

# Evaluation of weaning parameters for weaning readiness from mechanical ventilation among elderly patients

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The data and code were available upon reasonable request (Dujrath Somboonviboon, email address: dujrath@gmail.com).

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## ABSTRACT:

**Background:** Numbers of elderly patients with acute respiratory failure continue to rise with increasing age of the general population worldwide. Ventilatory reserve decreases substantially with age as a result of multiple interrelated physiologic changes.

**Objective:** This study aimed to evaluate the predictive value of conventional and composite weaning parameters among elderly patients.

**Methods:** We conducted an observational prospective study among intubated patients  $\geq 70$  years old and readied for undergoing spontaneous breathing trial (SBT). Weaning parameters were recorded [heart rate, respiratory rate, tidal volume, minute ventilation (MV)] at 1 min, 30 min, and 2 hr after beginning of SBT. Cough peak expiratory flow (CPEF) and diaphragmatic thickness (DT) were also measured at 1 min after SBT. Weaning parameters were compared between the 2 patient groups (weaning success vs. weaning failure). Primary outcome was difference in weaning parameters between the 2 groups of patients.

**Results:** All 48 subjects were enrolled. The mean ( $\pm$ SD) age was 80.2 ( $\pm$ 6) years. Altogether, 38 patients (79.2%) were in the weaning success group and 10 patients (20.8%) in the weaning failure group. All baseline characteristics did not significantly differ between the 2 groups. While no difference was observed in other isolated weaning parameters between the 2 patient groups, we found that patients in the weaning success group had significantly lower MV than patients in the weaning failure group ( $8.3 \pm 1.8$  vs.  $9.9 \pm 2.5$  L/min,  $p=0.025$ ). Composite weaning parameters included MV/CPEF and MV/(CPEF  $\times$  DT) increased predictive values for weaning failure than isolated MV with area under the receiver operating characteristics curves of 0.78, 0.80, and 0.72 respectively. The best cutoff point to predict weaning failure were MV  $\geq 8.4$  L/min, MV/CPEF  $\geq 0.12$ , and MV/(CPEF  $\times$  DT)  $\geq 0.45$  cm $^{-1}$ .

**Conclusion:** MV was the only parameter associated with weaning failure among the elderly. Composite parameters demonstrated better predictive value for assessing weaning readiness among elderly patients.

**Keywords:** Weaning readiness, Weaning parameters, Mechanical ventilator, Elderly patients.

## BACKGROUND

The number of elderly patients with acute respiratory failure continues to rise with increasing age of the general population worldwide[1,2]. No consensus has been reached about the influence of age on mortality [3]. Disease severity on admission, nosocomial infection, and presence of significant comorbid conditions mainly decided the patient's outcomes in compared with age alone [4,5]. However, regarding weaning from mechanical ventilation, it seems that elderly subjects were associated with difficult weaning [6]. In previous studies, 20 to 30% of elderly patients were re-intubated within 48 to 72 hours after extubation, while the general population ranged from 3 to 19% [7,8]. Re-intubation is associated with an 8-fold increase in nosocomial pneumonia and a 3-fold increase in hospital deaths [9]. Because of age-related physiologic changes, the elderly develop stiffening of the thoracic cage, higher residual volume, weakened diaphragmatic and respiratory muscle strength, decreased sensitivity of cough center of the brain, and decline in cardiac function[10,11]. All these factors cause difficult weaning from mechanical ventilation among the elderly rather than general adults. One related study found a threshold of RSBI <130 was more appropriate for the elderly than a conventional threshold of RSBI ≤105 in the general population[12,13]. Another study tested a composite weaning parameter called the integrative weaning index (IWI) which was calculated using three essential parameters (respiratory compliance, arterial oxygenation, and RSBI), and found a high predictive value for weaning among the elderly [14]. However, this index relied on respiratory compliance which may be affected by patient's inspiratory effort during the weaning process. To date, lung ultrasonography (LUS) is generally used for respiratory function assessment among patients receiving mechanical ventilation[14,15]. Therefore, we hypothesized that the composite weaning parameters comprising LUS parameters may increase the accuracy for predicting weaning readiness than isolated RSBI value in the elderly population.

## MATERIAL AND METHODS

### Study design

This prospective observational study was conducted between May 2019 and December 2019 in Phramongkutklao Hospital. The study was approved by the Ethics Committee Institutional Review Board of Royal Thai Army Medical Department (R076h/62).

The primary endpoint was the difference in weaning parameters including composite parameters and single parameters between weaning success vs. weaning failure among elderly patients.

### Patients

Inclusion criteria were age > 70 years old, receiving endotracheal intubation for more than 24 hours, in a medical ward or intensive care unit (ICU), meeting the readiness criteria [16,17] for spontaneous breathing trial (SBT) [using fraction of inspired oxygen ( $\text{FiO}_2$ ) < 0.5, PEEP < 5 cm  $\text{H}_2\text{O}$ ,  $\text{PaO}_2/\text{FiO}_2 > 200$ , or  $\text{SpO}_2/\text{FiO}_2 > 200$ , respiratory rate

### KEY MESSAGES:

- Minute ventilation was the only parameter associated with weaning failure among the elderly. Composite parameters comprising lung ultrasonography parameters and cough ability demonstrated better predictive value for assessing weaning readiness among elderly patients.

< 35/min, stable hemodynamics (absence or low-dose vasoconstrictors required), good consciousness and minimal secretion].

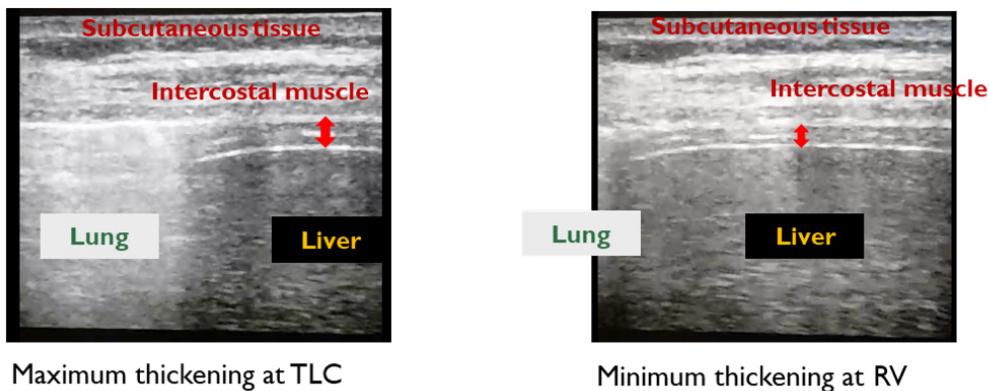
Exclusion criteria were receiving ventilation via tracheostomy tube, neuromuscular diseases, previously diagnosed diaphragmatic paralysis, and palliative care patients.

### Methods

Patients meeting the inclusion criteria above and readied for undergoing SBT were enrolled in this study. All patients received pressure support (PS) of 5 cm  $\text{H}_2\text{O}$  and PEEP 5 cm  $\text{H}_2\text{O}$  during SBT. Weaning parameters were recorded [heart rate, respiratory rate, tidal volume, minute ventilation (MV) and RSBI] at 1 min, 30 min, and 2 hr after the beginning of SBT. The RSBI was calculated as  $\text{RR}^2/\text{MV}$ . Cough peak expiratory flow (CPEF) was also measured at 1 min after SBT. Before measurement, head of bed was elevated in a semi-upright position, and secretions were removed by suction. CPEF was measured using internal flow meter of a ventilator. Each patient was asked to cough three times making as much effort as possible and the best flow velocity was recorded [18]. Then LUS was performed using 10 MHz linear probe to observe the zone of apposition by placing vertically to the chest wall at the 8<sup>th</sup> or 9<sup>th</sup> intercostal space between anterior axillary and midaxillary line. Three layers of diaphragm were identified with one hypoechoic central layer bordered by two echogenic layers. The patients were asked to fully inspire to total lung capacity (TLC) and then fully expire to residual volume (RV). At TLC, diaphragm thickness (DT) is in maximum thickening and minimum thickening at RV in the same breath [19] (Fig1). DT at TLC was recorded and diaphragmatic thickness fraction (DTF) was calculated from DT at TLC minus DT at RV, divided by DT at RV [20]. All LUS parameters in this study were conducted by a single well-trained physician for reducing interrater reliability. Weaning failure was defined as reintubation or death within 48 hours after extubation. Criteria regarding reintubation during SBT[17] were respiratory rate > 35 /min, heart rate > 130 /min, unstable hemodynamic status (systolic blood pressure > 180 mmHg or < 90 mmHg), obvious accessory respiratory muscle use, inability to protect the airway or change of mental status.

### Statistical analysis

Values are presented as mean ( $\pm\text{SD}$ ), median (IQR, interquartile range), and proportion (%). P-value corresponds to the Mann-Whitney U test and Fisher's exact test as appropriate. The diagnostic test was used to calculate sen-



**Figure 1.** Three layers of diaphragm structure was demonstrated (arrows), a) maximum thickening at TLC, b) minimum thickening at RV.

sitivity, specificity, positive predictive value, and negative predictive value of weaning parameters. Receiver operating characteristic (ROC) curve analysis was performed to assess the ability of conventional and composite weaning parameters regarding predicting weaning readiness. SPSS software (V.23.0) was used to analysis. To analyze the difference in weaning parameters between the 2 groups of patients, the adequate sample size of patients calculated from a previous study was 25 [5].

## RESULTS

All 48 subjects were enrolled. Average age was 80.2 ( $\pm 6$ ) years, and 25 (52%) were male. Most patients (68.8%) were admitted to the intensive care unit (ICU) and able to perform self-activity daily life before being hospitalized (77%). In all, 38 patients (79.2%) were in the weaning success group and 10 patients (20.8%) in the weaning failure group. All baseline characteristics did not significantly differ between 2 groups. However, hospital outcomes including ventilator-days, length of hospital stay and 30-day mortality

tended to increase in the weaning failure group (6 vs. 9 days;  $P=0.15$ , 22 vs. 37 days;  $P=0.057$ , and 5.1 vs. 20%;  $P=0.18$ , respectively) (Table 1). During SBT, while no difference was found in other isolated weaning parameters at 1 min SBT between the 2 patient groups, we found that patients in the weaning success group had significantly lower MV than patients in the weaning failure group ( $8.3 \pm 1.8$  vs.  $9.9 \pm 2.5$  L/min;  $p=0.025$ ) (Table 2).

According to our findings that MV, CPEF and DT may have played a potential role to use as composite parameters (Table 2), we then constructed models using these parameters to test whether they could better predict weaning readiness than isolated RSBI. These composite weaning parameters included MV/CPEF, MV/DT, and MV/(CPEF x DT). Our analysis found that, compared with the weaning success group, these composite parameters were significantly higher in the weaning failure group (Table 3) (Fig 2). MV/CPEF and MV/(CPEF x DT) increased predictive values for weaning failure than isolated MV with the area under the ROC curves of 0.78 (95% CI 0.64-0.91,  $p=0.008$ ), 0.80

**Table 1.** Patient characteristics between weaning success group and weaning failure group.

Variables	Success (n=38)	Fail (n=10)	p-value
Age, years	$80.6 \pm 6.3$	$78.9 \pm 5.6$	0.45
Male, n (%)	18 (47.4)	5 (50)	1.0
Body weight (kg)	$60.2 \pm 12.4$	$56 \pm 10.8$	0.33
Height (cm)	$160.1 \pm 7.0$	$160.4 \pm 7.7$	0.92
BMI ( $\text{kg}/\text{m}^2$ )	$23.5 \pm 4.7$	$21.6 \pm 3.9$	0.24
ICU admission, n (%)	26 (68.4)	7 (70)	1.0
Status of self-care ADL#, n (%)	30 (78.9)	7 (70)	0.68
Clinical Frailty Scale	$5.6 \pm 1.4$	$6.1 \pm 1$	0.28
APACHE II	$18.4 \pm 5.2$	$20.5 \pm 3.3$	0.23
<b>Hospital outcomes</b>			
• Previous intubation in same visit, n (%)	4 (10.5)	1 (10)	1.0
• Ventilator day (days)	$6 \pm 4.8$	$9 \pm 4.2$	0.15
• 30-day mortality, n (%)	2 (5.1)	2 (20)	0.18
• Hospital LOS, median (IQR) (days)	22 (14, 39)	37 (27, 62)	0.057

BMI: Body mass index, ICU: intensive care unit, ADL: Activities of daily living, APACHE: acute physiologic assessment and chronic health evaluation, LOS: Length of stay, #Status of self-care ADL: Having self-care ADL at baseline clinical status before intubation.

**Table 2.** Weaning parameters during SBT between weaning success group and weaning failure group.

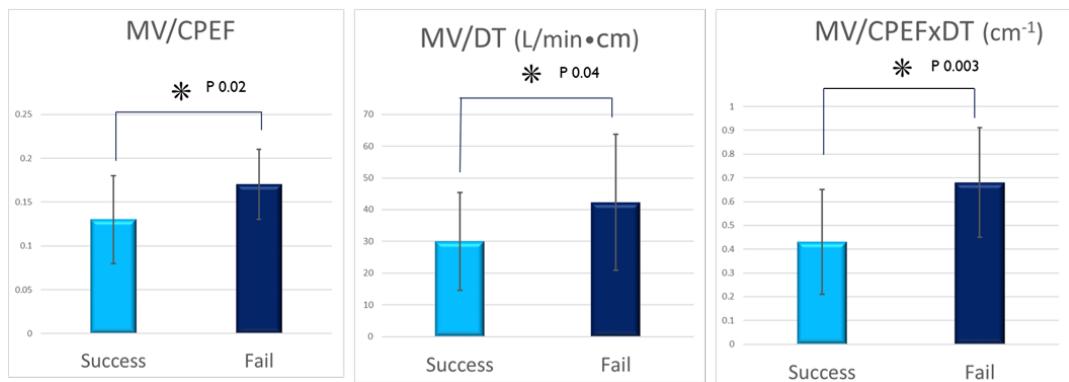
Variables	Success (n=38)	Fail (n=10)	p-value
Weaning parameters at pressure support 5 cmH <sub>2</sub> O			
• Minute ventilation (L/min)	8.3 ± 1.8	9.9 ± 2.5	0.025*
• Heart rate (/min)	90 ± 13.48	86 ± 14.02	0.41
• Respiratory rate (/min)	20 ± 5	21 ± 3	0.53
• RSBI at 1-min SBT	49.3 ± 20.4	45 ± 10.4	0.38
• Cough peak expiratory flow (L/min)	72.6 ± 23.0	62 ± 24.7	0.21
• Diaphragm thickness at TLC (cm)	0.34 ± 0.19	0.27 ± 0.12	0.26
• Diaphragmatic thickness fraction (%)	35.2 ± 18.4	48.3 ± 24.3	0.07

RSBI: rapid shallow breathing index, TLC: total lung capacity

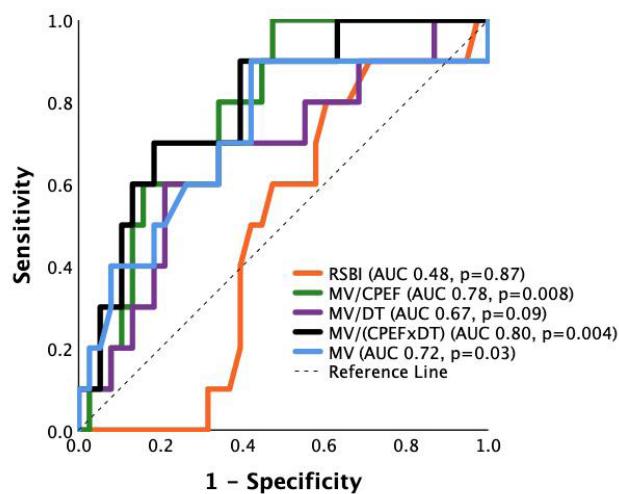
**Table 3.** Composite weaning parameters between weaning success group and weaning failure group.

Variables	Success (n=38)	Fail (n=10)	p-value
MV/CPEF	0.13 ± 0.05	0.17 ± 0.04	0.021*
MV/DT (L/min•cm)	29.97 ± 15.41	42.29 ± 21.46	0.044*
MV/CPEF x DT (cm <sup>-1</sup> )	0.43 ± 0.22	0.68 ± 0.23	0.003*

MV: minute ventilation, CPEF: Cough peak expiratory flow, DT: diaphragmatic thickness

**Figure 2.** Differences in composite weaning parameters between two patient groups (\*p<0.05).

MV: minute ventilation, CPEF: Cough peak expiratory flow, DT: diaphragmatic thickness

**Figure 3.** ROC curves for predicting weaning failure.

RSBI: Rapid shallow breathing index, MV: minute ventilation, CPEF: Cough peak expiratory flow, DT: diaphragmatic thickness

**Table 4.** Best cutoff point of weaning parameters for predicting weaning failure.

Variables	Threshold value	Sensitivity	Specificity	PPV	NPV	Accuracy	p-value
MV	≥ 8.40 (L/min)	90.0%	57.9%	36.0%	95.2%	64.6%	0.011*
MV/CPEF	≥ 0.12	90.0%	55.3%	34.6%	95.5%	62.5%	0.013*
MV/(CPEF x DT)	≥ 0.45 cm <sup>-1</sup>	90.0%	60.5%	37.5%	95.8%	66.7%	0.010*

MV: minute ventilation, CPEF: Cough peak expiratory flow, DT: diaphragmatic thickness

(95% CI 0.65-0.94, p=0.004), and 0.72 (95% CI 0.53-0.92, p=0.03), respectively (Fig 3). The best cutoff point to predict weaning failure of MV, MV/CPEF, and MV/(CPEF x DT) were 8.4 L/min, 0.12 and 0.45 cm<sup>-1</sup>, respectively (Table 4).

## DISCUSSION

The prevalence of weaning failure in this study was 20.8%, similar to recent studies among elderly patients [7]. The accuracy of RSBI and %change in RSBI might concurrently decrease with increased patient age because respiratory function declines gradually over a lifetime. Although receiving ventilation with low pressure support level using RSBI <75 breaths/min/L could demonstrate discrimination between weaning success and weaning failure in the overall population [21], we found no difference in RSBI between the two groups of elderly patients. Increased MV among the elderly during SBT may represent a high work of breathing as well as high metabolic demand, therefore leading to respiratory muscle fatigue and weaning failure. Our study found that DT in the weaning success group tended to exhibit more thickness than that of the weaning failure group (0.34 vs. 0.27 cm; p=0.26). This result was consistent with the studies from Pirompanich [22] and Ferrari [23]. Interestingly, while no statistically difference was observed in DTF between the two groups, we found that the weaning failure group tended to present a higher DTF than the weaning success group, contradicting previous studies demonstrating that weaning failure had lower DTF than weaning success patients [22-24]. One possible explanation of our finding is that during SBT among the elderly may result in a high work load of breathing and related to higher DTF. One related study [5] in elderly demonstrated that IWI, not otherwise single parameters, was significant for predicting weaning success. This can be explained by evaluating multiple essential functions representing higher predictive performance among elderly patients. However, IWI was calculated using a component of oxygenation, respiratory rate, tidal volume and respiratory compliance, which was difficult to perform during the weaning process. Meanwhile, ineffective clearing secretions were associated with extubation failure [7]. Therefore, we evaluated models of multiple essential respiratory functions including cough ability and diaphragmatic contractility. We found that composite weaning parameters demonstrated a good predictive value for weaning failure. Limitations of our study comprised the relatively small number of patients and single-center enrollment. Further, we did not perform the inter-rater reliability assessment of diaphragmatic ultrasonography.

## CONCLUSION

MV was the only isolated parameter associated with weaning failure in the elderly. MV ≥ 8.4 L/min, MV/CPEF ≥ 0.12, and MV/(CPEF x DT) ≥ 0.45 cm<sup>-1</sup> improved efficacy for prediction of weaning failure in the elderly. Composite parameters demonstrated better predictive value than isolated RSBI for weaning readiness assessment in elderly patients.

## CONFIDENTIALITY

Informed consents are obtained at medical ICU/ward. The subject's information is represented by a unique number, and the study data is stored at the pulmonary and critical care division, Phramongkutkla Hospital. The study data will be retained for 5 years after the study is finished. After that, all the study data will be disposed.

## DISSEMINATION POLICY

None

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## AUTHORS' CONTRIBUTIONS

(I) Conceptualization: Dujrath Somboonviboon; (II) Data collection: Dujrath Somboonviboon; (III) Writing original draft preparation: Dujrath Somboonviboon; (IV) Conceptualization: Nittha Oerareemitr, Petch Wacharasint; (V) Validation: Nittha Oerareemitr; (VI) Visualization: Nittha Oerareemitr, Petch Wacharasint; (VII) Formal analysis: Petch Wacharasint; (VIII) Writing – review & editing: Petch Wacharasint.

## SUPPLEMENTARY MATERIALS

None

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