

**Research Article** 

# Value of Integrated Lung and Diaphragm Ultrasonography in Predicting Extubation Outcomes from Mechanical Ventilation in Patients with Critical Illness

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Received date: September 19, 2019; Accepted date: October 10, 2019; Published date: October 15, 2019

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#### Abstract

**Background:** A primary priority for all intensivists is identifying strategies to reduce the duration of mechanical ventilation (MV) and deciding the ideal time for extubation.

Aim: To evaluate the role of the diaphragm and lung ultrasonography principally (DE, DTF, and LUS scores) in the prediction of extubation outcomes from MV.

**Patients and methods:** This prospective observational study included sixty-eight adult patients who required invasive MV for as a minimum of 24 hours and successfully passed a spontaneous breathing trial (SBT). At the end of a successful SBT, we assessed by ultrasound DE, DTF and lung parenchyma.

**Results:** 53 patients (78%) successfully extubated while, 15 patients (22%) experienced failed extubation. DTF% with cutoff value  $\ge$  30% had the highest sensitivity (100%), negative predictive value (100%) and the highest accuracy (89.24%). On combining DTF%  $\ge$  30% and LUS  $\le$  12, specificity and the diagnostic accuracy raised to (100% and 96% respectively) with highly precise AUC (0.97).

**Conclusion:** The integration of DTF  $\% \ge 30\%$  of the right hemi-diaphragm with LUS  $\le 12$  improved the expectation of successful extubation in comparison with DTF % alone.

**Keywords:** Diaphragm; Lung; Ultrasonography; Extubation; Mechanical ventilation

## Introduction

Nowadays Mechanical Ventilation (MV) is considered a fundamental life support strategy that is used in many patients with critical illness and has proven to decrease mortality rates [1]. Once mechanical ventilation initiated; planning for weaning should starts. Timing of weaning is crucial to avoid many complications [2]. Liberation from mechanical ventilation is considered a major issue in critical care practice. Traditionally; decision to start weaning process is taken after improvement of patient's clinical condition, arterial blood gas parameters and largely depends on clinical experience [3]. However, approximately 14% to 32% of the patients meeting these criteria undergoing extubation failure (EF).

For identifying the right time to extubate patients from invasive mechanical ventilation, several ventilatory indices have been established; however, none of them fulfilled the criteria necessary to deliver properly precise success rates [4]. In recent times, lung and diaphragm ultrasonography approaches have been presented to evaluate the patterns of the pulmonary airway and the diaphragmatic function. Moreover, lung ultrasonography can be used as an effective measure in the evaluation of lung aeration which is useful during the weaning procedure as it reflect the aeration loss and consequently predict the respiratory distress in the post extubation period, a validated score termed the lung ultrasound score (LUS) can be used to evaluate the loss of lung aeration [5]. Numerous data measured through diaphragmatic ultrasonography have been recommended for the same purpose [6-7], which involve measurement of diaphragmatic muscle movement during inspiration or excursion during the respiratory cycle (DE) [8], and diaphragmatic muscle thickening or diaphragmatic thickening fraction (DTF).

The primary aim of the present study was to evaluate the role of the lung and diaphragm ultrasound in particular the DE, DTF and LUS scores to predict extubation outcomes. The secondary outcome was to compare these ultrasonography data with the other traditional weaning criteria.

### **Patients and Methods**

This prospective observational study includes a total of 85 patients required invasive mechanical ventilation for a minimum of 24 hours and achieved the weaning criteria. Approval of the ethical committee and a written informed consent was given by surrogate decision maker. This study was conducted at the Surgical ICU in Aswan University Hospital, during the period from May 2017 to December 2018. Included patients underwent full clinical examination, Chest radiography, routine laboratory investigations (whenever needed) and arterial blood gases (ABG) on daily basis; also before and after start of SBT.

# Weaning procedure

All patients who meet the following weaning criteria undergo SBT, which include, improvement of disease acute phase which necessitated mechanical ventilation, stable neurological status, no hemodynamic instability (heart rate  $\leq 120$ /min, systolic blood pressure higher than 90 mmHg and lower than 160 mmHg) in the absence of any vasoactive support therapy, PaO<sub>2</sub>>60 mm Hg or SaO<sub>2</sub>  $\geq$  90% or more with FiO<sub>2</sub>  $\leq$  0.4, spontaneous respiratory rate (RR)<35 breath/min, exhaled tidal volume (VT)>5 ml/kg of ideal body weight, afebrile and there were no significant abnormalities in the electrolyte levels.

Patients who were hemodynamic unstable (heart rate>140, systolic blood pressure>180 or <90 mmHg), those with severe intracranial disease, with tracheostomy, severe ICU acquired neuromyopathy, with primary unilateral/bilateral absence of diaphragmatic mobility, and who had previously failed SBT, were excluded from the study.

## Variables monitored during SBT

Patients underwent a SBT for at least two hours by putting the patient on spontaneous mode of weaning with low-level pressure support (8 cm H<sub>2</sub>O) and PEEP level ( $\leq$  5 cm H<sub>2</sub>O) using GE ventilator (Carescape R860, USA). Dyspnea, fatigue, anxiety and distress were subjectively assessed. Vital signs were monitored and recorded. Ventilatory data were recorded including exhaled tidal volume, breathing rate, minute ventilation, maximal inspiratory pressure (PImax) and rapid shallow breathing index (RSBI). Patients, who passed the SBT without worsening, were extubated and received oxygen therapy with Venturi mask and then monitored for 48 hours after extubation. A successful extubation was defined as preservation of spontaneous breathing without any ventilatory support for  $\geq$  48 hours following extubation [9-10].

# Ultrasound examination

At the end of a successful SBT, lung and diaphragm ultrasound examination were done. All the included cases in our study were assessed in a semi-recumbent position. Ultrasound was accomplished using GE ULTRASOUND (LOGIQ C5 Premium, GE MEDICAL SYSTEMS (CHINA) CO, LTD).

# A- Diaphragm ultrasonography

Evaluation of diaphragmatic excursion: we measured the amplitude of diaphragmatic inspiratory excursion as the highest point of maximal inspiration in the motion mode (M-mode) with the use of 3.5-5 MHz curvilinear probe, which was positioned immediately underneath the right subcostal margin in the mid-clavicular line and was moved upward till better visualization of the posterior portion of the right hemi-diaphragm [11, 12] as shown in Figure 1.



**Figure 1:** Diaphragm excursion is evaluated in the M-mode with the use of 3.5-5 MHz curvilinear probe.

Evaluation of diaphragmatic thickness & thickness fraction: The diaphragmatic thickness was evaluated with the use of a 7-10 MHz linear probe in B mode as shown in Figure 2.



**Figure 2:** Diaphragmatic thickness is evaluated in the B-mode with the use of 7-10 MHz linear probe.

The right hemi-diaphragm was seen at the region of apposition, on the midaxillary line between the 8<sup>th</sup> and 10<sup>th</sup> intercostal spaces, where we viewed the diaphragm as three layered structure (two parallel echogenic lines demonstrating the diaphragmatic pleura and the peritoneum with central hypoechoic space representing the diaphragmatic muscle) [13]. Measurement of the degree of diaphragm thickening had been planned to be more accurate than the evaluation of thickness alone, the diaphragmatic thickness fraction (DTF) was considered as=[(Thickness at the end inspiration-thickness at the end expiration)/Thickness at the end expiration] [14].

**B-Lung ultrasound:** For the evaluation of Lung parenchyma, each lung was divided into 3 zones underwent evaluation anteriorly and posteriorly with the use of B-mode to check the degree of lung aeration with a total of 12 zones to be assessed [15], as shown in Table 1.

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Points for each lung zone (12 zones)	Status of lung aeration	Lung ultrasound pattern
0 point	Normal aeration	Horizontal A-line (no exceed three B-line)
1 point	Average loss of aeration	numerous B-line with regular or irregular spacement
2 point	Marked aeration loss	Multiple coalescent B-lines
3 point	Complete aeration loss	Lung consolidation
Total score	From 0 to 36	

**Table 1:** Illustrates the lung ultrasound score for detection of the degree of lung aeration.

## Statistical analysis

SPSS (Statistical Package for Social Science) software program version 19.0 (SPSS Inc., Chicago, IL) was used for data recording and handling. Data was presented as (mean  $\pm$  SD) for continuous variables. Student's t tests were used for the comparison of continuous variables and chi-square tests were used to compare numerical variables. Non-parametric tests were used for abnormal distributed data in the current study. To assess the accuracy of each weaning index, Receiver operator characteristic curves (ROC) were used and the non-parametric method of Delong was used to calculate the area under the ROC curves (AUC) for each weaning index. P value  $\leq$  0.05 considered significant.

#### Results

During the study period, we evaluated 85 patients (50 males and 35 females) eligible for weaning. Ten subjects were excluded from the study, three of which had hemodynamic instability, 4 cases had previously failed SBT and 3 had a decreased level of consciousness. Among the 75 patients underwent SBT, 7 patients failed SBT and were omitted from data analysis. Sixty-eight patients were successfully passed SBT then extubated and monitored for 48 hours to evaluate extubation outcome.

Patients were classified according to the fate of extubation into a successful extubation group (53 patients) (78%) and failed extubation group (15 patients) (22%), who required re-intubation within 48 hours post-extubation due to respiratory distress or hypoventilation with respiratory acidosis as shown in Figure 3.



With the exception of the length of mechanical ventilation, all the demographic and clinical data did not differ considerably between the successfully extubated and failed groups (Table 2).

Demographic variable		Successful extubation group (n=53)	Failed extubation group (n=15)	P Value	
Age	Mean ± SD	51.3 ± 16.5	54.5 ± 15.6	0.512	
Male no (%) 3		38 (71.7%)	8 (53.3%)	0.040	
Gender	Female no (%)	15 (28.3%)	7 (46.7%)	0.210	
Duration of MV (days)	Mean ± SD	2.8 ± 0.76	5.8 ± 1.8	0.001*	
Diagnosis on admission to ICU	Polytrauma (%)	15 (28.3%)	4 (26.7%)		
	Sepsis (%)	15 (28.3%)	5 (33.3%)	0.159	
	Postpartum hemorrhage (%)	2 (3.7%)	1 (6.7%)	0.156	
	Acute pancreatitis (%)	3 (5.7%)	1 (6.7%)		

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	Postoperative complications (%)	15 (28.3%)	2 (13.3%)	
	Pregnancy induced hypertension or eclampsia (%)	3 (5.7%)	2 (13.3%)	
MV: mechanical ventilation; ICU: intensive care unit; P value is considered significant at <0.05				

Table 2:Demographic and clinical data of the studied groups.

All the traditional weaning parameters including, (MAP, HR,  $PaO_2/FiO_2$  ratio, RR, RSBI and  $PI_{max}$ ), were significantly different in the successful extubation group in comparison with the failed one (P<0.05) (Table 3). The diaphragmatic ultrasound parameters

including DE and DTF% were considerably higher (P<0.001) in the successfully extubated group compared to the failed one, while LUS score was considerably lower (P<0.001) in the successfully extubated group in comparison with the failed one (Table 3).

	Successful extubation group (n=53)	Failed extubation group (n=15)	P Value	
	Mean ± SD	Mean ± SD		
MAP (mmHg)	96.2 ± 6.6	101.5 ± 9.04	0.015	
HR (beat/min)	93.2 ± 11.9	120.7 ± 21.9	<0.001	
PaO <sub>2</sub> /FiO <sub>2</sub> ratio	211.8 ± 31.2	174.0 ± 24.7	<0.001	
RR (breath/min)	24.8 ± 5.7	33.1 ± 6.2	0.001	
RSBI (breath/min/I)	74.4 ± 14.9	100.5 ± 6.1	0.001	
PI <sub>max</sub>	-57.3 ± 18.2	-22 ± 4.5	0.001	
DE (mm)	20.6 ± 7.3	8.5 ± 6.2	<0.001	
DTF (%)	34.1 ± 1.9	23.4 ± 3.8	<0.001	
LUS score	9.9 ± 5.3	18.9 ± 6.5	<0.001	

Abbreviations: MAP: Mean arterial pressure; HR: Heart rate; PaO<sub>2</sub>: Partial arterial oxygen pressure; FiO<sub>2</sub>: Fraction of inspired oxygen; RR: Respiratory rate; RSBI: Rapid shallow breathing index; PI<sub>max</sub>: Maximal inspiratory pressure; DE: Diaphragm excursion; DTF: Diaphragmatic thickness fraction; LUS score: Lung ultrasound score;

P-value is considered significant at<0.05

 Table 3: Comparison of the weaning parameters between the studied groups.

Diagnostic test performance of each index was used to predict extubation success (the traditional weaning parameters and ultrasonographic parameters) was shown in Table 4 and Figures [4-7]. DTF% with cutoff value  $\geq$  30% had the highest sensitivity (100%), negative predictive value (100%) and the highest accuracy (89.24%); while, its specificity and positive predictive value were (71.4% and 83.3% respectively). On combining DTF%  $\geq$  30% to LUS  $\leq$  12, specificity and positive predictive value raised to 100%, 96.0% accuracy and AUC was highly precise (0.97).

Diagnostic Validity	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
Traditional weaning parameters						
RR ≤ 28 breath/min	78.2	60	76.1	66.3	65.8	0.636
RSBI ≤ 102 (breath/min/L)	80	65.3	77.8	69.7	70.4	0.719
PImax ≤ -25 (cmH <sub>2</sub> O)	80	70	78.3	71.6	72	0.727
PaO2/FiO <sub>2</sub> ratio ≥ 188	79.3	80	93.3	52.2	79.4	0.832
Ultrasonography parameters						
DE ≥ 11 (mm)	84.4	73.9	86.4	70.8	80.9	0.868

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DTF ≥ 30	100	71.43	83.3	100	89.24	0.904
LUS score ≤ 12	80	78.3	87.8	66.7	79.4	0.889
DTF $\geq$ 30 and LUS score $\leq$ 12	95	100	100	92	96	0.971

Abbreviations: RR: Respiratory rate; RSBI: Rapid shallow breathing index;  $PI_{max}$ : Maximal inspiratory pressure;  $PaO_2$ : Partial arterial oxygen pressure;  $FiO_2$ : Fraction of inspired oxygen; DE: Diaphragm excursion; DTF: Diaphragmatic thickness fraction; LUS score: Lung ultrasound score; PPV: Positive predictive value; NPV: Negative predictive value; AUC: Area under the receiving operating characteristic curve

Table 4: Diagnostic Test Performance for Traditional and Ultrasonography Weaning Parameters.



**Figure 4:** Area under receiving operating characteristic curve for diaphragm excursion (DE).







**Figure 6:** Area under Receiver operator characteristic curve (ROC) for lung ultrasound score (LUS).



**Figure 7:** Area under Receiver operator characteristic curve (ROC) for combined diaphragmatic thickness fraction ( $\geq$  30) and lung ultrasound score ( $\leq$  12).

## Discussion

Determining the ideal time for extubation in mechanically ventilated patients is an exciting topic as the traditional weaning predictor tools are not precise. Our study found that a right DTF of more than or equal to 30% had a better diagnostic accuracy for predicting extubation successfulness. In harmony with our results, the studies from Ferrari et al. [16], DiNino et al. [17], Dube et al. [18], and Blumhof et al. [19] confirmed that DTF above or equal 36, 30, 29, and 20%, respectively, were related to successful extubation. Moreover, from our analysis, the combination of right DTF of  $\geq$  30% and LUS

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score  $\leq 12$  improved the specificities and accuracy for expecting the success of the extubation procedure from mechanical ventilation compared to the use of DTF alone.

In our results, 15 patients representing (22%) of the study population experienced failed extubation and re-intubated within 48 hours. Similarly, previous studies revealed failure rate about 20, 26.7 and 23.3 percentages correspondingly [20-22]. However, Ferrari et al. described 63 failure rate percentage in patients ventilated through a tracheostomy tube [16].

The mean length of mechanical ventilation was considerably prolonged in our failed extubation group (5.8  $\pm$  1.8 days) compared with the successful one (2.8  $\pm$  0.76 days]. Similarly, Baess et al. (2016) established that the mean length of MV in the successful weaned group was (4 days) versus (7 days) in the failed one [22].

We observed highly substantial difference between patients who succeeded or failed extubation in comparing the traditional weaning predictors including (RSBI, PImax, RR, and PaO<sub>2</sub>/FiO<sub>2</sub> ratio). Osman and Hashim [6] reported similar result regarding PImax, Nemer and Barbas [23] regarding RR, Farghaly and Hasan [24] regarding PaO<sub>2</sub>/FiO<sub>2</sub> ratio, Ferrari et al. [16] and Saeed et al. [21] regarding RSBI, However, Farghaly and Hassan [24] reported that RSBI measured during SBT was insignificantly different between their successful and failed extubation groups.

The mean diaphragmatic excursion (DE), in our study was considerably higher in the successfully extubated group  $(19.7 \pm 5.1 \text{ mm vs.} 6.2 \pm 3.1 \text{ mm})$  in comparison with the other group, the best cutoff value of diaphragmatic excursion that accurately prognosticate effective extubation in our study was minimally 11 mm with 84% sensitivity, however its specificity and negative predictive value were (73% and 70% respectively). This result was comparable with Farghally and Hasan [24] who reported that the best cutoff value of DE for prognostication of successful extubation was 10.5 mm.

In the present study, DTF percentage with cut off value  $\geq$  30 had 100% sensitivity but 71% specificity and 83% positive predictive value, similar result by Pirompanich and Romsaiyut in their study on 34 patients found that DTF percentage  $\geq$  26 had sensitivity of 0.96, specificity of 0.68, PPV of 0.89 and NPV of 0.86 [25], moreover, Osman and Hashim in their study on 68 patients demonstrated that DTF percentage more than 28 was the optimal cut off value that better predict successful weaning with 0.88 sensitivity and 1.00 specificity [6]. However, this result was in controversy to Ferrari et al. who described greater cut off value  $\geq$  36% with 0.82 sensitivity and 0.88 specificity [16], additionally, Farghaly and Hasan [24] reported that DTF percentage  $\geq$  34.2% was associated with the greatest sensitivity (0.90) in comparison with the other diaphragmatic parameters but with (0.64) specificity.

We found that the diagnostic test performance of LUS score to prognosticate extubation success with the best cut off value of  $\leq 12$  had sensitivity 80%, specificity 78%, NPV 66% and AUC 0.88 reflecting lower accuracy than previously mentioned weaning indices. In concordance with our results, Mayo et al. proposed that a LUS score<13 at the end of a SBT increased probability of achievement of extubation and a LUS score>17 was highly predictive of postextubation distress and increased the chance of failed extubation [26].

Finally, we found that the integration of DTF of more than or equal to 30% combined with LUS score of less than or equal to 12 improved the diagnostic accuracy for prediction of successful extubation compared to DTF alone (96% accuracy and the area under curve was 0.971).

# Limitations

Our study is a single center study with small sample of selected patients. Moreover, the main limitation of our study that ultrasonography was operator dependable technique with several ultrasound limitations such as the existence of pneumothorax as well as the morbid obesity interfering with the maximum window for diaphragm imaging.

## Conclusion

Ultrasonography measurement of DTF can provide appreciated data in the assessment of subjects during partial ventilatory support. Moreover, the integration of DTF  $\geq$  30% combined with LUS score  $\leq$ 12 improved the likelihood of successful extubation in comparison with DTF alone.

## Acknowledgments

The authors appreciate the ultimate help and support of the surgical intensive care unit residents and nurses in this research. No fund was paid by any institution.

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