$). In addition, there was a direct and significant relationship between right and left thickness ($P < 0.0001$, $r = 0.678$) and Right and Left Excursion ($P < 0.0001$, $r = 0.648$).

The results concerning the diagnostic capability, sensitivity, and specificity of diaphragm ultrasound parameters for predicting extubation success are presented in Table 3. The results of the ROC are also presented in Fig. 1, which shows the high excursion capability and the right and left thickness of the diaphragm by ultrasonography to predict extubation. Accordingly, the sensitivity and specificity of the excursion and thickness of the left side of the diaphragm are greater than that of the right to predict extubation.

Table 1: Diaphragm thickness and diaphragm excursion measured by ultrasound in ICU patients

| **Parameter** | Mean ± S.D | Median | IQR (CI 95%) | Min-Max |
|---|---|---|---|---|
| Right Thickness (mm) | 0.38 ± 1.94 | 1.90 | 2.01 – 1.86 | 4.0 -0.9 |
| Left Thickness (mm) | 0.36 ± 2.00 | 1.90 | 2.07 - 1.93 | 3.5– 0.8 |
| Right Excursion (mm) | 6.20 ± 34.59 | 33.50 | 33.40- 35.79 | 48 – 18 |
| Right Excursion (mm) | 7.04 ± 36.35 | 37.50 | 34.99 -37.71 | 53 – 10 |

IQR, interquartile range.

Table 2: Diaphragm thickness and excursion based on extubation success

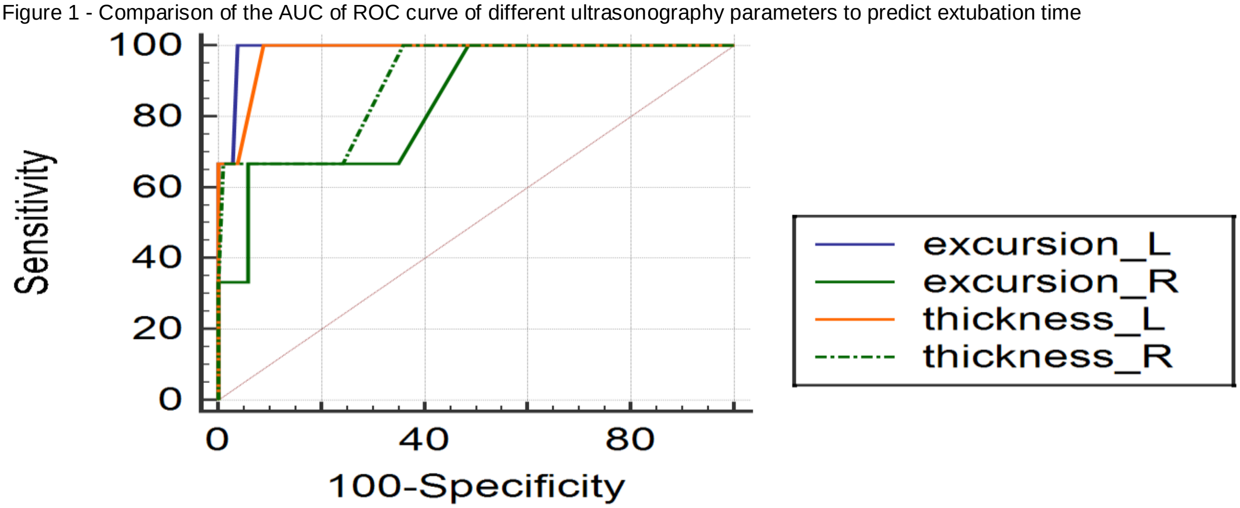
| **Parameter** | Successful extubation | Extubation failure | p-value |
|---|---|---|---|
| Right Thickness (mm) | 0.36 ± 1.96 | 0.47 ± 1.26 | 0.012 |
| Left Thickness (mm) | 0.33 ± 2.02 | 0.40 ± 1.16 | 0.0001 |
| Right Excursion (mm) | 5.98 ± 37.84 | 7.50 ± 25.00 | 0.042 |
| Right Excursion (mm) | 91.69± 36.91 | 8.18 ± 17.00 | 0.0001 |

Table 3: Diagnostic capability of diaphragm ultrasound parameters for prediction of extubation time and success

| **Variable** | **Sensitivity%** | **Specificity%** | **Cut off** | **AUC** | **95% CI** | **P value** |
|---|---|---|---|---|---|---|
| Excursion L | 100 | 96.12 | 26 ≥ (15≥ تا 26≥) | 0.989 | 1.000 – 0.945 | 0.0001> |
| Excursion R | 66.67 | 94.17 | 24 ≥ (18≥ تا 33≥) | 0.841 | 0.905 – 0.785 | 0.002 |
| Thickness L | 100 | 26/91 | 6/1 ≥ (1/1≥ تا 6/1≥) | 975/0 | 0.977 – 0.930 | 0.0001> |
| Thickness R | 67/66 | 03/99 | 1/1 ≥ (9/0≥ تا 8/1≥) | 898/0 | 0.948 – 0.824 | 0.0001> |

AUC: Area Under the Curve; CI: Confidence Interval.

Figure 1 - Comparison of the AUC of ROC curve of different ultrasonography parameters to predict extubation time




## DISCUSSION

This study aimed to evaluate diaphragm dysfunction using ultrasonography to predict extubation time in ICU patients. In the present study, extubation failure was observed in 2.83% of patients, whose diaphragm thickness and excursion was significantly lower than those with successful extubation. Besides, ultrasonography excursion parameters and diaphragm thickness had high sensitivity and specificity to predict extubation time. Similar results were reported in Yoo et al. These findings suggest that diaphragm ultrasonography can be a useful tool for predicting successful extubation.

Numerous studies have evaluated diaphragm function using ultrasonography in critically ill patients[18-12]. Kim et al[12] reported that 29% of patients with SBT had diaphragm dysfunction, which was detectable as diaphragm excursion less than 10 mm as assessed by M-mode ultrasound. They also showed that the best cut-off values for right and left diaphragm excursions were 14 and 12 mm, respectively, and diaphragm ultrasound could be a useful tool to diagnose patients at high risk of endotracheal intubation. Lerolle et al. showed that diaphragm excursion could indicate diaphragm dysfunction[19]. These results are in agreement with the findings of the present study. Saeed et al[20] by examining 30 patients with COPD under mechanical ventilation showed a cut-off value of 11 mm for diaphragm excursion with a sensitivity of 86.4% and a specificity of 87.5%. Osman and Hashim[21] found that the cut-off value for diaphragm excursion less than 10 mm predicts extubation failure and has a sensitivity of 83.3%, a specificity of 100% and the under curve area of 0.830. In another study, Farghaly et al[22] found that the diaphragm excursion cut-off values greater than or equal to 10.5 mm during normal breathing with a sensitivity of 87.5% and a specificity of 71.5% were able to predict extubation success. The reason for the lower cut-off values compared to the present study may be the small number of extubation failures in the present study and differences in the characteristics of the studied subjects. Other studies have also shown that excursion measurements can predict the likelihood of a patient removal from ventilator and the success or failure of extubation[8,15, 23]. The results of Huang et al[5] showed that larger diaphragm movements and faster contractions are good factors in Extubation success (AUC of 0.839 and 0.833, respectively). Li et al[3] in a meta-analysis showed that diaphragm ultrasound is a valuable tool with high diagnostic accuracy for predicting the isolation of patients undergoing mechanical ventilation and extubation results. In another study, DiNino et al[13] concluded that diaphragm thickness measurement by apposition ultrasound could be useful in predicting extubation success or failure in the apposition area. Other past studies have also shown that diaphragm thickness (atrophy) determines the duration of ventilation or extubation failure[24] and measuring diaphragm thickness changes helps to predict ventilator[13,14]. All of these results confirm the findings of the present study and suggest that diaphragm performance evaluation by ultrasound is a useful indicator for predicting extubation time or success.

In the present study, the best predictor of successful extubation was the left diaphragm excursion rate. The results of Yoo et al[2] showed that diagram excursion was a more accurate criterion for predicting extubation than its thickness, and the AUC of ROC for prediction of extubation success was higher for excursion than diaphragm thickness. These results are in agreement with the findings of the present study and show that the diaphragm excursion rate is a better predictor of successful extubation than diaphragm thickness.

In the present study, there was a direct and significant relationship between thickness and diaphragm excursion on the left and right sides. Similar results were found in Theerawit et al[25]. Moreover, in this study, excursion and left-diaphragm thickness measurements are better predictors of success of extubation and endotracheal tube separation (due to AUC, sensitivity and specificity) compared to the right side. The results of Huang et al[5] also confirm these findings.

The results of Flevari et al[15] showed that left side excursion with 7 mm cut-off rate is a better indicator for predicting wearing success in patients with long wearing compared to the right side (10 mm cutoff). These results are in agreement with the findings of the present study. However, the large difference between the left and right thresholds in the study by Flevari et al[15] was most likely due to differences in probe position. It should be noted that in ultrasound examination, movement is usually better assessed on the right side, while in the left ultrasound, the lower part of the lung, intestine, and the involvement of gases during the inhalation usually cover the diaphragm. Moreover, according to the results of some studies, it is not always possible to evaluate the thickness of the left diaphragm[16,26]. Therefore, in most studies, only the right diaphragm ultrasound was performed because the acoustic window created by the liver facilitates the measurement of parameters in this direction[2,25], which may affect the results.

In the present study, diaphragm thickness in male patients was significantly higher. However, there was no significant difference in diaphragm excursion between men and women. Li et al. reported that diaphragm thickness was higher in men than in women[3]. These results are in agreement with the findings of the present study. On the other hand, Flevari et al[15] examined the role of ultrasound in predicting the success of removing patients with long and difficult wearing from ventilator and showed that there was no significant difference between diaphragm excursion rate in male and female patients. However, one study found that diaphragm excursion rates varied in terms of gender[11].

Finally, it should be noted that differences in the population and characteristics of the studied subjects, differences in device type and ultrasound technique and operator experience could be the reason for the differences in the results of different studies. In addition, several factors are involved in extubation failure, including changes in airway resistance, respiratory system compliance, load-related cardiac dysfunction, respiratory muscle weakness, or airway clearance failure[23]. These factors may influence the results of this study and cause less sensitivity or specificity than previous studies. Besides, since diaphragm dysfunction is the main cause of extubation failure, but not the only cause, it is necessary to pay attention to the information obtained from diaphragm ultrasound with clinical and laboratory data as well as information obtained from other imaging technologies such as X-ray, CT and echocardiography[3].

The present study also had limitations: First, the study population was heterogeneous and critically ill patients with different etiologies were included. Therefore, future studies should be conducted on populations with similar diseases. Second, diaphragm thickness or excursion measurements were not performed just before extubation. Ultrasound time can affect the amount of excursion and the measured thickness. Third, the reliability of interobserver and intraobserver was not investigated in the present study. However, previous studies have reported high reliability for ultrasound parameters[11]. Fourth, RSBI was not calculated at time similar to ultrasound, so it was not possible to compare ultrasound indices with RSBI. In addition, in this study, the diaphragm strength was not measured evaluate using phrenic nerve stimulation as the gold standard[6] and the results were not compared with the ultrasound findings. Therefore, because of the small sample size and mentioned limitations, larger randomized controlled trials can help to confirm the results.

## CONCLUSION

The results of the present study showed that ultrasonography is a reliable and effective noninvasive technique in the evaluation of diaphragm dysfunction and predicting the success of extubation in critically ill patients with different etiologies in ICU and measurement of both excursion and diaphragm thickness indices helps to resolve this issue. The present study showed that the excursion rate and thickness of the left side of diaphragm were better indices for predicting extubation time in critically ill ICU patients than the parameters on the right side. In addition, ultrasound measurement of diaphragm excursion seems to be a better predictor of extubation success than ultrasound thickness measurement.

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