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# Diaphragm ultrasound as a new index of discontinuation from mechanical ventilation

Giovanni Ferrari<sup>1\*</sup>, Giovanna De Filippi<sup>1</sup>, Fabrizio Elia<sup>1</sup>, Francesco Panero<sup>1</sup>, Giovanni Volpicelli<sup>2</sup> and Franco Aprà<sup>1</sup>

## Abstract

**Background:** Predictive indexes of weaning from mechanical ventilation are often inaccurate. Among the many indexes used in clinical practice, the rapid shallow breathing index is one of the most accurate. We evaluated a new weaning index consisting in the diaphragm thickening fraction (DTF) assessed by ultrasound.

**Methods:** Forty-six patients were prospectively enrolled. All patients were ventilated in pressure support through a tracheostomy tube. Patients underwent a spontaneous breathing trial (SBT) when they met all the following criteria:  $FiO_2 < 0.5$ ,  $PEEP \leq 5$  cmH<sub>2</sub>O,  $PaO_2/FiO_2 > 200$ , respiratory rate  $< 30$  breaths per minute, absence of fever, alert and cooperative, and hemodynamic stability without vaso-active therapy support. During the trial, the right hemi-diaphragm was visualized in the zone of apposition using a 10-MHz linear ultrasound probe. The patient was then instructed to perform breathing to total lung capacity (TLC) and then exhaling to residual volume (RV). Diaphragm thickness was recorded at TLC and RV, and the DTF was calculated as percentage from the following formula:  $\text{Thickness at end inspiration} - \text{Thickness at end expiration} / \text{Thickness at end expiration}$ . Also, the rapid shallow breathing index (RSBI) was calculated. Weaning failure was defined as the inability to maintain spontaneous breathing for at least 48 h, without any form of ventilatory support.

**Results:** A significant difference between diaphragm thickness at TLC and RV was observed both in patients who succeeded SBT and patients who failed. DTF was significantly different between patients who failed and patients who succeeded SBT. A cutoff value of a DTF  $> 36\%$  was associated with a successful SBT with a sensitivity of 0.82, a specificity of 0.88, a positive predictive value (PPV) of 0.92, and a negative predictive value (NPV) of 0.75. By comparison, RSBI  $< 105$  had a sensitivity of 0.93, a specificity of 0.88, a PPV of 0.93, and a NPV of 0.88 for determining SBT success.

**Conclusions:** This study shows that in our cohort of patients, the assessment of DTF by diaphragm ultrasound may perform similarly to other weaning indexes. If validated by other studies, this method may be used in clinical practice.

**Keywords:** Diaphragm; Ultrasonography; Weaning

## Background

Difficulties in weaning from mechanical ventilation are encountered in approximately 20% of patients, and more than 40% of the time passed in the intensive care unit is spent to try to wean off from mechanical ventilation [1]. Several indexes have been employed to assess the patient's ability to recover spontaneous breathing. Variables such as minute ventilation ( $V_e$ ), maximum inspiratory pressure ( $PI_{max}$ ), breathing frequency, rapid shallow breathing index (RSBI, i.e., respiratory frequency/tidal volume), tracheal airway occlusion pressure 0.1 s ( $P_{0.1}$ ), and a

combined index named CROP (compliance, rate,  $O_2$ , pressure index) have been used in common clinical practice [2]. RSBI was found to be one of the most accurate predictors of failure [3]. However, values of sensitivity and specificity and negative predictive values for the suggested threshold of rapid shallow breathing index  $< 105$  were highly variable in different studies [4-6].

The diaphragm is a fundamental respiratory muscle whose dysfunction may be very common in patients undergoing mechanical ventilation. Diaphragm dysfunction is associated to prolonged mechanical ventilation and weaning failure [7-10]. The diagnostic tools traditionally used to study diaphragm dysfunction, like fluoroscopy, phrenic nerve conduction study, and trans-diaphragmatic

\* Correspondence: giovanniferrarister@gmail.com

<sup>1</sup>High Dependency Unit, San Giovanni Bosco Hospital, P.za Donatore del Sangue 3, Turin 10154, Italy

Full list of author information is available at the end of the article

pressure measurement, present some limitations and disadvantages, including the use of ionizing radiation, low availability, invasiveness, and the need for patient transportation and skilled or specifically trained operators. Recently, ultrasound has been used to evaluate diaphragmatic function [10]. Advantages of ultrasound include safety, avoidance of radiation hazards, and availability at the bedside.

Ultrasound may be used to measure diaphragmatic excursion, the thickening of the diaphragm, and the speed of diaphragmatic contraction [10]. Among patients requiring mechanical ventilation, detection of diaphragmatic dysfunction by ultrasound performed during spontaneous breathing trial is associated with both longer weaning time and longer total ventilation time [11]. Ultrasound may be used to evaluate diaphragm excursions and also diaphragmatic thickness [9,12]. The evaluation of the diaphragmatic thickening fraction (DTF) may be helpful to assess diaphragmatic function and its contribution to respiratory workload [12]. However, to our knowledge, no studies have assessed diaphragmatic thickening as a predictor index for weaning from mechanical ventilation.

The aim of our study was to assess whether the degree of diaphragm thickening, measured by ultrasound during a weaning trial and expressed as thickening fraction, may be used to predict successful weaning.

## Methods

This was a prospective study, performed between December 2009 and December 2011 in the High Dependency Unit of the S. Giovanni Bosco Hospital in Turin, Italy. Patients were referred to our institution from the intensive care unit of our hospital after failing one or more attempts of weaning. The institutional ethic committee of the hospital approved the study. Patients gave their informed consent to participate in the study, which was conducted in accordance with the Declaration of Helsinki. Researchers involved in the study were all well trained in point-of-care ultrasound, with specific interest in lung ultrasound and diaphragm ultrasound imaging.

## Subjects

All patients were ventilated in pressure support ventilation through a tracheostomy tube. Patients underwent a spontaneous breathing trial when they met all the following criteria:  $\text{FiO}_2 < 0.5$ ,  $\text{PEEP} \leq 5 \text{ cmH}_2\text{O}$ ,  $\text{PaO}_2/\text{FiO}_2 > 200$ , respiratory rate  $< 30$  breaths per minute, absence of fever, alert and cooperative, and hemodynamic stability in the absence of any vaso-active therapy support. Subjects with diaphragm paralysis or neuromuscular diseases were excluded from the study.

## Study design

When the abovementioned criteria were reached, patients were disconnected from the tube and a spontaneous breathing trial was attempted for 1 h administering supplemental oxygen to achieve a peripheral oxygen saturation ( $\text{SpO}_2$ )  $> 94\%$ . Then, each diaphragm was evaluated by B-mode and M-mode ultrasound subcostal views to rule out abnormalities in muscle movement [13]. When dysfunction of a single hemi-diaphragm was detected, patients were excluded from the study. Hereafter, right hemi-diaphragm ultrasound scans were performed with patients lying down at a semi-recumbent position ( $45^\circ$ ). Rapid shallow breathing index and maximum inspiratory pressure (PI<sub>max</sub>) were also recorded. Weaning failure was defined as the inability to maintain spontaneous breathing for at least 48 h, without any ventilatory support. Criteria for failure to the spontaneous breathing trial were the following: change in mental status, onset of discomfort, diaphoresis, respiratory rate (RR)  $> 35$  breaths/min, hemodynamic instability (heart rate  $> 140$ , systolic blood pressure  $> 180$  or  $< 90$  mmHg), or signs of increased work of breathing [14]. Clinicians in charge of the patient's care were blinded to ultrasound measurements.

## Diaphragm ultrasound

All patients were evaluated in a semi-recumbent position. Ultrasound was performed using an Esaote MyLab 40 ultrasound system (Esaote, Genova, Italy) equipped with a 10-MHz linear probe.

Ultrasound evaluation was performed as previously described [15]. Briefly, the diaphragm was visualized by placing the transducer perpendicular to the chest wall, in the eighth or ninth intercostal space, between the anterior axillary and the midaxillary lines, to observe the zone of apposition of the muscle 0.5 to 2 cm below the costophrenic sinus. The diaphragm is imaged as a structure with three distinct layers, including two parallel echoic lines (the diaphragmatic pleura and the peritoneal membrane) and a hypoechoic structure between them (the muscle itself) [15,16]. The patient was then instructed to perform breathing to total lung capacity (TLC) and then to exhale to residual volume (RV). Several images of the diaphragm were captured and stored, including at least three at the point of maximum thickening at TLC and at least three at minimum thickening at RV.

On each frozen B-mode image, the diaphragm thickness was measured from the middle of the pleural line to the middle of the peritoneal line. Then, the DTF was calculated as percentage from the following formula:  $\text{Thickness at end inspiration} - \text{Thickness at end expiration} / \text{Thickness at end expiration}$ .

### Data analysis

Data were collected using Epi Info statistical software (Centers for Disease Control and Prevention, Atlanta, GA, USA) and analyzed using R version 2.15.0 (R Development Core Team: <http://www.R-project.org>).

Data are presented as mean (SD) or median [interquartile range] when appropriate. Descriptive statistics are shown for both the whole cohort and the subgroups of interest. Differences of continuous variables between the subgroups for the independent variable were assessed by non-parametric tests. The  $\chi^2$  test, with Fisher correction when appropriate, was used for comparisons among categorical variables. Intra-observer variability was assessed measuring diaphragm thickness at least 24 h after the first measurement. To assess inter-observer variability, 23 patients were analyzed by two different operators. Pearson correlation analysis and Bland-Altman plotting were performed to evaluate the reproducibility of diaphragm ultrasound studies. Receiver operating characteristic (ROC) curve analysis was performed to assess diaphragm DTF ability to discriminate between patients who succeeded weaning and those who failed. The Spearman coefficient was used to evaluate correlations. A two-tailed *p* value of less than 0.05 was taken to indicate statistical significance.

### Results

During the study period, 75 patients were referred to the High Dependency Unit for weaning. Two showed signs of neuromuscular disorders and were excluded from the study. The remaining 73 were analyzed. Of these, 27 were weaned while the remaining 46 failed after the first spontaneous breathing trial. Table 1 summarizes the

main clinical-demographic characteristics of the population enrolled in the study.

Ultrasound examination was feasible in all patients, including those with body mass index >30. On occasion, the presence of pleural effusion or parenchymal lung consolidation did not affect the quality of ultrasound studies targeted to diaphragm evaluation.

Diaphragm thickness differed significantly between TLC and RV in patients who succeeded spontaneous breathing trial but not in patients who failed (Figure 1). Diaphragm thickness at both TLC and RV was positively correlated with body mass index ( $\rho = 0.52$ ,  $p = 0.0008$  and  $\rho = 0.57$ ,  $p = 0.0002$ , respectively). A significant difference in DTF was observed between success and failure groups (Figure 2). A ROC curve was used to assess the diagnostic accuracy of DTF in predicting failure to the spontaneous breathing test (Figure 3). A cutoff value >36% was associated with a successful spontaneous breathing test with a sensitivity of 0.82, a specificity of 0.88, a positive predictive value (PPV) of 0.92, and a negative predictive value (NPV) of 0.75. By comparison, RSBI <105 showed a sensitivity of 0.93, a specificity of 0.88, a PPV of 0.93, and a NPV of 0.88 for determining success to the spontaneous breathing test.

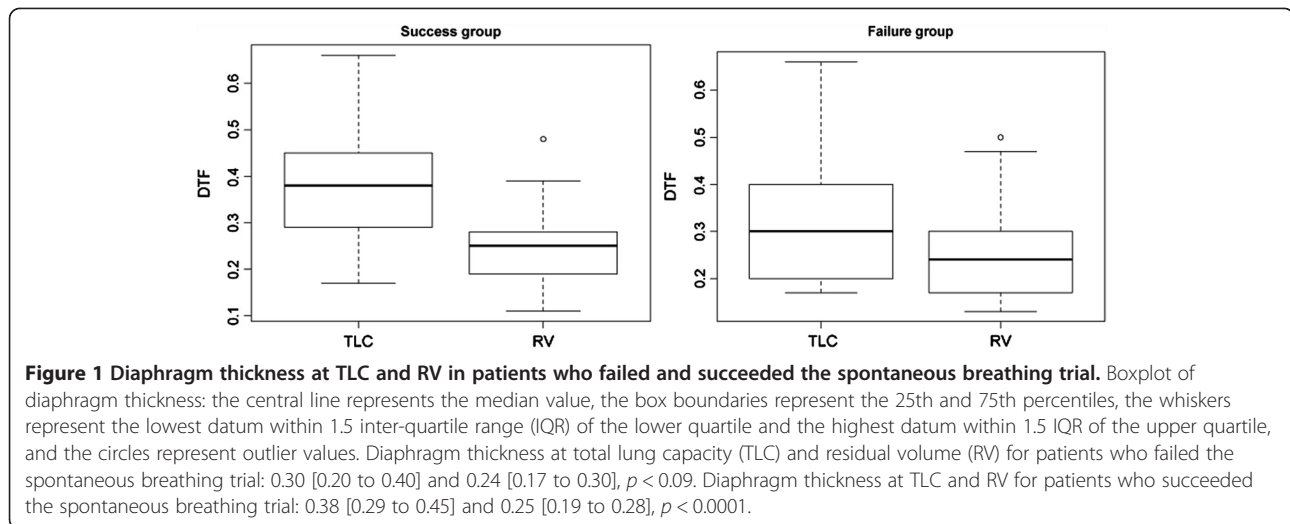
A good correlation between DTF and PImax was observed ( $\rho = 0.75$ ,  $p < 0.001$ ) (Figure 4).

Expiratory tidal volume was significantly different between success and failure groups, showing 360 ml [340 to 400 ml] vs 280 ml [236 to 300 ml], respectively, with  $p < 0.001$ . Moreover, DTF was positively correlated with expiratory tidal volume ( $\rho = 0.55$ ,  $p < 0.001$ ). The duration of ventilatory treatment and hospital length of

**Table 1 Patient characteristics**

	All (n = 46)	Success (n = 29)	Failure (n = 17)	p value
Age	64.6 (12.1)	64.3 (13.7)	65.8 (10)	0.72
Male/female	34/12			
BMI	23 [22 to 27]	24 [22 to 27]	23 [20 to 26]	0.66
SAPS II	34 [33 to 39]	33 [29 to 45]	36 [33 to 43]	0.12
$D_{TLC}$	0.34 [0.26 to 0.44]	0.38 [0.29 to 0.45]	0.30 [0.20 to 0.40]	0.08
$D_{RV}$	0.24 [0.17 to 0.30]	0.25 [0.19 to 0.28]	0.24 [0.17 to 0.30]	0.81
DTF	0.38 [0.29 to 0.44]	0.56 [0.38 to 0.64]	0.26 [0.22 to 0.30]	<0.0001
RSBI	85 [65 to 112]	70 [57 to 83]	120 [110 to 148]	<0.0001
RR	28 [18 to 58]	27 [18 to 32]	31 [24 to 58]	0.001
PImax	67.5 (23.9)	82.9 (13.6)	41.2 (11.2)	<0.0001
Vte	340 [290 to 380]	360 [260 to 700]	280 [210 to 500]	0.007
HDU length of stay	15 [11 to 23]	15 [11 to 19]	22 [15 to 28]	0.02
Duration of ventilatory treatment	28 [22 to 37]	26 [19 to 30]	37 [28 to 45]	0.011
Mortality	3	1	2	

BMI, body mass index; SAPS, Simplified Acute Physiology Score;  $D_{TLC}$ , diaphragm thickness at total lung capacity;  $D_{RV}$ , diaphragm thickness at residual volume; DTF, diaphragm thickening fraction; RSBI, rapid shallow breathing index; RR, respiratory rate; PImax, maximum inspiratory pressure; Vte, expiratory tidal volume; HDU, high dependency unit.



stay were significantly higher in patients who failed the spontaneous breathing test (Table 1).

#### Intra- and inter-observer variability

Measurements of diaphragm thickness at both TLC and RV showed significantly high intra- and inter-observer correlations ( $\rho = 0.98$ ,  $p < 0.001$  at TLC and  $r = 0.98$ ,  $p < 0.001$  at RV for intra-observer variability;  $\rho = 0.96$ ,  $p < 0.001$  at TLC and  $\rho = 0.98$ ,  $p < 0.001$  at RV for inter-observer variability).

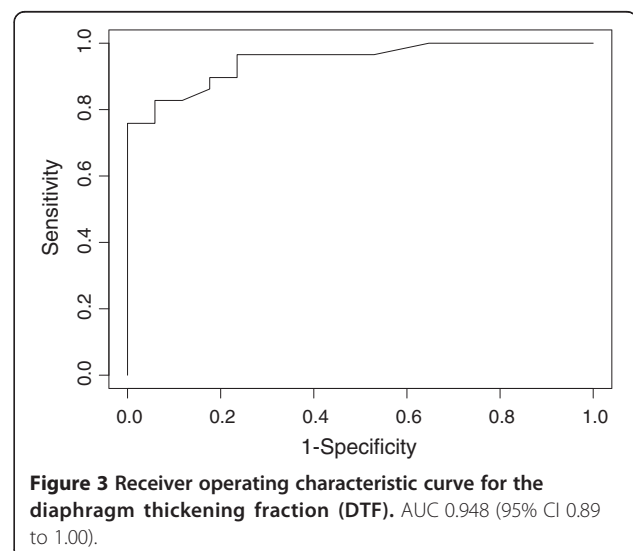
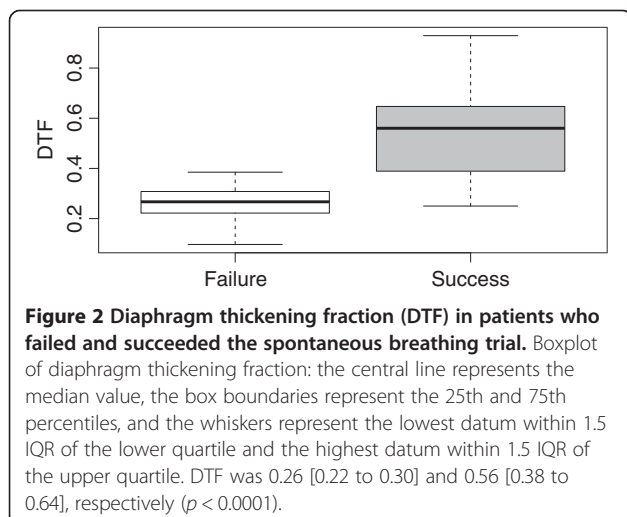
#### Discussion

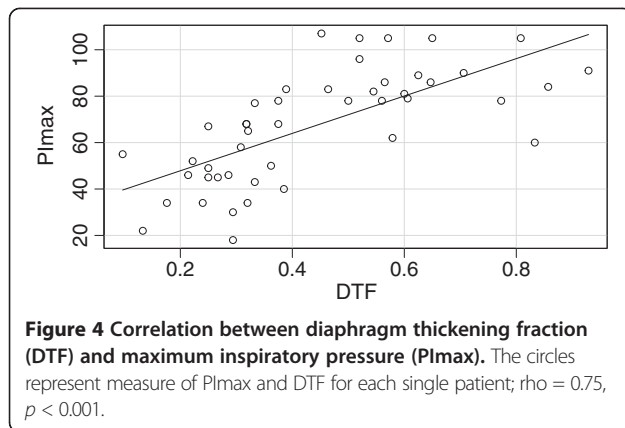
To our knowledge, this is the first study that evaluates the DTF as a predictive index of weaning after a spontaneous breathing trial. The present study shows that a DTF  $>36\%$  is associated with a successful weaning.

The important role of ultrasound in assessing diaphragm function has already been studied, but there are few data concerning the usefulness of diaphragm ultrasound evaluation as a weaning predictor.

In an elegant study, Lerolle and co-workers assessed the ultrasound criteria to determine diaphragmatic dysfunction after cardiac surgery [9]. They found that ultrasound determination of diaphragm excursion, expressed as the greater excursion of the muscle on a maximal inspiratory effort in patients requiring prolonged mechanical ventilation, may help identify those patients with severe diaphragmatic dysfunction. They also showed that their ultrasound measurement correlated well with trans-diaphragmatic pressure. However, this study was not designed to predict success of a weaning trial.

To assess the usefulness of diaphragmatic ultrasound in predicting successful weaning, Kim and co-workers





studied the amplitude of diaphragm movements [11]. A diaphragm dysfunction was diagnosed by ultrasound if an excursion  $<10$  mm or a paradoxical movement was observed. Diaphragmatic dysfunction was associated with weaning failure, and the authors conclude that ultrasound may identify patients at risk of difficult weaning.

Another ultrasound method, described since the last decade of the 1990s, is to evaluate the diaphragm thickness [15]. Ultrasound measures accurately the thickness of the muscle in the zone of apposition, with high reproducibility. Thickening ratio was reported to be a good indicator of diaphragm strength [15]. B-mode ultrasound may be used to assess the thickness of the muscle over a wide range of lung volumes from RV to TLC, as was demonstrated by Cohn and co-workers [16].

Diaphragm thickness may also be estimated in M-mode, although this method was criticized [16,17]. Nevertheless, Vivier and co-workers concluded that diaphragm thickness evaluated in M-mode is a non-invasive and reproducible ultrasound method, useful to evaluate muscle function and its contribution to respiratory workload [12]. However, the great majority of diaphragm ultrasound studies have measured diaphragm thickness in B-mode. Some evaluated the variation of thickness at different lung volumes from RV to TLC in normal subjects [15,18]. Another study measured diaphragm thickness in patients with diaphragm paralysis to monitor recovery of the muscle over time [19]. Interestingly, in this latter study, no thickening was observed by ultrasound in patients who did not recover from paralysis, thus providing useful information for both diagnosing diaphragm paralysis and indicating recovery.

We decided to measure diaphragm with B-mode ultrasound because this technique provides a greater anatomical definition of the muscle and its adjacent structures together with a more panoramic view in comparison with M-mode [16,18].

Conventional methods used to assess diaphragm function are the measurement of trans-diaphragmatic pressure (Pdi) and phrenic nerve stimulation. Also, fluoroscopy and electromyography have been largely used. However, all these methods are invasive and uncomfortable or expose the patients to radiations.

B-mode diaphragm ultrasound is a simple, rapid, reproducible, and non-invasive test that can be repeated several times without any risk for patients and provides important information on its respiratory function. Our data suggest that DTF has a potential in predicting those patients who may fail a weaning attempt, similarly to other already established weaning parameters and tests.

Our study has some limitations. The first is that, except with PImax, we did not perform a comparison with other methods that may be considered a gold standard in the assessment of diaphragmatic function, to validate ultrasound. A previous study found a good correlation between trans-diaphragmatic pressure-time product and DTF [12]. Although trans-diaphragmatic pressure-time may be considered a gold standard in studies that evaluate new tests of diaphragmatic function, it is highly invasive and uncomfortable for the patient. Furthermore, other studies already concluded that diaphragm ultrasound is a reliable method to evaluate its respiratory function, because measurements correlated well with lung volumes and with PImax [15,19]. Nevertheless, a future prospective trial comparing diaphragm ultrasound with trans-diaphragmatic pressure in patients with difficult weaning may be of high scientific interest and further validate this ultrasound method.

Another limitation of our study is the validity of the DTF cutoff that we obtained. We have studied a very selected population referred to our unit from the ICU of our hospital, after failure of a first gross attempt of weaning. This selection may only be obtained from the path specifically designed for our patients in our hospital. Our data cannot be automatically generalized to other populations of ordinary polyvalent ICUs. For this reason, other prospective studies should be designed to confirm the reliability of diaphragm US and to propose the most generalizable DTF threshold value.

## Conclusions

Ultrasound of the diaphragm is a simple method useful to evaluate the thickness of the muscle in the zone of apposition. This technique is highly feasible, harmless, and repeatable in the same patients. Assessment of DTF by diaphragm ultrasound in B-mode represents an easy-to-obtain new weaning index that, if further validated by other studies, may be introduced as a bedside method in the clinical practice.



### Competing interests

The authors declare that they have no competing interests.

### Authors' contributions

GF conceived and designed the study; acquired, analyzed, and interpreted the data; drafted the manuscript and edited it for important intellectual and scientific content; served as the principal author; and edited the internal revision. GDF and FP acquired the data. FE acquired the data and edited the internal revision. FA conceived and designed the study and edited the internal revision. GV revised the article for important intellectual content. All authors read and approved the final manuscript.

### Author details

<sup>1</sup>High Dependency Unit, San Giovanni Bosco Hospital, P.zza Donatore del Sangue 3, Turin 10154, Italy. <sup>2</sup>Department of Emergency Medicine, San Luigi Gonzaga University Hospital, Turin 10043, Italy.

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