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Original research article

Diaphragm Thickening Fraction for Predicting Weaning Success in COPD Patients

Pongpat Klumusuk[1, 2], Apichart Kanitsap[1], Pitchayapa Ruchiwit[1], Narongkorn Saiphoklang[1], Thiti Sricharoenchai[1], Pattarin Pirompanich[1,*]

[1]*Division of Pulmonary and Critical Care Medicine, Department of Medicine, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand*
[2]*Department of Medicine, Pathum Thani hospital, Pathum Thani 12120, Thailand*

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ABSTRACT

Weaning failure in mechanically ventilated chronic obstructive pulmonary disease (COPD) patients is a major concern in clinical practice. Rapid shallow breathing index (RSBI), a well-known weaning index, has some limitations in predicting weaning outcomes. Diaphragm thickening fraction (DTF) has potential benefits for improving the accuracy of weaning success prediction. The aim of this study was to evaluate the effectiveness of DTF compared to RSBI for predicting weaning success in COPD patients. This prospective study enrolled COPD patients who were ready for weaning from mechanical ventilator. Patients underwent a spontaneous breathing trial (SBT) for 1 hr, and then, both hemi-diaphragms were visualized using a 10-MHz linear probe. Diaphragm thickness was recorded at the end of inspiration and expiration. The DTF was calculated as a percentage. In addition, RSBI was calculated at 1 minute and 1 hour after SBT. Of the 24 patients enrolled, the mean (± SD) age was 80 (± 8.78) years. Twenty-two patients succeeded in weaning and the rest failed. DTF in both sides was not significantly different between patients whose weaning succeeded and whose weaning failed (right DTF: success group 67.22 ± 41.65%, failure group 44.84 ± 47.7%, $p = 0.478$). The ROC curves of the right DTF and RSBI for the prediction of successful weaning were 0.636 and 0.607, respectively, but these data were not statistically significant. In conclusion, DTF appears not to help in predicting weaning success in COPD patients. However, there was a trend toward higher right DTF in the weaning success group. (Trial registration: TCTR20201103003 registered November 01, 2020).

Keywords: Chronic obstructive pulmonary disease; Diaphragm; Diaphragm thickening fraction; Ultrasound; Weaning

***Corresponding author:** pattarin@tu.ac.th
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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide [1]. The COPD exacerbation rate ranges from 0.5 to 3.5 exacerbations per patient per year and the hospitalization rate is about 0.1 to 2.4 per patient per year [2]. In-hospital mortality makes up about 15% to 20% of acute exacerbations [3, 4] overall, and up to 36% of acute exacerbations in patients who failed extubation [4]. Weaning failure is defined as either failing a spontaneous breathing trial (SBT) or requiring reintubation within 48 hours post-extubation [5]. COPD appears to be an independent risk factor for increased duration of weaning and weaning failure, with a prevalence of 46% to 66% [6-8].

Weaning parameters frequently used in clinical practice are minute ventilation (MV), negative inspiratory force (NIF), maximum inspiratory pressure (MIP), tidal volume (VT), respiratory rate (RR), rapid shallow breathing index (RSBI) represented by the ratio of RR to VT, $P_{0.1}$/MIP represented by the ratio of airway occlusion pressure 0.1 s after the onset of inspiratory effort to maximal inspiratory pressure, and CROP (integrative index of compliance, RR, oxygenation, and pressure) [9]. Among these, RSBI is the most accurate weaning parameter;[10] however, it has relatively low specificity and can produce false positive predictions for successful weaning [11].

The diaphragm is the principal muscle of inspiration. Impaired diaphragm function can lead to respiratory complications and increased intensive care unit (ICU) length of stay [12]. Several studies have reported that diaphragm dysfunction is common during mechanical ventilation [13, 14] and is associated with a higher rate of weaning failure and mortality [15]. Point-of-care ultrasound is increasingly used in critically ill patients [16]. It can provide bedside structural and functional assessment of the diaphragm [17].

Diaphragm thickening fraction (DTF), assessed by point-of-care ultrasound, defined as the percentage change in diaphragm thickness from end expiration to peak inspiration during tidal breathing, is a reliable indicator of diaphragm contractile activity [18]. As determined from previous studies, DTF can be used to predict weaning success in mechanically ventilated patients [19-21]. In COPD, the diaphragmatic rapid shallow breathing index (D-RSBI), represented by the ratio of RR to diaphragmatic displacement, is superior to the traditional RSBI in predicting weaning outcomes [22]. Moreover, a DTF of less than 20% is associated with NIV failure and a higher mortality rate [23]. One case control study reported that DTF was significantly decreased in COPD patients and decreased with increasing severity of COPD [24]. In this study, we aim to evaluate the effectiveness of DTF as compared to RSBI, for the predicted success rate of weaning in COPD patients.

2. Material and Methods

2.1 Methods

This prospective study was performed over a 13-month period from April 2020 to April 2021 in a tertiary care teaching hospital. Mechanically ventilated patients who had underlying COPD were enrolled in this study from medical wards, medical intensive care units, cardiac care units, and respiratory care units if they were ready to wean from mechanical ventilation and could tolerate the SBT through a T-tube for 60 minutes. Approval was obtained from the ethics committee of the Faculty of Medicine, Thammasat University, Thailand (IRB No. MTU-EC-IM-1-095/63), and the study was conducted according to the Declaration of Helsinki. All patients or relatives of the patients gave written informed consent prior to participation. The principal investigator of this study (PK), a pulmonology fellow, worked with a corresponding author (PP), an intensivist well trained in point-of-care ultrasound, with a specific interest in thoracic ultrasound.

2.2 Patient selection

Inclusion criteria were age ≥ 40 years, and with an underlying COPD diagnosis according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria supported by spirometric evidence of airflow obstruction (forced expiratory volume in 1 second [FEV1]/forced vital capacity [FVC] < 0.70) when clinically stable. Other inclusion cirteria included being intubated and mechanically ventilated due to respiratory failure from any cause for more than 24 hours, and the ability to tolerate SBT for 1 hour before ultrasound. Patient readiness for weaning must have had met all the following criteria: using fraction of inspired oxygen (FIO2) < 0.5 and PEEP ≤ 5 cmH2O, PaO2/FIO2 > 200, RR ≤ 30 breaths/min, stable hemodynamics (absence or low-dose vasopressors required), good consciousness, minimal secretion, and effectiveness of cough. Exclusion criteria were having any neuromuscular diseases, diaphragmatic paralysis, or being tracheostomized.

2.3 Study design

The patients who met the aforementioned inclusion criteria were disconnected from their ventilator to SBT through T-tube flow 10 l/min for 1 hour with oxygen supplementation (FIO2 of 0.21-0.5) to achieve a pulse oxygen saturation (SpO2) ≥ 94%. Weaning parameters were measured by the attending physicians uninvolved in the study. The 1st RSBI was recorded 1 min after SBT. One hour later, the 2^{nd} RSBI was taken, along with RR, MV, MIP, and maximum expiratory pressure (MEP). MIP and MEP were measured by the same pressure gauge in all patients, in a semi-upright position; each participant was asked to perform three maneuvers and the highest pressure achieved during these maneuvers was recorded. Then, sitting in a semi-recumbent position, both diaphragms were evaluated by B-mode and M-mode ultrasound subcostal views to exclude paradoxical movement [25]. Diaphragm ultrasound scans on both sides were performed. Attending physicians were blinded to the results of ultrasound measurements.

Weaning failure is defined as either failing a spontaneous breathing trial (SBT) or requiring reintubation within 48 hours post-extubation [5]. Criteria regarding the inability for spontaneous breathing were: change in mental status, RR > 35 breaths/min, hemodynamic instability (heart rate > 140/min, systolic blood pressure > 180 or < 90 mmHg), and signs of increased effort for breathing. Weaning success was defined by the ability to maintain spontaneous breathing for at least 48 h without ventilator support and without criteria for failure of spontaneous breath.

2.4 Diaphragm ultrasound

Ultrasound was performed using a 10-MHz linear probe Philips Lumify (USA) by a single well-trained operator (PK) to minimize inter-observer variability. The patients were in a semi-recumbent position. The transducer was placed vertically to the chest wall, at the eighth or ninth intercostal space, between the anterior axillary and the mid-axillary lines, to observe the zone of apposition of the muscle 0.5 to 2 cm below the costophrenic sinus [26]. The inferior border of the costophrenic sinus can be determined based on the level of lung artifact caused by ultrasound reflecting off air in the lung.

The diaphragm structure has three layers (Fig. 1): two parallel hyperechoic lines (diaphragmatic pleura and the peritoneal membrane) and a hypoechoic structure between them (muscle). All patients were asked to deeply inhale to total lung capacity (TLC) and then fully exhale to residual volume (RV). Diaphragm images were captured, stored, and analyzed to measure maximum diaphragm thickening at TLC and minimum diaphragm thickening at RV, in the same breath. On B-mode, diaphragm thickness was measured from the middle of the pleural line to the middle of the peritoneal line. Then, the DTF percentage was calculated by the following formula: thickness at the end of inspiration minus thickness at the end of expiration, divided by thickness at the end of expiration, then multiplied by 100 [27]. DTF was measured from three breaths on each side and the mean was used for analysis.

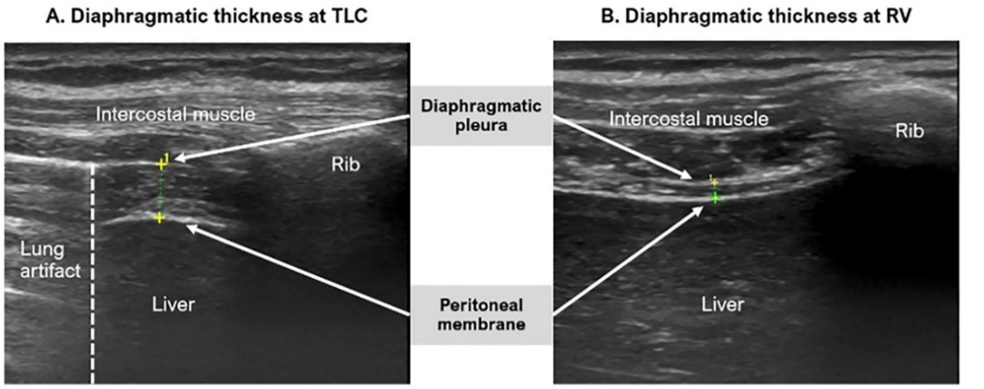

Fig. 1. Diaphragmatic ultrasound showing three layers of diaphragm and diaphragmatic thickness at total lung capacity (TLC) in (a) and residual volume (RV) in (b).

3. Results

A total of 24 COPD patients were enrolled, of which 20 (83.3%) were male. The mean age was 80 (± 8.78) years and the mean body mass index (BMI) was 21.16 (± 3.32) kg/m^2. From the total number of patients, 8 (33.3%) patients received ICS/LABA/LAMA, 9 (37.5%) patients received ICS/LABA, 2 (8.3%) patients received LABA/LAMA, and 3 (12.5%) patients received LAMA only. All participants received mechanical ventilation through the endotracheal tube and showed readiness for weaning. Twenty-two (91.6%) patients were successfully weaned from the mechanical ventilator. The baseline characteristics were not significantly different between the weaning success and failure groups, as shown in Table 1.

Table 1. Baseline characteristics.

Parameters (mean ± SD)	All (n=24)	Success (n=22)	Failure (n=2)	p value
Sex				
Male	20 (83.3)	19 (86.4)	1 (50)	0.312
Female	4 (16.7)	3 (13.6)	1 (50)	0.312
Age (years)	80.00 ± 8.78	79.23 ± 8.71	88.50 ± 4.95	0.157
Weight (kg.)	55.26 ± 11.09	56.08 ± 10.58	46.25 ± 17.32	0.238
Height (cm.)	161.00 ± 7.00	161.55 ± 6.82	155.00 ± 8.49	0.213
BMI (kg/m^2)	21.16 ± 3.32	21.38 ± 3.18	18.78 ± 5.35	0.299
Number of exacerbations in previous year				
0	13 (54.2)	11 (50)	2 (100)	1.000
1	8 (33.3)	8 (36.4)	0 (0)	1.000
2	2 (8.3)	2 (9.1)	0 (0)	1.000
4	1 (4.2)	1 (4.5)	0 (0)	1.000
Number of intubations due to exacerbation in previous year				
0	21 (87.5)	19 (86.4)	2 (100)	0.422
1	3 (12.5)	3 (13.6)	0 (0)	1.000

Current medications				
ICS/LABA/LAMA	8 (33.3)	8 (36.4)	0 (0)	1.000
ICS/LABA	9 (37.5)	8 (36.4)	1 (50)	1.000
LABA/LAMA	2 (8.3)	2 (9.1)	0 (0)	1.000
LAMA	3 (12.5)	2 (9.1)	1 (50)	0.239
Underlying diseases				
Hypertension	15 (62.5)	14 (63.6)	1 (50)	1.000
Dyslipidemia	12 (50.0)	11 (50.0)	1 (50)	1.000
Benign prostatic hyperplasia	8 (33.3)	8 (36.4)	0 (0)	1.000
Atrial fibrillation	5 (20.8)	5 (22.7)	0 (0)	1.000
Diabetes mellitus	4 (16.7)	4 (18.2)	0 (0)	0.504
Old pulmonary tuberculosis	4 (16.7)	4 (18.2)	0 (0)	0.504
Bronchiectasis	4 (16.7)	3 (13.6)	1 (50)	0.312
Chronic kidney disease	4 (16.7)	3 (13.6)	1 (50)	0.312
Coronary artery disease	4 (16.7)	3 (13.6)	1 (50)	0.312
Stroke	1 (4.2)	1 (4.5)	0 (0)	0.230
Malignancy	1 (4.2)	1 (4.5)	0 (0)	0.230
Spirometric parameters				
Post BD FEV1/FVC (%)	53.72 ± 12.32	52.09 ± 12.27	64.28 ± 7.74	0.204
Post BD FEV1 (L.)	1.11 ± 0.51	1.06 ± 0.52	1.40 ± 0.37	0.402
Post BD FEV1 (%)	60.41 ± 29.94	55.08 ± 28.52	95.05 ± 4.31	0.077
Ventilator days (days)	4.38 ± 2.34	4.18 ± 2.30	6.50 ± 2.12	0.185

DTF, in both sides, was not significantly different between patients whose weaning succeeded and whose weaning failed (right DTF: success group 67.22 ± 41.65%, failure group 44.84 ± 47.7%, p = 0.478; left DTF: success group 57.50 ± 33.14%, failure group 97.30 ± 50.92%, p = 0.135), as shown in Fig. 2. In addition, maximum and minimum diaphragm thickness alone did not have a statistically significant difference between groups (right diaphragm: p = 0.125 and 0.127, respectively; left diaphragm: p = 0.657 and 0.948, respectively), as shown in Table 2. There was no significant correlation between right DTF and MIP, post BD FEV1 or post BD FEV1/FVC (r = 0.123, -0.293, 0.085, p = 0.718, 0.290, 0.764, respectively).

The ROC curves of right and left DTF and the second RSBI for the prediction of successful weaning were 0.636, 0.237, and 0.607, respectively, though these results were not statistically significant p = 0.531, 0.231 and 0.623, respectively, as shown in Table 3. The best cutoff value for predicting weaning successfulness of right DTF was not identified.

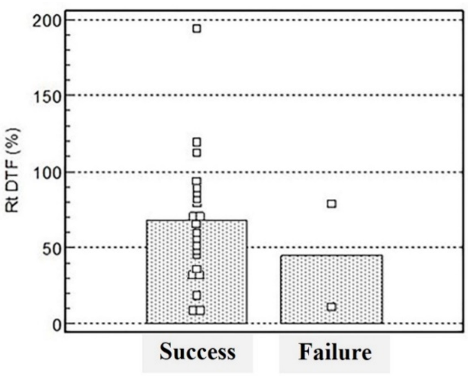

Fig. 2. Dot plot of the right diaphragm thickening fraction (Rt DTF) in weaning success and failure groups (success group 68.11 ± 45.76%, failure group 44.84 ± 47.70%, p = 0.507).

Table 2. Weaning parameters.

Parameters	All	Success	Failure	p value
1st RSBI (breaths/min/L)	50.02 ± 14.91	51.84 ± 14.17	30	0.171
2nd RSBI (breaths/min/L)	57.83 ± 19.63	58.25 ± 20.22	53.40 ± 16.11	0.746
Maximum right DT (mm)	4.3 ± 1.9	4.4 ± 1.9	2.3 ± 0.4	0.125
Minimum right DT (mm)	2.6 ± 0.9	2.6 ± 0.9	1.6 ± 0.3	0.127
Right DTF (%)	65.36 ± 41.51	67.22 ± 41.65	44.84 ± 47.70	0.478
Maximum left DT (mm)	3.7 ± 1.7	3.7 ± 1.7	4.3 ± 1.1	0.657
Minimum left DT (mm)	2.4 ± 1.2	2.4 ± 1.2	2.3 ± 1.1	0.948
Left DTF (%)	61.29 ± 35.51	57.50 ± 33.14	97.30 ± 50.92	0.135
RR (breaths/min)	19.94 ± 3.80	19.67 ± 3.77	24	0.285
MV (L)	7.45 ± 2.36	7.36 ± 2.41	8.89	0.548

Data shown as mean ±SD

SD; standard deviation, RSBI; rapid shallow breathing index, DT; diaphragmatic thickness, DTF; diaphragmatic thickness fraction, RR; respiratory rate, MV; minute ventilation.

Table 3. Receiver operating characteristic (ROC) analysis.

	AUC	95%CI.	p-value
Right DTF (%)	0.636	0.23 - 1.00	0.531
Left DTF (%)	0.237	0.00 - 0.54	0.231
1st RSBI	1.000	1.00 - 1.00	0.111
2nd RSBI	0.607	0.34 - 0.87	0.623

DTF; diaphragmatic thickness fraction, RSBI; rapid shallow breathing index

4. Discussion

The European Respiratory Society statement on thoracic ultrasound states that low DTF was reproducible and a good predictor of weaning outcome [28]. However, a large multicenter randomized controlled trial was not able to demonstrate a difference in DTF between successful and unsuccessful extubation patients [29]. Most of the study population of the previous study was a mix of critically ill patients, and data on COPD patients are scant. Our study, done specifically in COPD patients, revealed no significant difference of right DTF between cases of successful and failed weaning.

Several studies in stable COPD patients were not able to demonstrate a correlation between DTF and symptoms, symptom severity, lung function, or risk of exacerbation [30, 31]. A study in stable COPD patients from our group revealed that the mean right DTF was relatively high compared to the normal population (140% and 105%, respectively) [30, 32]. The increased baseline DTF in stable COPD, from increased work of breathing, might have lead to the negative result found in this study.

In contrast, diaphragm force reserve ratio assessed by 1-(DTF during resting breathing/maximal DTF) was lower in COPD patients than in control healthy subjects, and it fell with decreasing lung function, which suggests an increased diaphragm workload in more severe patients [33]. A recent study demonstrated reduced DTF during acute exacerbation of COPD compared to recovery after exacerbation [31]. The inconsistency of the data might suggest heterogeneity in COPD phenotypes; the emphysematous type might result in air trapping which could impair diaphragm function, while the chronic bronchitis type might not affect diaphragm function.

Ultrasound is a noninvasive bedside test that becomes an extension of the physical examination in clinical practice. However, due to the fact that ultrasound is an operator-dependent method, some important techniques were used to decrease variation. First, the patients' posture was identical and anatomical landmarks were employed for probe positioning. Second, measurements of diaphragm thickness at TLC and RV were conducted intra-breath to decrease effort variation between breaths. Following this same technique, a previous study reported a high degree of inter-observer correlation on both sides of the diaphragm [21].

There were some limitations in this study. First, the COVID-19 outbreak in Thailand, beginning in April 2020, lead to mask wearing, increased hygienic practices, and social distancing, which could have contributed to the lower rate of COPD exacerbations observed [34, 35]. Second, the small sample size, especially in the weaning failure group, did not produce high enough statistical power that would be needed to confirm any difference between the two groups. Third, both participants in the failure group were re-intubated due to delirium and agitation the next day after extubating, which is not associated with impaired diaphragm function. Fourth, our participants were quite old, which could have affected diaphragm function, ultimately producing the negative study results we reported.

5. Conclusion

DTF appears not to help in predicting weaning success in COPD patients. However, there was a trend toward higher right DTF in the weaning success group. A larger study population is required to confirm these results. Future research would likely benefit from including younger patients and healthy control patients as well.

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