End-Expiratory Lung Volumes During Spontaneous Breathing Trials in Tracheostomized Subjects on Prolonged Mechanical Ventilation

Jui-Chen Cheng, Hui-Chuan Chen, Jih-Shuin Jerng, Ping-Hung Kuo, and Huey-Dong Wu

BACKGROUND: The role of end-expiratory lung volume (EELV) during a spontaneous breathing trial (SBT) in patients who were tracheostomized and on prolonged mechanical ventilation is unclear. This study aimed to assess EELV during a 60-min SBT and its correlation with weaning success. METHODS: Enrolled subjects admitted to a weaning unit were measured for EELV and relevant parameters before and after the SBT. RESULTS: Of the 44 enrolled subjects, 29 (66%) were successfully liberated, defined as not needing mechanical ventilation for 5 d. The success group had fewer subjects with chronic kidney disease (41% vs 73%, $P = .044$), stronger mean ± SD maximum inspiratory pressure (41.6 ± 10.4 vs 34.1 ± 7.1 cm H_2O; $P = .02$) and mean ± SD maximum expiratory pressure (46.9 ± 11.7 vs 35.3 ± 16.9 cm H_2O; $P = .01$) versus the failure group. Toward the end of the SBT, the success group had a significant increase in the mean ± SD EELV (before vs after: 1,278 ± 744 vs 1,493 ± 867 mL; $P = .040$) and a decrease in the mean ± SD rapid shallow breathing index (83.8 ± 39.4 vs 66.3 ± 29.4; $P = .02$), whereas there were no significant changes in these 2 parameters in the failure group. The Cox regression analysis showed that, at the beginning of SBT, a greater difference between EELV with a PEEP of 0 cm H_2O and with a PEEP of 5 cm H_2O was significantly correlated to a higher likelihood of weaning success. Toward the end of the SBT, a greater EELV level at a PEEP of 0 cm H_2O was also correlated with weaning success. Also, the greater difference of EELV at a PEEP of 0 cm H_2O between the beginning and the end of the SBT was also correlated with a shorter duration to weaning success. CONCLUSIONS: The change in EELV during a 60-min SBT may be of prognostic value for liberation from prolonged mechanical ventilation in patients who had a tracheostomy. Our findings suggest a model to understand the underlying mechanism of failure of liberation from mechanical ventilation in these patients. *Key words: respiratory failure; mechanical ventilation; weaning; lung volumes; tracheostomy; ventilator dependence.*
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Introduction

Patients with prolonged mechanical ventilation, generally defined as the requirement of at least 6 h of mechanical ventilation for ≥ 21 consecutive d,[1,2] accounts for 10% of those experiencing acute respiratory failure. This prolonged mechanical ventilation status is correlated with a poor prognosis[3] and imposes a significant care burden on health-care systems.[4] Liberation from mechanical ventilation is an essential goal in the care of patients who survive acute life-threatening respiratory failure; however, only 30%–53% of patients can be successfully liberated.[3] A multi-national prospective multi-center observational study reported that only 67% of the subjects on mechanical ventilation had a weaning process of <1 week; the rest of them had a longer weaning course or never started a weaning process.[2]

Results of a previous report suggest that frequent screening for preparedness for weaning and early initiation of a spontaneous breathing trial (SBT) can result in a higher weaning rate.[5] Although patients may tolerate a reduction in mechanical ventilation settings and proceed with a final SBT, failure in this last stage is common.[6] A possible reason for this failure is an increased respiratory mechanical load coupled with insufficient capability and endurance of the respiratory muscles.[7] The change from mechanical ventilation support to unassisted breathing can impose markedly increased work of breathing[8]; however, in real-world patient care, measuring work of breathing may not be

practical in a post-acute setting due to the need for the invasive placement of pressure sensors.

An alternative approach is to assess the loss of end-expiratory lung volume (EELV) during an SBT to explain the lack of respiratory endurance. Functional residual capacity (FRC) is the amount of gas that remains in the lungs after expiration during tidal breathing, not necessarily during rest.[9] Previous studies proposed that EELV[10] or accessible pulmonary gas volume[11] can be used to assess lung volumes in abnormal conditions or during mechanical ventilation. During normal tidal breathing with adequate expiratory time, EELV approximates FRC,[12] which is a valuable indicator for aeration and recruitment of lung tissue.[13] The FRC is normally 30–35 mL/kg per predicted body weight in healthy individuals.[14] In patients who are critically ill and on mechanical ventilation, the level of PEEP and the degree of patient relaxation determine the FRC; therefore, it is better to use EELV.[15]

After a patient starts an SBT, commonly through a T-piece, CPAP is immediately lost, especially toward the end-expiratory time point. Lungs previously affected by acute respiratory failure may be less aerated, which results in a reduced EELV. Traditional methods of measuring FRC or EELV include gas dilution, nitrogen washout,[16,17] body plethysmography, and computed tomography;[12,15,18] however, applying these approaches is difficult in patients on mechanical ventilation in the ICU. New techniques have been developed to address this issue, with the advantage of not interrupting breathing with mechanical ventilation,[15,19]: nitrogen multiple breath washout techniques integrated into ventilators,[19-23] electrical impedance tomography,[24,25] and the capnodynamic method.[26]

Most previous studies on the correlation between the FRC or EELV and ventilator weaning focused on patients who were endotracheally intubated. A lower FRC before extubation has been reported to have a negative impact on weaning outcomes.[18] However, studies on EELV during SBTs for patients who were tracheostomized, especially those on prolonged mechanical ventilation, are lacking. In this study, we hypothesized that an evolution of EELV might occur during unassisted breathing in patients with prolonged mechanical ventilation. We aimed to evaluate the correlation between the changes in EELV and weaning outcomes in these patients.

QUICK LOOK

Current knowledge

Only 30%-53% of patients on prolonged mechanical ventilation can be successfully liberated from the ventilator. The change from ventilatory support to unassisted breathing can impose markedly increased work of breathing and a change of lung volume.

What this paper contributes to our knowledge

The difference of measured end-expiratory lung volume during the 60-min spontaneous breathing trial and the end-expiratory lung volume at the end of the trial correlated with the days to successful weaning of subjects who were tracheostomized and on prolonged mechanical ventilation. Our findings suggest the loss of end-expiratory lung volume during a spontaneous breathing trial to explain the lack of respiratory endurance.

Methods

Design and Settings

This prospective single-center observational study was conducted since August 2017 at the Respiratory Care Center, a dedicated weaning unit of National Taiwan University Hospital, a university-affiliated medical center in Taiwan. The study was performed in accordance with current ethics guidelines (Declaration of Helsinki), and the Research Ethics Committee B of National Taiwan University Hospital approved the study protocol (201606049RINB). Informed consent was obtained from the subjects or their surrogates. The Respiratory Care Center has 15 beds and receives patients with prolonged mechanical ventilation from ICUs for liberation from the ventilator. Since 2014, the Respiratory Care Center has implemented a standardized weaning protocol.[5] The decision to initiate the weaning process is determined by the consensus of attending physicians, residents, and respiratory therapists.

Briefly, the clinicians gradually reduce the ventilator settings to a pressure support level of 10 cm H_2O and 5 cm H_2O PEEP for at least 8 h. A screening process with a 12-h

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SBT is then conducted for 2 consecutive days with humidified oxygen delivered through a T-piece. If there is no distress during the screening period, a direct liberation trial with continuous unassisted breathing is provided for 5 consecutive days. If this screening process fails in the patient, then a stepwise liberation trial ensues with the daily duration of the SBT starting from 2 h, then extending to 2 h twice daily, 4 h daily, 4 h twice daily, 8 h daily, 12 h daily, 16 h daily, 20 h daily, and finally continuous unassisted breathing for 5 days. A slow weaning trial is used for patients in whom the stepwise trials failed, with either external positive airway pressure breathing through a T-piece or stepwise liberation with a slow increment of the SBT duration. Patients who tolerate the liberation process and a final 5 days of continuous unassisted breathing are transferred to a general ward.

Participants

Patients admitted to the Respiratory Care Center were screened; the patients were considered eligible to participate in the study if they fulfilled all of the following criteria: ages $\geq$ 20 y, tracheostomized after intubation due to acute respiratory failure, which required at least 14 d of continuous mechanical ventilation; and no fever or clinical evidence of active infection. Also, the ventilator settings for the included subjects had to be successfully reduced to and maintained at a low level of support for at least 24 h, including: $S_{pO_2} > 90\%$, $P_{aCO_2} < 52$ mm Hg, frequency <35 breaths/min under a pressure support mode with $F_{IO_2} \leq 0.4$, and PEEP of <8 cm H_2O. In addition, patients were excluded if they met any one of the following criteria: unstable hemodynamics, active bleeding, frequent seizures, myoclonus, tremors, or involuntary movements.

Measurement of EELVs and Relevant Parameters

Measurement of the EELV was performed when the subject was put on a ventilator equipped with the ability to measure EELV (Engstrom, GE Healthcare, Chicago, Illinois). This was based on a previous report of a simplified and modified nitrogen multiple breath washout technique[19-22] integrated with an Engstrom ventilator, with breath-by-breath calculation of nitrogen-based on carbon dioxide production, end-tidal oxygen concentration, and end-tidal P_{aO_2} without using supplementary gases. After written informed consent was obtained, the ventilator settings were reduced to a pressure support level of $\leq$10 cm H_2O and PEEP of 5 cm H_2O with F_{IO_2} 0.4, and the subject was observed for at least 8 h to ensure stable respiratory and hemodynamic conditions. The subject then underwent an SBT for 60 min through an open breathing circuit composed of a T-piece connected to a central oxygen source with F_{IO_2} 0.4 and air flow of 10 L/min. Before and after an SBT of 60 min, the investigator measured EELV when the subject was temporarily reconnected to the specified ventilator (Engstrom) for this study after the patient received oxygen for 1 h through a T-piece. After the EELV measurement, the subject continued the T-piece trial. The settings during this measurement included the cuff pressure of the tracheostomy tube was checked to prevent air leakage, and tracheostomy suction was performed to remove possible airway secretions. Therefore, the measured EELV was an estimate of the EELV at the end of the T-piece trial. EELV was measured[27] with the FRC INview system (GE Healthcare).

During the measurement, the subjects were positioned semi-recumbent, at 45°; the humidifier was turned off, and the data were captured after a steady sate had been reached for at least 10 min. The subjects were allowed to receive necessary bedside care tasks, including suctioning of airway secretions, administering nutrition, intravenous fluids, oral and intravenous medications, and physical restraints if needed. However, percussion, rehabilitation activities, nebulized medications, and bedside procedures were avoided. Before and after the SBT, the rapid shallow breathing index, the ratio of breathing frequency to tidal volume (V_T), was measured with a handheld Wright spirometer (NSpire, Health Ltd, Hertford, UK) placed on the tracheotomy tube. The maximum inspiratory pressure and maximum expiratory pressure were also measured by using a manometer with a unidirectional valve. For subjects' EELV, the mean value of 2 readings of EELV was recorded. For those with the difference between 2 readings that exceeded 25%, the measurement was repeated. The ratio of EELV to predicted body weight was also calculated, with the predicted body weight being calculated as $50 + 0.91 \times$ (height [cm] – 152.4) kg for men and as $45.5 + 0.91 \times$ (height [cm] – 152.4) kg for women.[27]

Collection of Clinical Data

For each subject, we collected the following data from the health-care information system of the hospital: age, sex, comorbidities, etiology of respiratory failure and reason to initiate mechanical ventilation, date of initiating ventilator use, the APACHE II (Acute Physiology and Chronic Health Evaluation II) score on ICU admission, and documentation of extubation and tracheostomy. In addition, the following clinical, laboratory, and physiologic data were also collected before the SBT: body height, weight, Glasgow coma scale, blood cell counts, hemoglobin, and C-reactive protein levels. During the SBT, blood oxygen saturation was measured by using continuous pulse oximetry, whereas blood pressure was measured every 15 min by using an electronic sphygmomanometer. The definitions of failure to liberate from mechanical ventilation were adopted from a previous study as follows: systolic blood

Table 1. Demographic and Clinical Characteristics of the Subjects and Comparisons Between the Success and Failure Groups

Characteristic	Total ($N = 44$)	Weaning Success ($n = 29$)	Weaning Failure ($n = 15$)	P	Effect Size*
Age, y	66.1 ± 17.6	66.0 ± 16.9	66.2 ± 19.4	.98	0.01
Men	26 (59)	18 (62)	8 (53)	.58	0.08
Conditions that contributed to acute respiratory failure					
Sepsis and/or septic shock	20 (4)	13 (45)	7 (47)	.90	0.02
Hospital-acquired pneumonia	15 (34)	10 (35)	5 (33)	.94	0.01
Community-acquired pneumonia	8 (18)	6 (21)	2 (13)	.70	0.09
Central nervous system diseases	6 (14)	5 (17)	1 (7)	.41	0.15
Pulmonary edema	3 (7)	2 (7)	1 (7)	>.99	0.01
Cardiopulmonary arrest	4 (9)	2 (7)	1 (7)	.60	0.11
ARDS	2 (5)	1 (3)	1 (7)	>.99	0.07
Others	4 (9)	2 (7)	2 (13)	.60	0.11
Comorbidities					
Chronic kidney disease	23 (52)	12 (41)	11 (73)	.044	0.30
Cardiovascular diseases other than heart failure	22 (50)	14 (48)	8 (53)	.75	0.05
Malignancy	16 (36)	9 (31)	7 (47)	.31	0.15
Central nervous system diseases	13 (30)	10 (35)	3 (20)	.49	0.15
Congestive heart failure	10 (23)	6 (21)	4 (27)	.71	0.07
Obstructive airway diseases	6 (14)	3 (10)	3 (20)	.65	0.13
Others	7 (1)	5 (17)	2 (13)	>.99	0.05
APACHE II score on ICU admission	15.5 ± 3.9	15.0 ± 3.5	16.5 ± 4.7	.23	0.38
Duration of mechanical ventilation before study, d	40.0 ± 23.5	35.1 ± 20.2	49.2 ± 27.2	.058	0.62
Extubation failure before tracheostomy	41 (93)	26 (87)	15 (100)	.20	0.20
Mode of weaning before RCC discharge					
Protocol (direct liberation + stepwise weaning)	34 (77)	27 (93)	7 (47)	<.001	0.53
Non-protocol (slow weaning)	10 (23)	2 (7)	8 (53)	NA	NA

Data are expressed as mean ± SD or *n* (%).
*Cohen d for continuous variable or Cramer V for categorical variable.
APACHE II = Acute Physiology and Chronic Health Evaluation II
RCC = Respiratory Care Center
NA = not applicable

pressure > 180 mm Hg; heart rate > 120% of baseline, or the development of arrhythmia; frequency > 150% of baseline; S_{pO_2} < 90%; the blood CO_2 or end-tidal P_{aO_2} increase > 8 mm Hg, or serum pH < 7.2; the clinical judgment of a primary physician who was not involved in this study, including intolerable subjective dyspnea, accessory muscle use, diaphoresis, cyanosis, and loss of consciousness.[6]

Statistical Analysis

Data of clinical, physiologic, and outcome data are expressed as mean ± SD for continuous variables and were compared by using independent-sample *t* tests between the success and failure groups. However, the paired-sample *t* test was used to compare data between the beginning and the end of the SBT. Categorical variables were compared between the groups by using the chi-square or the Fisher exact test as appropriate. Linear regression analysis was performed to evaluate the relationships between EELV parameters and other physiologic variables, including V_T, frequency, and oxygen uptake. Also, the relationships between EELV parameters and the survival outcome of the days to successful liberation from mechanical ventilation during hospitalization were investigated by using the Cox proportional hazard model. All tests were 2-tailed, and $P <$ .05 was considered statistically significant. Data analyses were conducted by using SPSS 25 (SPSS Chicago, Illinois).

Results

Participants

During the study period, 44 subjects (26 men, 18 women) were included; their demographic and clinical characteristics are summarized in Table 1. Sepsis and/or septic shock and hospital-acquired pneumonia were the most common conditions that contributed to acute respiratory failure; heart diseases, including congestive heart failure and other cardiovascular diseases, were the most frequent comorbidities. Of the subjects, 29 (66%) were successfully liberated from mechanical ventilation at discharge from the Respiratory Care Center. The

Table 2. Physiologic Parameters of the Subjects and Comparisons Between the Success and Failure Groups

Parameter	Total ($N = 44$)	Weaning Success ($n = 29$)	Weaning Failure ($n = 15$)	P	Effect Size*
Glasgow coma scale	13.6 ± 3.0	14.2 ± 2.5	12.6 ± 3.7	.11	0.54
WBC count, cells/μL	8.84 ± 3.84	8.56 ± 3.64	9.43 ± 4.37	.54	–0.22
Hemoglobin, g/dL	9.1 ± 1.0	9.3 ± .9	8.7 ± 1.2	.11	0.59
C-reactive protein	23.1 ± 110.7	4.7 ± 5.4	61.9 ± 194.7	.16	–0.51
P_{Imax}, cm H_2O	39.0 ± 10.0	41.6 ± 10.4	34.1 ± 7.1	.02	0.80
P_{Emax}, cm H_2O	43.0 ± 14.6	46.9 ± 11.7	35.3 ± 16.9	.01	0.85
Beginning of SBT					
EELV at PEEP 0 cm H_2O, mL	1,279 ± 688	1,278 ± 744	1,279 ± 590	> .99	–0.001
EELV/PBW at PEEP 0 cm H_2O, mL/kg	22.1 ± 11.5	21.9 ± 12.4	22.5 ± 9.8	.87	–0.05
EELV at PEEP 5 cm H_2O, mL	1671 ± 936	1738 ± 1070	1542 ± 611	.52	0.21
EELV/PBW at PEEP 5 cm H_2O, mL/kg	28.8 ± 15.7	29.7 ± 18.1	27.1 ± 9.9	.61	0.16
RSBI	88 ± 42	83.8 ± 39.4	97.1 ± 45.7	.32	–0.32
V_T, mL	330 ± 114	350 ± 125	291 ± 77	.11	0.53
Frequency, breaths/min	25.8 ± 6.7	25.8 ± 6.3	25.8 ± 7.6	.99	< 0.001
Mean blood pressure, mm Hg	86.9 ± 13.9	87.2 ± 12.9	86.7 ± 16.2	.85	0.04
Heart rate, beats/min	84.5 ± 14.2	84.8 ± 13.4	84.0 ± 16.2	.86	0.06
S_{pO_2}, %	98.8 ± 1.8	99.0 ± 1.8	98.6 ± 2.0	.53	0.21
Carbon dioxide production, mL/min	173.0 ± 65.0	167.8 ± 60.6	182.9 ± 73.3	.47	–0.23
End of SBT					
EELV at PEEP 0 cm H_2O, mL	1,402 ± 747	1,493 ± 867	1,224 ± 401	.26	0.36
EELV/PBW at PEEP 0 cm H_2O, mL/kg	24.2 ± 12.4	25.4 ± 14.3	21.8 ± 7.4	.37	0.29
EELV at PEEP 5 cm H_2O, mL	1,605 ± 717	1670 ± 787	1479 ± 558	.41	0.27
EELV/PBW at PEEP 5 cm H_2O, mL/kg	27.9 ± 12.1	28.5 ± 12.8	26.7 ± 10.8	.65	0.15
RSBI	71.9 ± 36.4	66.3 ± 29.4	82.7 ± 46.2	.16	–0.46
V_T, mL	369 ± 118	375 ± 98	357 ± 154	.63	0.15
Frequency, breaths/min	23.7 ± 6.6	23.2 ± 6.8	24.7 ± 6.5	.47	–0.22
Mean blood pressure, mm Hg	88.8 ± 12.1	89.0 ± 11.6	88.6 ± 13.5	.92	0.03
Heart rate, beats/min	89.4 ± 15.6	89.7 ± 12.5	88.8 ± 20.7	.87	0.06
S_{pO_2}, %	98.5 ± 2.4	98.8 ± 2.2	97.7 ± 2.7	.15	0.46
Carbon dioxide production, mL/min	184.3 ± 50.6	182.2 ± 40.9	188.4 ± 66.9	.70	–0.12
Difference (end-beginning)					
EELV at PEEP 0 cm H_2O, mL	123 ± 497	215 ± 537	–55 ± 360	.09	0.56
EELV/PBW at PEEP 0 cm H_2O, mL/kg	2.1 ± 8.2	3.5 ± 8.7	–0.7 ± 6.4	.11	0.55
EELV at PEEP 5 cm H_2O, mL	–66 ± 584	–68 ± 659	–62 ± 429	.98	–0.01
EELV/PBW at PEEP 5 cm H_2O, mL/kg	–0.9 ± 10.1	–1.2 ± 11.3	–0.4 ± 7.7	.80	–0.08

Data are expressed as mean ± SD.
*Cohen d for continuous variable or Cramer V for categorical variable.
WBC = white blood cell
P_{Imax} = maximum inspiratory pressure
P_{Emax}= peak expiratory pressure
SBT = spontaneous breathing trial
EELV = end-expiratory lung volume
PBW = predicted body weight
RSBI = rapid shallow breathing index
V_T = tidal volume

demographic and clinical features of the success and failure groups were similar, except that more subjects in the failure group had chronic kidney disease versus those in the success group (73% vs 41%; $P = .044$).

Physiologic Parameters

The measured data of physiologic parameters and comparisons between the 2 groups are summarized in Table 2. The success group had better mean ± SD maximum inspiratory pressure (success vs failure, 41.6 ± 10.4 vs 34.1 ± 7.1 cm H_2O; $P = .02$) and mean ± SD maximum expiratory pressure (43.0 ± 14.6 vs 35.3 ± 16.9 cm H_2O; $P = .01$) than the failure group; however, there were no significant differences in the other physiologic parameters at the same time points, including at baseline, at the beginning of the SBT, and toward the end of the SBT (Table 2).

Table 3. Outcomes of the Subjects and Comparisons Between the Success and Failure Groups

Variable	Total ($N = 44$)	Weaning Success ($n = 29$)	Weaning Failure ($n = 15$)	P	Effect Size*
Duration of mechanical ventilation since the test, d	11.5 ± 12.0	4.9 ± 4.7	24.4 ± 11.3	<.001	–2.58
Duration of mechanical ventilation in the RCC, d	18.9 ± 13.1	10.8 ± 6.5	34.6 ± 6.5	<.001	–3.66
RCC length of stay, d	22.9 ± 10.9	16.9 ± 7.1	34.6 ± 6.5	<.001	–2.56
Length of since the test, d	48.0 ± 32.9	54.5 ± 36.6	36.4 ± 20.7	.09	0.56
In-hospital mortality	10 (23)	6 (2.7)	4 (26.7)	.71	0.07

Data are expressed as mean ± SD or *n* (%).
*Cohen d for continuous variable or Cramer V for categorical variable.
RCC = Respiratory Care Center

Table 4. The Relationships Between EELV and Days to Successful Liberation from Mechanical Ventilation (survival outcome)

SBT Parameter	Hazard Ratio (95% CI)	P
Beginning of the SBT		
EELV at PEEP 0 cm H_2O per 100 mL	1.01 (0.96–1.06)	.82
EELV/PBW at PEEP 0 cm H_2O	1.00 (0.97–1.03)	.97
EELV at PEEP 5 cm H_2O per 100 mL	1.02 (0.98–1.06)	.30
EELV/PBW at PEEP 5 cm H_2O	1.01 (0.99–1.03)	.38
End of SBT		
EELV at PEEP 0 cm H_2O per 100 mL	1.05 (1.02–1.08)	.002
EELV/PBW at PEEP 0 cm H_2O	1.03 (1.01–1.05)	.01
EELV at PEEP 5 cm H_2O, per 100 mL	1.03 (0.99–1.08)	.13
EELV/PBW at PEEP 5 cm H_2O	1.02 (0.99–1.04)	.28
Difference, end of SBT and beginning of SBT		
EELV at PEEP 0 cm H_2O per 100 mL	1.10 (1.01–1.19)	.02
EELV/PBW at PEEP 0 cm H_2O	1.06 (1.003–1.11)	.040
EELV at PEEP 5 cm H_2O per 100 mL	1.01 (0.93–1.09)	.84
EELV/PBW at PEEP 5 cm H_2O	1.00 (0.96–1.04)	>.99

EELV = end-expiratory lung volume
SBT = spontaneous breathing trial
PBW = predicted body weight

For all 44 subjects, unassisted breathing for 60 min resulted in significantly decreased mean ± SD rapid shallow breathing index (before vs after: 88.0 ± 42.0 vs 71.9 ± 36.4; $P = .004$) and mean ± SD frequency (25.8 ± 6.7 vs 23.7 ± 6.6 breaths/min; $P = .039$), with increased mean ± SD heart rate (84.5 ± 14.2 vs 89.4 ± 15.6 beats/min; $P = .02$) and mean ± SD V_T (330 ± 114 vs 369 ± 118 mL; $P = .02$). On average, the success group also had a significantly increased mean ± SD EELV at PEEP of 0 cm H_2O (1,278 ± 744 vs 1,493 ± 867 mL; $P = .040$), and mean ± SD EELV per predicted body weight (21.9 ± 12.4 mL/kg vs 25.4 ± 14.3 mL/kg; $P = .038$) also increased toward the end of the SBT, with a significantly decreased mean ± SD rapid shallow breathing index (83.8 ± 39.4 vs 66.3 ± 29.4; $P = .02$).

In contrast, toward the end of the SBT, there were no significant changes in EELV or rapid shallow breathing index in the failure group; however, the mean ± SD V_T increased significantly (291 ± 77 vs 357 ± 154 mL, $P = .03$). The difference of the mean ± SD EELV at PEEP of 0 cm H_2O (215 ± 537 vs – 55 ± 360 mL; $P = .09$) and the mean ± SD EELV per predicted body weight at PEEP of 0 cm H_2O (3.5 ± 8.7 vs – 0.7 ± 6.4 mL; $P = .11$) between the measurements of end and beginning of SBT tended to be increased in the success group and decreased in the failure group. The results of the linear regression of EELV and ventilation parameters showed that EELV, either at PEEP of 0 cm H_2O or 5 cm H_2O, was significantly positively correlated with carbon dioxide production at the beginning of the SBT but not at the end of SBT are summarized in Table 1 of the supplementary materials (see the supplementary materials at http://www.rcjournal.com). The V_T and the frequency were not correlated to the EELV (see the supplementary materials at http://www.rcjournal.com).

Weaning Outcome and Prognostic Significance of EELV

The secondary outcomes and comparisons between the 2 groups are summarized in Table 3. The failure group had a longer duration of mechanical ventilation after measuring the EELV ($P < .001$) and a longer duration of mechanical ventilation at the Respiratory Care Center ($P < .001$). The failure group also had a longer stay at the Respiratory Care Center ($P < .001$), but the stay after measuring the EELV was similar to the success group, with a similar in-hospital mortality rate.

The results of univariable Cox regressions for the weaning outcome are summarized in Table 4. At the beginning of the SBT, a more significant difference between EELV with PEEP of 0 cm H_2O and PEEP of 5 cm H_2O was significantly correlated to a higher likelihood of weaning success. Toward the end of SBT, a greater EELV level at PEEP of 0 cm H_2O was also correlated with a higher chance of weaning success. Also, the more significant difference of the EELV at PEEP of 0 cm H_2O between the beginning and the end of the SBT was also correlated with a shorter duration to weaning success (Table 4).

Discussion

In this study, we found that the difference of the measured EELV during the 60-min SBT and the EELV at the end of SBT was correlated with the days to successfully weaning of the subjects who were tracheostomized and with prolonged mechanical ventilation. To the best of our knowledge, the prognostic significance of the kinetics of EELV during open-circuit SBT in subjects with tracheostomy and with prolonged mechanical ventilation has not previously been reported. Thus, our findings suggest a potentially feasible model to understand the underlying mechanism of failure to be liberated from mechanical ventilation in these patients.

Previous studies measured the FRC in subjects on pressure-support spontaneous breathing or CPAP when the breathing circuit was connected to the ventilator.[27,28] FRC is not correlated with P_{aO_2}/F_{IO_2} in patients on mechanical ventilation, and is only moderately correlated with respiratory-system compliance.[29,30] Despite concerns whether measured EELV data can represent the FRC during unassisted breathing, FRC is influenced more by mechanical ventilation settings than by physiologic variables as in spontaneous breathing.[29] However, in this study, there was significant diversity in the evolution of the EELV. In general, the success group had a significant increase (215 mL on average) in the EELV. This indicated that multiple factors could influence the measurement of the EELV, such as pulmonary and extrapulmonary medical disorders, the breathing pattern during SBT, the presence of expiratory flow limitation due to underlying obstructive airway disease, dynamic airway compression, or retained airway secretions, peak inspiratory pressure, minute ventilation, and body weight.[29] Therefore, further studies with a larger population of subjects on prolonged mechanical ventilation stratified based on underlying mechanisms related to EELV are needed. Also, we focused on absolute EELV values rather than the EELV per predicted body weight. Indexing measured FRC values to predicted FRC values did not improve the correlation between P_{aO_2}/F_{IO_2} and respiratory-system compliance.[29]

The correlation between changes in the EELV during an SBT with weaning outcomes in this study suggests that patients in whom the weaning process failed may develop unfavorable changes in pulmonary aeration status during unassisted breathing. Because patients who have unassisted spontaneous breathing are not monitored by ventilators that measure respiratory mechanics, alternative approaches to understand the potential changes after starting unassisted breathing may be indicated. Measurement of the FRC or EELV during mechanical ventilation to assess the amount of ventilated alveoli[31] can be accomplished with new measurement technology incorporated into commercially available ventilators.[32] In patients with acute respiratory failure, atelectasis with decreased FRC and increased shunt, results in decreased oxygenation;[33] therefore, attempts at increasing the FRC might improve pulmonary gas exchange. However, in patients on ventilation, the FRC is influenced by multiple factors; therefore, a single FRC value could be misleading.[34] In contrast, FRC changes during the weaning process may reflect different states of alveolar recruitment and de-recruitment.

Our findings had several implications. Bedside measurement of the EELV or FRC with clinically acceptable accuracy and repeatability has the potential to be included in established assessments known as "weaning parameters."[19,35] The development of a progressive reduction in the EELV may also be an early indicator of weaning failure before the patient exhibits overt clinical manifestations, such as impaired gas exchange, paradoxical breathing movement, or severe distress. Rehabilitation to enhance the respiratory muscles and clearance of potentially obstructing airway secretions can also enhance the EELV. Measuring the EELV might not be feasible as a routine practice in the weaning units, mainly because of its cost and technical demand.

However, as our main finding was the tendency of the EELV reduction during SBT in subjects for whom weaning failed, clinicians might consider measuring EELV in those patients who tolerated continuous minimal support from the ventilator but with a failed SBT later. Maneuvers to restore EELV might also be considered during the SBT process in those patients in whom weaning failed and showed a reduced EELV. In some patients with a low EELV or with a significant reduction in EELV during unassisted breathing, a strategy of intermittent ventilatory support to maintain an adequate EELV may be considered. Nevertheless, how FRC measurements can guide the weaning process is still under debate, and our findings may provide more in-depth insight into how weaning failure develops during SBTs intended to impose a fixed work of breathing.

This study's strengths included the use of a protocolized weaning process in the weaning unit, the measurement of the EELV by a noninvasive device in an open-circuit setting of breathing, and simultaneous measurement of multiple respiratory physiologic variables. Nevertheless, there also were limitations to this study. First, this single-center study included only a small number of subjects, whereas the analysis of the data suggested high variations of the measured EELVs and other physiologic data in a patient population with diverse causes of respiratory failure. Second, we performed only one session of EELV measurements during the SBT because of a standardized weaning protocol, unless the process had been interrupted by clinical events or had failed. The feasibility of repeated measurements of the EELV needs further investigation. Third, the measurement of the EELV during subjects' spontaneous breathing movements did not exclude any condition that might affect the lung volumes,

such as severe cough, obstruction of airways by secretion, which resulted in atelectasis of the lung units, suctioning of airway secretion, and medications that affected ventilation and the drive for breathing. Nevertheless, our primary focus was not to interfere with the breathing pattern during the SBT, as seen in a real-world scenario. Fourth, because of the small number of subjects ($n = 15$) with failed tests, the multivariate analysis could not include more potential variables, such as clinical characteristics and other physiologic parameters. Fifth, because this study was based on a noninvasive design, we did not obtain the data to calculate work of breathing by using esophageal pressure measurements. Further studies are needed to investigate the exact role of work of breathing in the mechanism of weaning failure and its correlation with the EELV.

Conclusions

In this study, we hypothesized that the evolution of the EELV might occur during unassisted breathing in subjects on prolonged mechanical ventilation. Although we were unable to perform multivariate analysis in this single-centered study secondary to a small sample size, analysis of our data suggests that the changes in EELV during a 1-h SBT may be of prognostic value in the liberation of patients who were tracheostomized and with prolonged mechanical ventilation. However, further large-scale studies are warranted.

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