The evolution of diaphragm activity and function determined by ultrasound during spontaneous breathing trials

Nuttapol Rittayamai *, Sivaporn Hemvimon, Nitipatana Chierakul

Division of Respiratory Disease and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

A B S T R A C T

Purpose: Rapid shallow breathing index (RSBI) is a commonly used index for predicting the outcome of spontaneous breathing trial (SBT). Ultrasound is a non-invasive technique for assessing diaphragm activity and function. This study aimed to investigate changes in diaphragm activity during SBT, and to compare diaphragm function between patients with and without SBT success.

Materials and methods: Forty-five patients undergoing SBT were enrolled. Thickening fraction of the diaphragm was assessed during tidal breathing ($TFdi_{tidal}$), and RSBI was measured during 30 min of SBT. Diaphragm function measured by maximum TFdi ($TFdi_{max}$) and diaphragmatic excursion (DE_{max}) was also evaluated.

Results: $TFdi_{tidal}$ and RSBI significantly increased during SBT ($TFdi_{tidal0}$ *vs.* $TFdi_{tidal30}$ = 29.8 ± 13.8 *vs.* 37.4 ± 13.0%; $p < .001$, and $RSBI_0$ *vs.* $RSBI_{30}$ = 64.8 ± 25.9 *vs.* 70.8 ± 29.1 breaths/min/L; $p = .034$). In SBT failure ($n = 13$), there was no significant difference in $TFdi_{tidal}$ compared to SBT success, except at the beginning of the trial ($p = .043$); however, RSBI significantly increased throughout SBT. No differences in $TFdi_{max}$ or DE_{max} were observed between groups.

Conclusions: Patient inspiratory efforts significantly increased during SBT. $TFdi_{tidal}$ measured by diaphragm ultrasound could not distinguish between patients with SBT success and failure. RSBI was significantly higher during SBT in patients with SBT failure.

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1. Introduction

Weaning from mechanical ventilation is an important process after patient recovery from acute respiratory failure, and it is a process that may account for approximately 40% of the total duration of mechanical ventilation. Weaning can be divided into two parts, including 1) assessment of readiness to wean, and 2) spontaneous breathing trial (SBT) [1]. Several parameters have been used to assess pulmonary function and to predict weaning success, including respiratory rate, minute ventilation, vital capacity, and rapid shallow breathing index (RSBI) [2]. RSBI, which is the ratio of respiratory frequency divided by average tidal volume in one minute, is the most accurate and commonly used parameter in

routine clinical practice [3]. The cut-off point below 105 breath/min/L can predict the likelihood of successful weaning from mechanical ventilation [4]. Once the patient is ready to wean, SBT should be performed as a diagnostic test to determine the likelihood of successful weaning [5]. Several SBT techniques can be used, including T-tube, flow-by technique, or low-level pressure support for 30–120 min. Each of these 3 techniques may have different impact on inspiratory effort and clinical outcome [6-8].

In mechanically ventilated patients, the diaphragm can develop atrophy and weakness leading to prolonged duration of mechanical ventilation. Many studies reported a high prevalence of diaphragm dysfunction during weaning, and it was found to be associated with poorer clinical outcomes [9-11]. Several factors are associated with the development of diaphragm dysfunction, including inappropriate pressure support setting, days of mechanical ventilation, and use of sedative drugs and neuromuscular blocking agents [12,13]. Fluoroscopy, measurement of transdiaphragmatic pressure, and electrical activity of the diaphragm are all techniques that can be used to evaluate the diaphragm; however, these techniques are not easy to perform at bedside. In contrast, diaphragm ultrasound is a non-invasive, real-time, and widely available technique for assessing the activity and function of the diaphragm, and it is being used with increasing frequency in mechanically ventilated patients. Assessment of diaphragm activity by

measuring the thickening fraction of the diaphragm during tidal breathing ($TFdi_{tidal}$) was shown to be well correlated with the effort exerted by the diaphragm during breathing as measured by diaphragmatic pressure-time product (PTP_{di}) [14]. Measurement of maximum TFdi ($TFdi_{max}$) and diaphragmatic excursion (DE_{max}) has also been used to evaluate diaphragm function. However, few studies have evaluated diaphragm activity using diaphragm ultrasound during the course of SBT. The objectives of this study were to evaluate changes in diaphragm activity by serial measurement of $TFdi_{tidal}$ and RSBI during the course of SBT, to compare changes in $TFdi_{tidal}$ between patients with SBT success and SBT failure in comparison to RSBI, to evaluate diaphragm function between patients with SBT success and patients with SBT failure, and to assess the effect of duration of mechanical ventilation on diaphragm function.

2. Materials and methods

2.1. Subjects and study design

A prospective cohort study (Thai Clinical Trial Registry #TCTR20160808001) was conducted at the Respiratory Intensive Care Unit, Division of Respiratory Disease and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during the August 2016 to February 2017 study period. The protocol for this study was approved by the Siriraj Institutional Review Board (COA no. 358/2559[EC3]). Written informed consent to participate was obtained from each subject or their relatives.

Patients who met all of the following criteria were eligible for inclusion: 1) age ≥ 18 years; 2) receiving pressure support ventilation; and, 3) readiness to wean in addition to meeting all of the following criteria: fraction of inspired oxygen (FiO_2) ≤ 0.5, positive end-expiratory pressure (PEEP) ≤ 8 cmH_2O, partial pressure of oxygen in arterial blood (PaO_2)/FiO_2 ratio ≥ 200, respiratory rate ≤ 30/min, stable hemodynamics, and cooperative. Patients with diaphragm paralysis, neuromuscular diseases, or Glasgow Coma Scale score ≤ 8 were excluded.

2.2. Study protocol

All patients were positioned at a head-of-bed elevation of 30–45 degrees throughout the study. During SBT, patients were ventilated using flow-by technique with pressure support and PEEP at 0 cmH_2O for 30 min. FiO_2 was set at the same level used prior to SBT. The criteria for SBT failure included agitation, diaphoresis, decreased level of consciousness, cyanosis, systolic blood pressure > 180 mmHg, diastolic blood pressure < 90 mmHg, respiratory rate > 35 breaths/min, and/or heart rate > 140 beats/min [1].

Baseline characteristics that were recorded included age, gender, Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, co-morbidity, reason for intubation, and Richmond Agitation Sedation Scale (RASS) score. RSBI was recorded at 0, 5, 10, 15, and 30 min of SBT. The average of 3 consecutive RSBI values displayed on the ventilator at each time point was recorded. At the completion of the SBT, the attending physician decided to continue the SBT, resume mechanical ventilation, or extubate the patient.

Ultrasonography was performed by two investigators (NR and SH), both of whom are experienced in diaphragm ultrasonography using the Vivid e ultrasound system (GE Healthcare, Chicago, IL, USA). Diaphragm thickness (Tdi) was measured in the zone of apposition between the right 8th and 10th intercostal spaces at the anterior- to mid-axillary line [15] using a 10 MHz linear probe in the M-mode. The diaphragm was identified as a low echogenic structure located between parietal pleura and the peritoneum (Fig. 1a). Tdi was measured at the end of both inspiration and expiration. Thickening of the diaphragm was calculated using the following formula: [Tdi at the end of inspiration - Tdi at the end of expiration]/Tdi at the end of expiration.

Diaphragmatic excursion was measured using a 5 MHz cardiac probe at the right subcostal area between the mid-clavicular and anterior axillary line. The diaphragm was identified by the hyperechoic line attached to the liver (Fig. 1b). The amplitude of its movement during respiration in the M-mode was defined as diaphragm excursion.

2.3. Assessment of diaphragm activity and function

Diaphragm activity, which represents patient inspiratory effort [14,16], was assessed by measuring thickening of the diaphragm during tidal breathing ($TFdi_{tidal}$). $TFdi_{tidal}$ was measured at 0, 5, 10, 15, and 30 min of SBT. The average of 3 $TFdi_{tidal}$ values from 3 consecutive breaths at each time point was recorded.

Diaphragm function was assessed during coached maximum inspiratory effort. Maximum thickening of the diaphragm ($TFdi_{max}$) and diaphragmatic excursion (DE_{max}) were measured before starting the SBT.

2.4. Outcomes

The primary outcomes were changes in $TFdi_{tidal}$ and RSBI during the 30-minute SBT. The secondary outcomes were 1) changes in $TFdi_{tidal}$ between patients with SBT success and patients with SBT failure compared to RSBI, 2) $TFdi_{max}$ and DE_{max} compared between patients with SBT success and patients with failure, and 3) diaphragm function compared between patients who were ventilated <7 days and patients who were ventilated ≥7 days.

2.5. Sample size calculation and statistical analysis

Based on the results of a previous study [17], the proportion of patients who had $TFdi_{max}$ > 30% in the SBT success group and the SBT failure group was 80% and 30%, respectively. For this study, we postulated a
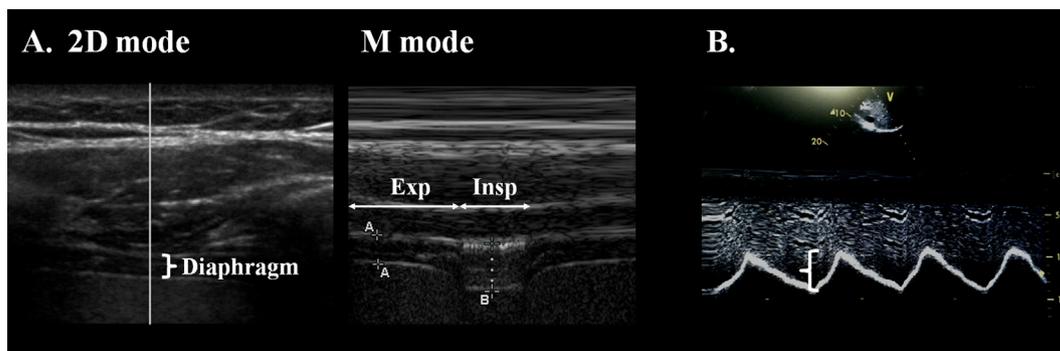
Fig. 1. Diaphragm ultrasound. A) Measurement of diaphragm thickness at the end of inspiration (Insp) and expiration (Exp) (double arrowhead) in the 2D mode and the M-mode. B) Measurement of diaphragm excursion in the M-mode (bracket).

SBT success to SBT failure ratio of 2:1. Using a 2-sided α value of 0.05 and a power of 90%, a minimum sample size of 41 subjects was calculated. To compensate for patients that would withdraw or have to be withdrawn from the study for any reason, we increased the sample size by approximately 10% to 45 patients.

Demographic and clinical characteristics were summarized using descriptive statistics. Continuous variables are expressed as mean ± standard deviation, and categorical variables shown as frequency and percentage. Chi-square test or Fisher's exact test was used to compare categorical variables, and Student's *t*-test or Mann-Whitney *U* test was used to compare continuous variables. A two-sided *p*-value <.05 was regarded as being statistically significant. All statistical analyses were performed using PASW Statistics version 18 (SPSS, Inc., Chicago, Illinois, USA).

3. Results

Forty-five patients were enrolled in this study. Mean age was 70 ± 13 years, and 66.7% of patients were men. Nearly half of enrolled subjects had underlying pulmonary disease. The average ± standard deviation duration of mechanical ventilation before enrollment was 7 ± 4 days. Other baseline characteristics are presented in Table 1. Thirty-two patients (71.2%) successfully passed SBT, and all of them were extubated. The rate of reintubation within 48 h was 15.6% (5/32 patients). Overall 28-day mortality in our study was 13.3% (6/45 patients).

3.1. Changes in thickening fraction of the diaphragm during tidal breathing, and rapid shallow breathing index during spontaneous breathing trial

During SBT, $TFdi_{tidal}$ significantly increased from 29.8 ± 13.8% at the start of SBT to 37.4 ± 13.0% at the end of SBT ($p < .001$). RSBI also significantly increased during the course of SBT ($RSBI_0$: 64.8 ± 25.9 *vs.* $RSBI_{30}$: 70.8 ± 29.1 breaths/min/L; $p = .034$). All data relating to $TFdi_{tidal}$ and RSBI during 30 min of SBT are shown in Table 2.

3.2. Changes in thickening fraction of the diaphragm during tidal breathing, and rapid shallow breathing index compared between SBT success and SBT failure

Thirteen of forty-five patients (28.8%) were classified as SBT failure. No significant difference was observed between groups for baseline characteristics or ventilator days before enrollment (Table 3).

At the beginning of the trial, $TFdi_{tidal}$ was significantly higher in the SBT failure group than in the SBT success group (36.3 ± 16.4 *vs.* 27.1

Table 1
Baseline demographic and clinical characteristics ($N = 45$).

Age, years	70 ± 13
Male gender, n (%)	30 (66.7%)
Underlying disease, n (%)	
Pulmonary disease	22 (48.9%)
Cardiovascular disease	15 (33.3%)
Neurological disease	18 (40.0%)
Renal disease	14 (31.1%)
Malignancy	6 (13.3%)
Ventilator days before enrollment,	7 ± 4
APACHE II score	12.1 ± 3.5
SOFA score	3.2 ± 1.7
RASS score	−0.3 ± 0.5
Cause of respiratory failure, n (%)	
Hypoxemic respiratory failure	33 (73.3%)
Airway protection	5 (11.1%)
Hypercapnic respiratory failure	4 (8.9%)
Shock	3 (6.7%)
Glasgow Coma Scale	14.0 ± 1.0

Continuous variables are presented as mean ± SD and categorical variables are presented as absolute value (%). *APACHE;* acute physiologic and chronic health evaluation, *RASS;* Richmond agitation and sedation scale, *SOFA;* sequential organ failure assessment.

Table 2
Changes in thickening fraction of the diaphragm during tidal breathing ($TFdi_{tidal}$), and changes in rapid shallow breathing index (RSBI) during 30 min of spontaneous breathing trial.

Parameters	Time 0	Time 5	Time 10	Time 15	Time 30	p
$TFdi_{tidal}$, %	29.8 ± 13.8	35.2 ± 17.5*	36.3 ± 15.0*	38.1 ± 15.6*	37.4 ± 13.0*	**<0.001**
RSBI, breaths/min/L	64.8 ± 25.9	72.2 ± 26.5#	70.1 ± 32.5#	69.3 ± 32.2#	70.8 ± 29.2#	**0.003**

Data are presented at mean ± SD.
* and # $p < .05$ compared to the value at Time 0.

± 11.8%, respectively; $p = .043$). However, no difference was observed for $TFdi_{tidal}$ between groups at any of the other evaluated time points (Table 3 and Fig. 2).

In addition, we found that patients who had a $TFdi_{tidal}$ value within the range of 20–50% at 5 min of SBT (which is within normal range in healthy subjects at rest) had a significantly higher rate of SBT success than patients who had a $TFdi_{tidal}$ value outside of this range at 5 min of SBT (odds ratio [OR]: 5.5, 95% confidence interval [95% CI]: 1.8–17.0; $p = .001$).

At the start of SBT, RSBI was significantly higher in the SBT failure group than among patients with SBT success (80.6 ± 2.7 *vs.* 57.1 ± 20.1 breaths/min/L, respectively; $p = .005$) (Table 3). RSBI was also significantly greater throughout SBT in patients with SBT failure than in patients with SBT success (Fig. 3).

3.3. Diaphragm function compared between SBT success and SBT failure, and between patients ventilated <7 days and those ventilated ≥7 days

No significant differences in $TFdi_{max}$ and DE_{max} were found between patients who failed SBT compared to patients with SBT success (40.4 ± 23.6 *vs.* 42.9 ± 15.7%; $p = .68$, and 1.98 ± 0.88 *vs.* 2.49 ± 0.85 cm.; $p = .078$ – all respectively).

Regarding mechanical ventilation before enrollment, we found a significantly higher DE_{max} in patients who were ventilated for <7days (n=25) before enrollment compared to those who were on mechanical ventilation for at least 7 days prior to enrollment (2.68 ± 0.90 *vs.* 1.92 ±

Table 3
Clinical parameters and outcomes between spontaneous breathing trial (SBT) success and failure. Bold indicates statistically significant difference (p < 0.05) between SBT success and SBT failure.

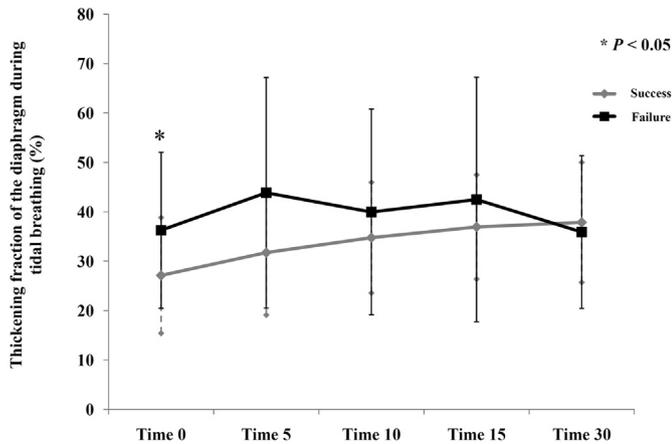| Clinical parameters	SBT success ($n = 32$)	SBT failure ($n = 13$)	p
Age, years	70 ± 11	70 ± 18	0.98
Male, n (%)	22 (68.8%)	7 (53.9%)	0.34
APACHE II score	12.1 ± 3.3	11.9 ± 4.1	0.84
SOFA score	3.1 ± 1.9	3.7 ± 1.1	0.17
Ventilator days before enrollment, days	6 ± 3	9 ± 5	0.09
Maximum diaphragm excursion, cm.	2.49 ± 0.84	1.98 ± 0.88	0.07
$TFdi_{max}$, %	42.9 ± 15.7	40.4 ± 23.6	0.68
$TFdi_{tidal}$, %			
At 0 min	27.1 ± 11.8	36.3 ± 16.4	**0.04**
At 5 min	31.7 ± 12.8	43.9 ± 24.1	0.11
At 10 min	34.7 ± 11.4	40.0 ± 21.7	0.40
At 15 min	36.8 ± 10.7	42.5 ± 26.1	0.50
At 30 min	37.7 ± 12.4	35.8 ± 16.7	0.70
RSBI, breaths/min/L			
At 0 min	58.1 ± 19.5	80.6 ± 32.7	**0.007**
At 5 min	64.2 ± 19.2	91.9 ± 32.1	**0.010**
At 10 min	57.9 ± 21.1	100.2 ± 36.5	**0.001**
At 15 min	61.0 ± 25.5	95.9 ± 38.0	**0.019**
At 30 min	63.2 ± 21.9	105.5 ± 34.7	**<0.001**

Continuous variables are presented as mean ± SD and categorical variables are presented as absolute value (%). *APACHE*; acute physiologic and chronic health evaluation, *RSBI*; rapid shallow breathing index, *SBT*; spontaneous breathing trial, $TFdi_{max}$; maximum thickening fraction of the diaphragm, $TFdi_{tidal}$; thickening fraction of the diaphragm at tidal breathing, *SOFA*; sequential organ failure assessment.
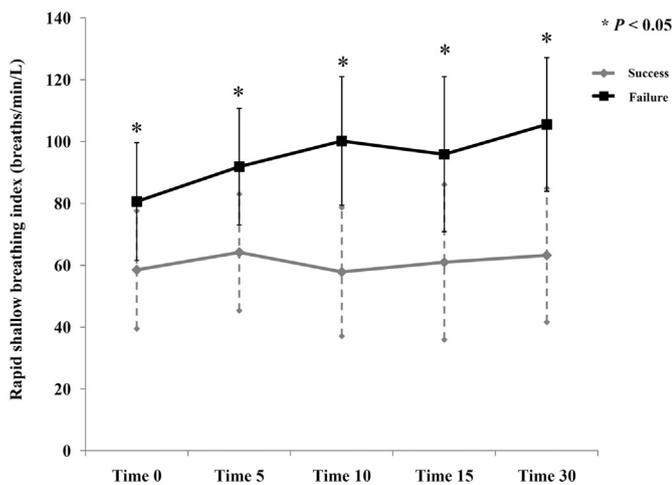
Fig. 2. Thickening fraction of the diaphragm during tidal breathing between spontaneous breathing trial (SBT) success (grey line) and failure (black line). *Indicates statistically significant difference ($p < .05$) between SBT success and SBT failure.

0.64 cm., respectively; $p = .003$). No difference in $TFdi_{max}$ was found between patients with shorter pre-enrollment ventilator days (< 7 days) compared to patients who were pre-enrollment ventilated for at least 7 days (46.0 ± 18.9 vs. $37.3 \pm 16.2\%$; $p = .109$).

4. Discussions

In our study, diaphragm ultrasound was used to evaluate diaphragm activity by serial measurement of $TFdi_{tidal}$ during the course of SBT, and to evaluate diaphragm function in mechanically ventilated subjects. We found $TFdi_{tidal}$ and RSBI to be significantly increased during the 30 min of SBT. However, no difference in $TFdi_{tidal}$ was observed between patients with SBT success and patients with SBT failure, except for time point 0 at the beginning of the trial. In contrast, RSBI was significantly greater throughout the SBT in patients with SBT failure than in those with SBT success. Furthermore, no difference in diaphragm function relative to $TFdi_{max}$ and DE_{max} was found between the success and failure groups.

Diaphragm ultrasound is a non-invasive and useful technique for assessing the activity and function of the diaphragm in mechanically ventilated patient [18]. Measurement of Tdi and $TFdi_{tidal}$ using diaphragm ultrasound was shown to be feasible and highly reproducible in ventilated subjects [19]. In addition, a study by Vivier et al. [14] has demonstrated strong correlation between $TFdi_{tidal}$ and PTP_{di} in 12

Fig. 3. Change in rapid shallow breathing index between spontaneous breathing trial (SBT) success (grey line) and failure (black line). *Indicates statistically significant difference ($p < .05$) between SBT success and SBT failure.

subjects that required non-invasive ventilation after extubation. A study by Goligher EC and colleagues [12] reported changes in Tdi to be very common during the first week of mechanical ventilation, and that changes in Tdi are associated with changes in ventilator driving pressure. Our study showed that $TFdi_{tidal}$ significantly increased during the course of SBT, which represented an increase in diaphragmatic workload and patient inspiratory effort. Change in $TFdi_{tidal}$ during SBT in our study was also correlated with change in RSBI. Increased patient inspiratory effort during SBT can be explained by several mechanisms, including higher airway resistance from endotracheal tube or secretion [20,21], decreasing lung compliance due to pulmonary congestion [22,23], and diaphragm muscle weakness [9,24,25]. We, therefore, hypothesized that serial measurement of $TFdi_{tidal}$ may be used as a surrogate marker for assessing increase in patient inspiratory effort during SBT.

We found that 28.8% of subjects in our study experienced SBT failure. We found $TFdi_{tidal}$ at the beginning of SBT to be significantly higher in the failure group than in the success group, and this may be explained by increased diaphragmatic workload and increased patient inspiratory effort due to the aforementioned reasons. However, there was no significant difference in $TFdi_{tidal}$ at the end of SBT between groups. Regarding RSBI, which is a gold standard metric and the most reliable index, we found significantly higher values during the course of SBT in patients with SBT failure compared to those who experiences SBT success. The discrepancy between changes in $TFdi_{tidal}$ and RSBI in patients who failed SBT might be explained by diaphragm muscle fatigue and the recruitment of other accessory inspiratory muscles, such as sternocleidomastoid, scalene, and intercostal muscles to compensate for excessive workload [26]. $TFdi_{tidal}$ in patients with SBT failure did not further increase or even decrease during SBT. RSBI represents the complex interaction among neural drive, the loads, and the capacity of all respiratory muscles. Not surprisingly, we observed increased RSBI during SBT in patients with SBT failure. Other studies also reported that patients with SBT failure had a significant increase in RSBI [27,28]. However, a study by Jubran, et al. in 31 patients with COPD during weaning trials found esophageal pressure-time product (PTP_{es}) to be significantly increased during the course of SBT in patients with weaning failure. Those authors mentioned increased patient inspiratory effort compared to patients with successful weaning, but there was no significant difference in RSBI between patients with SBT success and patients with SBT failure [21]. These studies confirm our hypothesis that $TFdi_{tidal}$ specifically represents diaphragm workload, whereas RSBI reflects overall patient inspiratory effort comprehensively performed by all inspiratory muscles. Thus, measuring $TFdi_{tidal}$ using diaphragm ultrasound could be useful for assessing patient inspiratory effort during SBT, but it might be inferior to RSBI (which is a simple index that is practical and easy to calculate at the bedside) for differentiating between patients with SBT success and SBT failure. Further study is needed in a larger group of subjects to identify the cut-off value of $TFdi_{tidal}$ for detecting SBT failure.

In addition and importantly, we found that evaluation of $TFdi_{tidal}$ at 5 min of SBT may be useful for early detection of patients who develop diaphragm fatigue or excessive diaphragm workload. In our study, patients who had a $TFdi_{tidal}$ value at 5 min of SBT within normal range (within 20–50%) had a higher likelihood of passing the SBT when compared to patients who had a $TFdi_{tidal}$ value outside of this range. This may be explained by diaphragm fatigue (< 20%) and/or too much workload on the diaphragm (> 50%). However, further study is needed to assess whether $TFdi_{tidal}$ at this specific time point can and should be used to assess patient inspiratory effort during SBT.

Diaphragm dysfunction commonly occurs in mechanically ventilated patients, and it adversely impacts treatment outcomes, including difficult weaning, longer duration of mechanical ventilation, prolonged ICU length of stay, and higher mortality [11]. Many studies have used diaphragm ultrasound to assess diaphragm weakness and atrophy by measuring $TFdi_{max}$ and DE_{max}. Di Nino, et al. [17] found that patients

with TFdi$_{max}$ > 30% had a higher probability of successful weaning from mechanical ventilation. Ferrari and colleagues [29] used TFdi$_{max}$ > 36% as a cut-off value to predict successful weaning. Other studies proposed values of DE$_{max}$ ranging from 0.95 to 1.00 cm as cut-off values for predicting weaning success [30-32]. Two recent meta-analyses reported that assessing diaphragm function using ultrasound might be helpful for predicting weaning outcome, but the accuracy of this method may vary according to the study population since there was high heterogeneity among the evaluated studies [33,34]. In our study, we found no differences in TFdi$_{max}$ and DE$_{max}$ when they were compared between the SBT success and SBT failure groups. However, we demonstrated that patients with a longer duration of ventilatory support (≥ 7 days) before the SBT had a significantly lower DE$_{max}$, which reflected poorer diaphragm function. This finding is consistent with the findings of other studies that reported longer duration of mechanical ventilation to be associated with diaphragm dysfunction that could lead to a poorer clinical outcome [12,25].

4.1. Limitations

This study has some mentionable limitations. First, the duration of SBT in our study was 30 min, so our findings may not be generalizable to SBTs with a duration longer than 30 min. Second, the subjects enrolled in this study had a relatively low mean APACHE II score (12.1 ± 3.5), and there were twice as many male subjects as female subjects. This suggests that our findings may not be generalizable to all patient populations, especially seriously ill intensive care patients. Third, diaphragm ultrasound is operator-dependent; however, good intra- and inter-observer reliability was reported by a previous study [19]. Fourth, measurement of diaphragm function during maximal inspiratory effort requires patient cooperation, and getting intubated patients to sufficiently cooperate can be a challenge in mechanically ventilated patients. Fifth and last, we did not measure the activity and function of other respiratory muscles, including the sternocleidomastoid, scalene, and intercostals muscles, that might contribute to patient inspiratory effort.

5. Conclusions

Patient inspiratory efforts determined by TFdi$_{tidal}$ significantly increase during SBT. TFdi$_{tidal}$ did not significantly differ throughout the trial between the success and the failure group except at the beginning of the trial with a higher TFdi$_{tidal}$ in the failure group. In contrast, RSBI was significantly greater throughout SBT in patients with failed weaning when compared to those who wean successfully. Diaphragm ultrasound might be inferior to RSBI for distinguishing patients with SBT success and failure.

Declarations of interests

None.

Funding statement

Authors' contributions

NR, SH, and NC conceived and designed the study. NR and SH collected the data. NR, SH, and NC analyzed and interpreted the data. NR and SH prepared the first draft of the manuscript. All authors contributed to the critical revision and final approval of the manuscript.

References

[1] Boles J-M, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. Eur Respir J 2007;29:1033–56. https://doi.org/10.1183/09031936.00010206.

[2] El-Khatib MF, Bou-Khalil P. Clinical review: liberation from mechanical ventilation. Crit Care 2008;12:221. https://doi.org/10.1186/cc6959.

[3] Meade M, Guyatt G, Cook D, Griffith L, Sinuff T, Kergl C, et al. Predicting success in weaning from mechanical ventilation. Chest 2001;120 [400S-24S].

[4] Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 1991;324:1445–50. https://doi.org/10.1056/NEJM199105233242101.

[5] Epstein SK. Weaning from ventilatory support. Curr Opin Crit Care 2009;15:36–43. https://doi.org/10.1097/MCC.0b013e3283220e07.

[6] Thille AW, Richard J-CM, Brochard L. The decision to extubate in the intensive care unit. Am J Respir Crit Care Med 2013;187:1294–302. https://doi.org/10.1164/rccm.201208-1523CI.

[7] Sklar MC, Burns K, Rittayamai N, Lanys A, Rauseo M, Chen L, et al. Effort to breathe with various spontaneous breathing trial techniques. A physiologic meta-analysis. Am J Respir Crit Care Med 2017;195:1477–85. https://doi.org/10.1164/rccm.201607-1338OC.

[8] Burns KEA, Soliman I, Adhikari NKJ, Zwein A, Wong JTY, Gomez-Builes C, et al. Trials directly comparing alternative spontaneous breathing trial techniques: a systematic review and meta-analysis. Crit Care 2017;21:127. https://doi.org/10.1186/s13054-017-1698-x.

[9] Demoule A, Jung B, Prodanovic H, Molinari N, Chanques G, Coirault C, et al. Diaphragm dysfunction on admission to the intensive care unit. Prevalence, risk factors, and prognostic impact-a prospective study. Am J Respir Crit Care Med 2013;188:213–9. https://doi.org/10.1164/rccm.201209-1668OC.

[10] Jung B, Moury PH, Mahul M, de Jong A, Galia F, Prades A, et al. Diaphragmatic dysfunction in patients with ICU-acquired weakness and its impact on extubation failure. Intensive Care Med 2016;42:853–61. https://doi.org/10.1007/s00134-015-4125-2.

[11] Dres M, Demoule A. Diaphragm dysfunction during weaning from mechanical ventilation: an underestimated phenomenon with clinical implications. Crit Care 2018;22:73. https://doi.org/10.1186/s13054-018-1992-2.

[12] Goligher EC, Fan E, Herridge MS, Murray A, Vorona S, Brace D, et al. Evolution of diaphragm thickness during mechanical ventilation. Impact of inspiratory effort. Am J Respir Crit Care Med 2015;192:1080–8. https://doi.org/10.1164/rccm.201503-0620OC.

[13] Goligher EC, Dres M, Fan E, Rubenfeld GD, Scales DC, Herridge MS, et al. Mechanical ventilation-induced diaphragm atrophy strongly impacts clinical outcomes. Am J Respir Crit Care Med 2018;197:204–13. https://doi.org/10.1164/rccm.201703-0536OC.

[14] Vivier E, Mekontso Dessap A, Dimassi S, Vargas F, Lyazidi A, Thille AW, et al. Diaphragm ultrasonography to estimate the work of breathing during non-invasive ventilation. Intensive Care Med 2012;38:796–803. https://doi.org/10.1007/s00134-012-2547-7.

[15] Matamis D, Soilemezi E, Tsagourias M, Akoumianaki E, Dimassi S, Boroli F, et al. Sonographic evaluation of the diaphragm in critically ill patients. Technique and clinical applications. Intensive Care Med 2013;39:801–10. https://doi.org/10.1007/s00134-013-2823-1.

[16] Umbrello M, Formenti P, Longhi D, Galimberti A, Piva I, Pezzi A, et al. Diaphragm ultrasound as indicator of respiratory effort in critically ill patients undergoing assisted mechanical ventilation: a pilot clinical study. Crit Care 2015;19:161. https://doi.org/10.1186/s13054-015-0894-9.

[17] DiNino E, Gartman EJ, Sethi JM, McCool FD. Diaphragm ultrasound as a predictor of successful extubation from mechanical ventilation. Thorax 2014;69:423–7. https://doi.org/10.1136/thoraxjnl-2013-204111.

[18] Dres M, Goligher EC, Heunks LMA, Brochard LJ. Critical illness-associated diaphragm weakness. Intensive Care Med 2017;43:1441–52. https://doi.org/10.1007/s00134-017-4928-4.

[19] Goligher EC, Laghi F, Detsky ME, Farias P, Murray A, Brace D, et al. Measuring diaphragm thickness with ultrasound in mechanically ventilated patients: feasibility, reproducibility and validity. Intensive Care Med 2015;41:734. https://doi.org/10.1007/s00134-015-3724-2.

[20] Cabello B, Thille AW, Roche-Campo F, Brochard L, Gómez FJ, Mancebo J. Physiological comparison of three spontaneous breathing trials in difficult-to-wean patients. Intensive Care Med 2010;36:1171–9. https://doi.org/10.1007/s00134-010-1870-0.

[21] Jubran A, Tobin MJ. Pathophysiologic basis of acute respiratory distress in patients who fail a trial of weaning from mechanical ventilation. Am J Respir Crit Care Med 1997;155:906–15. https://doi.org/10.1164/ajrccm.155.3.9117025.

[22] Lemaire F, Teboul JL, Cinotti L, Giotto G, Abrouk F, Steg G, et al. Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation. Anesthesiology 1988;69:171–9.

[23] Lamia B, Maizel J, Ochagavia A, Chemla D, Osman D, Richard C, et al. Echocardiographic diagnosis of pulmonary artery occlusion pressure elevation during weaning from mechanical ventilation. Crit Care Med 2009;37:1696–701. https://doi.org/10.1097/CCM.0b013e31819f13d0.

[24] Levine S, Nguyen T, Taylor N, Friscia ME, Budak MT, Rothenberg P, et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. N Engl J Med 2008; 358:1327–35. https://doi.org/10.1056/NEJMoa070447.

[25] Jaber S, Petrof BJ, Jung B, Chanques G, Berthet J-P, Rabuel C, et al. Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans. Am J Respir Crit Care Med 2011;183:364–71. https://doi.org/10.1164/rccm.201004-0670OC.

[26] Parthasarathy S, Jubran A, Laghi F, Tobin MJ. Sternomastoid, rib cage, and expiratory muscle activity during weaning failure. J Appl Physiol Bethesda Md 2007;103:140–7. https://doi.org/10.1152/japplphysiol.00904.2006.

[27] Krieger BP, Isber J, Breitenbucher A, Throop G, Ershowsky P. Serial measurements of the rapid-shallow-breathing index as a predictor of weaning outcome in elderly medical patients. Chest 1997;112:1029–34.

[28] Segal LN, Oei E, Oppenheimer BW, Goldring RM, Bustami RT, Ruggiero S, et al. Evolution of pattern of breathing during a spontaneous breathing trial predicts successful extubation. Intensive Care Med 2010;36:487–95. https://doi.org/10.1007/s00134-009-1735-6.

[29] Ferrari G, De Filippi G, Elia F, Panero F, Volpicelli G, Aprà F. Diaphragm ultrasound as a new index of discontinuation from mechanical ventilation. Crit Ultrasound J 2014; 6:8. https://doi.org/10.1186/2036-7902-6-8.

[30] Dres M, Dubé B-P, Mayaux J, Delemazure J, Reuter D, Brochard L, et al. Coexistence and impact of limb muscle and diaphragm weakness at time of liberation from mechanical ventilation in medical intensive care unit patients. Am J Respir Crit Care Med 2017;195:57–66. https://doi.org/10.1164/rccm.201602-0367OC.

[31] Jiang J-R, Tsai T-H, Jerng J-S, Yu C-J, Wu H-D, Yang P-C. Ultrasonographic evaluation of liver/spleen movements and extubation outcome. Chest 2004;126:179–85. https://doi.org/10.1378/chest.126.1.179.

[32] Kim WY, Suh HJ, Hong S-B, Koh Y, Lim C-M. Diaphragm dysfunction assessed by ultrasonography: influence on weaning from mechanical ventilation. Crit Care Med 2011;39:2627–30. https://doi.org/10.1097/CCM.0b013e3182266408.

[33] Llamas-Álvarez AM, Tenza-Lozano EM, Latour-Pérez J. Diaphragm and lung ultrasound to predict weaning outcome: systematic review and meta-analysis. Chest 2017;152:1140–50. https://doi.org/10.1016/j.chest.2017.08.028.

[34] Li C, Li X, Han H, Cui H, Wang G, Wang Z. Diaphragmatic ultrasonography for predicting ventilator weaning: a meta-analysis. Medicine (Baltimore) 2018;97: e10968. https://doi.org/10.1097/MD.0000000000010968.