

Diaphragmatic ultrasound as a predictor of successful extubation from mechanical ventilation: thickness, displacement, or both?

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Background Best predictor of successful extubation after mechanical ventilation is a matter of debate.

Objective The aim of this study was to assess whether the degree of diaphragm thickening and/or diaphragm displacement (DD) as measured by means of ultrasound during a weaning trial can predict extubation outcomes.

Methods Thirty patients who were planned for weaning after being intubated and mechanically ventilated were prospectively enrolled in the study between January and June 2015. The rapid-shallow breathing index (RSBI) was subsequently calculated, and diaphragmatic ultrasound was then carried out to assess DD and diaphragm thickening during tidal inspiration. The primary outcome was extubation success or failure.

Results Of the 30 patients included in the study, 15 were male. The mean age of patients was 59.17±13.17 years. The median duration of intubation before weaning was 4 days. There was a significant difference between mean inspiratory and expiratory diaphragmatic thickness (TDI) ($t=9.66$, $P=0.001$). An receiver operating characteristic curve was constructed for the end inspiratory TDI, end expiratory TDI, delta TDI, DD, and RSBI. The RSBI performed better than all other parameters, with an area under the curve of 0.968. A cut-off value of 73.5 had 87% sensitivity and 100%

specificity for predicting extubation success. All other parameters had an area under the curve less than 0.7. (0.559, 0.624, 0.655, and 0.512 for end inspiratory TDI, end expiratory TDI, delta TDI, and diaphragmatic displacement, respectively).

Conclusion Sonographically measured TDI performed better than displacement in predicting value for weaning outcome. In a respiratory ICU, however, the RSBI seems to be a more reliable and accurate tool for the purpose and should be considered in every weaning protocol. Whether TDI can be evaluated using low-frequency ultrasound probes needs to be validated by further studies.

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Introduction

Difficulty in weaning from mechanical ventilation (MV) is one of the most frequently encountered problems in modern ICUs. An estimated 20% of mechanically ventilated patients face failed extubation (requiring reintubation within 48 h of extubation) [1]. A trial of failed extubation induces several detrimental consequences, including cardiorespiratory stress, prolonged ICU stay, and increased mortality [1–3]. Delay in attempting extubation also increases the likelihood that patients would face the inherent risks of MV, including ventilator-associated pneumonia and ventilator-induced diaphragmatic atrophy [4].

Attempts have been ongoing to devise tools that can accurately determine the ideal timing of extubation. Among these tools are measuring the minute ventilation, maximal inspiratory pressure, and tracheal occlusion pressure at 0.1 s with variable degrees of success [5,6]. Another predictive tool, the rapid-shallow breathing index (RSBI) has gained popularity as a more accurate index in predicting success of extubation, but this ability is limited in patients weaned through pressure support (PS) [7,8].

The diaphragm plays a central role in the process of spontaneous ventilation, and it seems intuitive that, in patients receiving MV, a properly functioning diaphragm should herald successful weaning. Although the maximal inspiratory pressure is an indirect method of assessing the diaphragm, the more traditional methods of studying diaphragmatic dysfunction include fluoroscopy, phrenic nerve conduction study, and transdiaphragmatic pressure measurement [6]. These latter methods have serious limitations, including the use of ionizing radiation, invasiveness, relative unavailability, and sometimes the need for patient transportation [6,9]. Ultrasound has emerged as a cheap, widely available, free-from-radiation, bed-side tool for assessment of the characteristics of diaphragmatic movement, such as amplitude, force, and velocity of contraction, special patterns of motion, and changes in

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diaphragmatic thickness (TDI) during inspiration [9,10]. Many of these parameters have been studied as a guidance in predicting the course of weaning from MV [6,7,9–12].

This study aimed to assess whether the degree of diaphragm thickening (DT) and/or diaphragm displacement (DD) as measured using ultrasound during a weaning trial can predict extubation outcomes.

Methods

Patients

Thirty patients were prospectively enrolled in the study between January and June 2015. Patients were intubated and mechanically ventilated in the general and respiratory ICU in Alexandria Main University Hospital. The study was approved by the Ethics Committee of the Faculty of Medicine, Alexandria University. Patients who were planned for weaning either using low-level PS or spontaneous breathing trial were included if they fulfilled the following criteria: age above 18 years, hemodynamic stability without need

for vasopressors, and a duration of continuous MV of 30 days or greater. Patients were excluded if the cause for intubation was upper airway obstruction or there was pregnancy, dressing on the right lower rib cage hindering sonographic access, recent intra-abdominal surgery, a history of empyema, or pleurodesis.

Study design

Eligible patients were subjected to full history taking and clinical examination after informed consent was obtained from the patient or their next of kin. The tidal volume and breathing frequency were recorded on the least PS the patient was given and the RSBI was subsequently calculated [frequency/tidal volume (l)]. Diaphragmatic ultrasound was then performed to assess the degree of excursion/displacement (DD) and muscle thickening (DT) during tidal inspiration. The procedure was performed by physicians who had no role in the management of patients. Sonographic examination was carried out for spontaneous breathing trial patients when they were disconnected from ventilator. For the PS group, diaphragm ultrasound was performed when the patients were still on

ventilatory support. Weaning then ensued. The primary outcome was extubation success or failure. Patients were divided into two groups: the successful group, which included patients who could sustain spontaneous breathing for more than 48 h following extubation, and the failure group (FG), which included patients who required reintubation or noninvasive ventilation within 48 h after extubation.

Diaphragm ultrasound

The right diaphragmatic cupola was examined with a 2–4 MHz phased-array probe (Philips Healthcare, Andover, Massachusetts, USA). The right side was chosen due to the better sonographic window provided by the liver [13]. Patients were seated in a semirecumbent position and the probe was put either immediately below the right costal margin at the midclavicular line or on the last two spaces at the anterior axillary line. The probe was then directed backward, caudally, and slightly medially until the dome of the diaphragm was visualized [9]. At B-mode, the TDI at the dome was measured in mm at end-inspiration and end-expiration. Consequently, the delta TDI was calculated as percentage from the following formula:

$$\left(\text{DeltaTDI} = \frac{\text{Thickness at end inspiration} - \text{Thickness at end expiration}}{\text{Thickness at end expiration}} \right).$$

Subsequently, using M-mode, the excursion of the diaphragm (DD) at the dome was also measured in centimeters. For each of the measurements, five readings were taken and the average was recorded.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package, version 20.0. Qualitative data were described using number and percentage. Normally distributed quantitative data were described using mean \pm SD, whereas non-normally distributed data were expressed in range (minimum–maximum) and median. The Mann–Whitney test (*Z*) was used for non-normally distributed quantitative variables to compare the success and failed groups, whereas Pearson's coefficient (*r*) was calculated to correlate between two normally distributed quantitative variables. Significance of the obtained results was judged at the 5% level.

Results

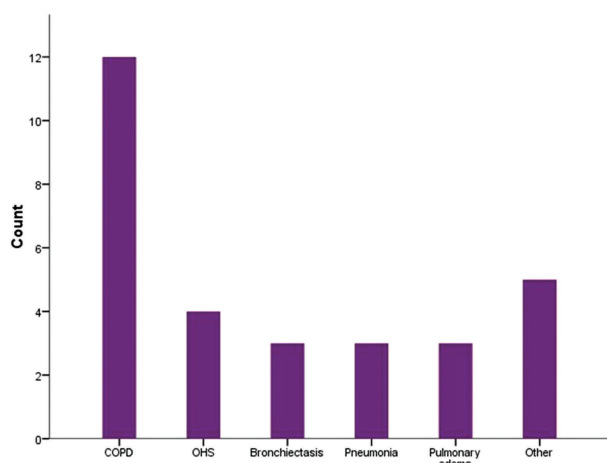
Of the 30 patients included in the study, 15 were male. The mean age of patients was 59.17 \pm 13.17 years.

Table 1 and Fig. 1 demonstrate the underlying causes that lead to intubation in the studied patients. Fifteen patients (50%) suffered from chronic airway obstruction in the form of chronic obstructive pulmonary disease or bronchiectasis. Only 13% of patients had an extrathoracic problem (opiate poisoning, cerebrovascular stroke, and polytrauma). The median duration of intubation before weaning was 4 days (1–30 days). Seventeen patients were weaned using PS and 13 using T-piece. The sonographic and clinical measurements for patients are shown in Table 1. Successful weaning was achieved in 23 patients (76.7%). The mean duration of MV in the successful group was 4 days (1–30 days), whereas it was 7 days (3–18 days) in the FG. The difference was not found to be statistically significant ($P=0.06$). There was a significant difference between mean inspiratory and expiratory TDI ($t=9.66$, $P<0.001$). A receiver operating characteristic curve was constructed for the end inspiratory TDI, end expiratory TDI, delta TDI, DD, and RSBI (Fig. 2). The areas under the curve (AUC), sensitivity, specificity, positive predictive value, negative predictive value, and proposed cutoffs are reported in Table 2. The RSBI performed better than all other parameters, with an AUC of 0.968. A cut-off value of 73.5 had 87% sensitivity and 100% specificity for predicting extubation success. All other parameters had an AUC less than 0.7.

Discussion

Since its development by Yang and Tobin [14], the RSBI has gained considerable popularity as a reliable tool for predicting weaning from MV. Given the central role of

Figure 1



Underlying disease in mechanically ventilated patients in both groups. COPD, chronic obstructive pulmonary disease; OHS, obesity hypoventilation syndrome.

the diaphragm in the process of ventilation and the widespread availability of ultrasound machines in the ICUs, attempts have been made to gauge the utility of diaphragmatic ultrasound in guiding the weaning procedure. Diaphragmatic displacement [7,10,12] and more recently diaphragmatic thickening [6,11] as measured using ultrasound are now used as a surrogate for diaphragmatic function. At our institution, the RSBI is a major determinant of the weaning decision. The current study was designed to assess whether DT and DD can be reliable like RSBI in terms of ability to predict the outcome of weaning. Both

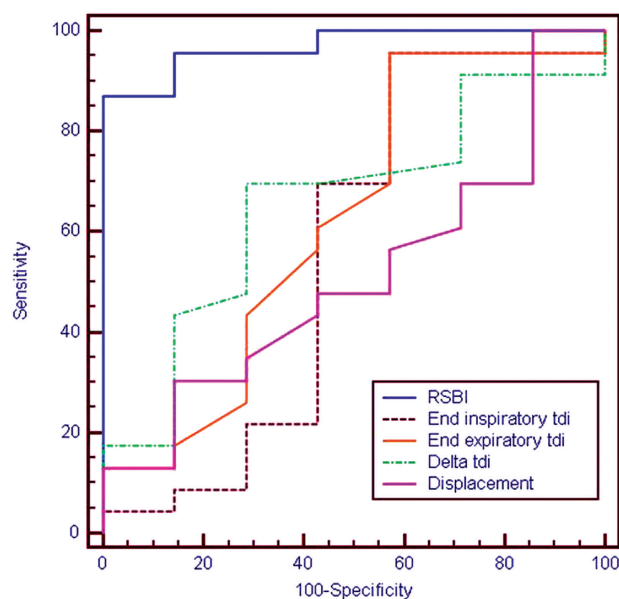
Table 1 Distribution of the studied cases according to different studied parameters (N=30)

	n (%)
Age (years)	59.17±13.17
Sex	
TDI	
End inspiratory TDI (mm)	0.67±0.16
End expiratory TDI (mm)	0.52±0.13
Delta TDI	28.67±15.35
Displacement (cm)	1.49±0.62
RSBI	65.33 (14.55–160.0)
Outcome	
Failed	7 (23.3)
Successful	23 (76.7)
Duration of MV (days)	4.0 (1.0–30.0)

Normally distributed quantitative data were expressed as mean ±SD, whereas non-normally distributed quantitative data were expressed as median (minimum–maximum).

MV, mechanical ventilation; RSBI, rapid-shallow breathing index; TDI, diaphragmatic thickness.

Figure 2



Receiver operating characteristic curve for different parameters to predict outcome (success). RSBI, rapid-shallow breathing index.

Table 2 Agreement (sensitivity, specificity, and accuracy) for different parameters to predict outcome (success)

	AUC	P	Youden index	Cutoff	Sensitivity	Specificity	PPV	NPV
RSBI	0.968*	<0.001*	0.869	≤73.53	86.96	100.0	100.0	70.0
End inspiratory TDI	0.559	0.772	0.385	>0.41	95.65	42.86	84.6	75.0
End expiratory TDI	0.624	0.384	0.385	>0.33	95.65	42.86	84.6	75.0
Delta TDI	0.655	0.192	0.409	≤30	69.57	71.43	88.9	41.7
Displacement	0.512	0.922	0.161	>1	69.57	14.29	72.7	12.5

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; RSBI, rapid-shallow breathing index; TDI, diaphragmatic thickness.

*Significance of the obtained results was judged at the 5% level

DT and DD were assessed using a low-frequency ultrasound probe.

Diaphragmatic excursion is the final product of diaphragmatic strength. As poor endurance is an important cause of failed weaning, evaluation of diaphragm movement using ultrasonography arises as an important tool. In this study, a low-frequency probe was used to assess the dome of the right hemidiaphragm at M-mode. Both B and M modes can be used for this purpose [9,13]. In a large study conducted on 210 healthy individuals, Boussuges *et al.* [13] used M-mode ultrasonography to determine normal values for diaphragmatic excursion. It was found that the lower limit for DD during quiet and deep breathing were 1 and 4.7 cm, respectively. In the present study, the mean DD was 1.5 cm (Table 1), which slightly exceeds values for normal individuals. Half of the studied patients had chronic airway obstruction. It has been shown that, when corrected for lung volume, the contractile strength of the diaphragm in chronic obstructive pulmonary disease is not reduced compared with controls [15] and may even be enhanced in some cases [16,17]. Lerolle *et al.* [10] evaluated the role of ultrasound in detecting diaphragmatic dysfunction in intubated postcardiac surgery patients and found that DD less than 2.5 cm at maximal breathing effort was a predictor of prolonged intubation. Kim *et al.* [12] determined that a DD less than 1 cm at tidal breathing is indicative of diaphragmatic dysfunction and predictive of weaning failure. For the specific goal of determining a cut-off point to predict successful weaning, Jiang *et al.* [7] studied 55 intubated patients and suggested 1.1 cm or more at quiet breathing as a cut-off value for successful weaning. Proponents of this index for prediction of weaning argue that it is more accurate compared with the RSBI [7,11]. Their explanation is that patients who sustain tidal volumes using accessory respiratory muscles before extubation, fatigue and fail extubation, which is why, they argue, relying on RSBI can be misleading [7,11]. As much as this holds true, the opposite is possible. Although diaphragmatic strength is only one factor for successful extubation (as measured by

DD), increased respiratory load might lead to failure, compromising the predictive strength of displacement (RSBI expresses the end product of the balance between strength and load). The present study did not find DD a useful parameter in predicting weaning outcome (AUC 0.51, $P=0.92$) when compared with the RSBI (AUC 0.97, $P<0.001$). In total, 87% of the studied patients suffered from a thoracic problem (imposing large ventilatory load), which might be why the RSBI performed better than DD. Moreover, the small size of the FG (seven of 30) may have obscured the relation between DD and weaning outcome.

Since its first description [18], sonographic DT evaluation has been carried out using high-frequency probes at the zone of apposition [9]. B-mode has been preferred over M-mode for evaluating DT [9]. Two studies (with different methodologies) have recently evaluated the concept of using DT (a surrogate for diaphragmatic strength) as a predictor index for weaning outcome. DiNino *et al.* [11] examined 63 intubated patients with ultrasonography before their first weaning trial and determined the degree of DT during tidal breathing. They found that a cutoff of 30% or more for DT was a good predictor for weaning success. However, Ferrari *et al.* [6], in their study on 46 tracheostomized patients who failed weaning at least once and underwent sonographic evaluation of DT during maximal inspiration during a weaning trial, found that a cut-off value of 36% was associated with successful weaning. Despite the different cut-off values, the two groups agreed that DT is more accurate compared with the RSBI in predicting successful extubation. They held a similar argument that the RSBI is a product of the work of diaphragm and accessory muscles (which are fatigable), whereas DT expresses the degree of the more sustainable power.

In our study, we tried to use the low-frequency probe – the available probe in our institution – to determine DT at frozen B-mode images during tidal breathing. As a proof of concept, DT could be evidenced using

this method. Our results show a significant difference between inspiratory and expiratory TDI (means 0.67 and 0.52 cm, respectively, $P < 0.001$). These values, however, are larger than the values reported from previous studies (0.24 to 0.35 cm at extremes of lung volumes) [6]. This is probably caused by the much lower resolution of low-frequency probes that make determining the exact boundaries of the muscle sheet challenging. Our data have shown that the values of DT had an AUC of 0.65, which means it can be predictive of weaning outcome with fair accuracy. Using a cut-off value of 30% or more, outcome could be predicted with 69% sensitivity and 71% specificity. This cutoff was identical to the one reported by DiNino *et al.* [11] but was smaller than that reported by Ferrari *et al.* [6] (36%). As previously discussed, this discrepancy is due to the different respiratory maneuver followed during the measurement. The rather lower sensitivity and specificity of DT in our studied patients might be due to the small size of the FG, which may have blurred the differences between the groups. Moreover, the disease profile of the studied cohort might have had an effect. It is noteworthy, however, that the range of DT found in the present study (0.16–0.62) was not far away from the values reported from researchers who used high-frequency ultrasound probe to detect DT (0.42–0.74) [18]. We thus can only conclude that examining DT using low-frequency probes needs further probing.

Among the challenges of using ultrasound-derived measurements to decide on the status of ventilatory apparatus is the considerable variability of results between different operators. It is a well-known caveat that results of ultrasonography are operator-dependent. We cannot exclude this element from being an obstacle toward getting a reproducible cut-off point to predict a certain outcome in the ICU. Another challenge inherent to measurements of minute structure (in fraction of cm) is the difficulty of reproducing exact results for serial measurements even by the same operator. With that said, our experience shows that, with enough practice, both interoperator and intraoperator fallacies can be fairly overcome.

This study has limitations. Sonographic measurements of the diaphragm were not complemented with more direct measurements of function (such as the maximal inspiratory pressure and transdiaphragmatic pressure). The small size of the FG and the relative homogeneity of the studied cohort do not allow generalization of the results.

Conclusion

Sonographically measured diaphragmatic thickening performed better than displacement in predicting value for weaning outcome. In a respiratory ICU, however, the RSBI seems to be a more reliable and accurate tool for the purpose and should be considered in every weaning protocol. Whether DT can be evaluated using low-frequency ultrasound probes needs to be validated by further studies.

Acknowledgements

Conflicts of interest

There are no conflict of interest.

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