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ACUTE RESPIRATORY FAILURE

Static Respiratory System Compliance as a Predictor of Extubation Failure in Patients with Acute Respiratory Failure

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Abstract

Purpose Ventilator weaning protocols rely in part on objective indices to best predict extubation failure in the critically ill. We investigated static respiratory system compliance (RC) as a predictor of extubation failure, in comparison to extubation readiness using rapid shallow breathing index (RSBI).

Material and Methods This was a cross-sectional, multi-institutional study of mechanically ventilated patients admitted between 12/01/2017 and 12/01/2019. All patients older than 18 years with a documented spontaneous breathing trial and extubation trial were included. RC and RSBI were calculated prior to the extubation trial. The primary outcome was extubation failure—defined as need for reintubation within 72 h from time of extubation.

Results Of the 2263 patients, 55.8% were males with a mean age of 68 years. The population consisted mostly of Caucasians (73%) and African Americans (20.4%). 274 (12.1%) patients required reintubation within 72 h. On multivariate logistic regression after adjusting for age, sex, body mass index (BMI), admission Sequential Organ Failure Assessment (SOFA) score, number of ventilator days, and the P/F ratio on the day of extubation, RC remained the strongest predictor for extubation failure at 24 h (aOR 1.45; 95% CI 1.00–2.10) and 72 h (aOR 1.58; 95% CI 1.15–2.17). There was no significant association between RSBI and extubation failure at 24 (aOR 1.00; 95% CI 0.99–1.01) or at 72 h (aOR 1.00; 95% CI 0.99–1.01).

Conclusion RC measured on the day of extubation is a promising physiological discriminant to potentially risk stratify patients with acute respiratory failure for extubation readiness. We recommend further validation studies in prospective cohorts.

Keywords Static respiratory system compliance · Extubation · Mechanical ventilation · Respiratory Failure · Rapid shallow breathing index

Introduction

Protocolized ventilator weaning trials attempt to identify readiness and likelihood of successful extubation. When compared to non-protocolized weaning practice, these trials significantly reduce total duration of ventilation, weaning duration, and intensive care unit length of stay [1–3]. Extubation failure or need for reintubation within 48 to 72 h after extubation is independently associated with increased mortality [2, 4, 5]. Failure of the SBT, whether through a T-tube or a low-level pressure support (< 8 cmH_2O), relies on objective and subjective weaning parameters [6]. Such parameters include tachypnea, hypertension, cardiac arrhythmia, diaphoresis, and agitation, which are only quantified in part by the rapid shallow breathing index (RSBI) or the ratio of respiratory frequency to tidal volume (f/V_T) [5, 7]. A RSBI value greater than 105 breaths/min/L was associated with weaning failure, while an RSBI less than 105 breaths/min/L predicted weaning success [5]. Despite these weaning predictors, extubation failure rates are still relatively high between 10 and 20% [2, 3, 8]. Further, there are insufficient data on the characteristics of patients who

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pass SBT with RSBI < 105 breaths/min/L, but require reintubation within 72-h.

Static respiratory system compliance (RC) relies on the elastic properties of the respiratory system. Normal static compliance in healthy adults is reported as 80–100 mL/cm H_2O, whereas in acute respiratory distress syndrome, static compliance is notably reduced at 29–42 mL/cm H_2O [9, 10]. A reduction in static compliance has also been demonstrated in other critically ill patients with pulmonary edema, pneumonia, pulmonary fibrosis, neuromuscular diseases, obesity, and abdominal distension [6]. Current weaning strategies remain insensitive to worsening respiratory load, particularly in critically older patients, owing to loss of respiratory muscle strength, elastic recoil, and exchange surface area [11]. We hypothesize that a decreased RC to a level less than 50 mL/cm H_2O is associated with an increased risk of reintubation within 72-h of extubation. In this study, we investigated the role of RC as a predictor of extubation failure and compared its predictive value to that of the RSBI after controlling for other clinically relevant patient factors.

Methods

Study Design

We conducted a retrospective analysis of all adult (age ≥ 18 years of age) mechanically ventilated patients admitted between December 1, 2017 and December 1, 2019 in a large academic health system composed of eight hospitals in Michigan. This study was reviewed and approved by the Institutional Review Board (IRB # 2020-048).

Patient demographics, comorbid diagnoses, admission and discharge diagnoses, ventilator data, and laboratory data were extracted from electronic medical records. RC was calculated from the following equation after completion of daily weaning trial:

$$RC = \frac{returned\ V_t}{P_{plateau} - PEEP},$$

where V_T represents the tidal volume (mL), $P_{Plateau}$ is the pressure measured from the onset of end-inspiratory occlusion (cmH_2O) and PEEP (positive end-expiratory pressure) (cmH_2O)) [9].

Those patients who underwent a change in code status to no reintubation after extubation or those, who were compassionately extubated or in those, who had a second intubation within the same hospital stay or were extubated without a documented spontaneous breathing trial were excluded from the analysis (Fig. 1). Patients with incomplete datasets were also excluded from the analysis.

A 30- to 60-min SBT was performed by the respiratory therapist based on institutional protocol for weaning on all ventilated patients. During the SBT, a continuous positive airway pressure (CPAP) of 0 to 5 cm H_2O, FiO2 ≤ 40%, and pressure support ventilation (PSV) of 4–5 cm H_2O were provided. The SBT was terminated if any of the following was observed: sustained oxygen saturation < 90%, change in blood pressure > 20% from baseline, heart rate > 120 or < 50 beats per minute or 20% change from baseline, respiratory rate > 30 breaths per minute, apnea > 30 s, and signs of increased work of breathing (accessory muscle use, paradoxical respiratory pattern, or change in Richmond Agitation Sedation Scale). SBT was successful if the patient obtained a negative inspiratory force ≥ 20 cm H_2O, vital capacity ≥ 10 mL/kg, and RSBI < 100. At completion of the trial, patients were returned to their prior ventilator settings. RC, and ratio of arterial oxygen partial pressure to fractional inspiratory oxygen (P/F ratio) was obtained from the last ventilator measurement.

Outcomes and Statistical Analysis

The main outcome was extubation failure (reintubation) occurring within 72 h of the first extubation attempt compared between patients with a lower (< 50 mL/cm H_2O) or higher (≥ 50 mL/H_2O) calculated RC on the day of extubation. We elected to transform RC into a dichotomous variable to allow for bedside application. A multivariate logistic regression model including RC as a binary variable was used to assess the impact of patient factors on extubation failure. Candidate variables were preliminarily identified as potentially significant in univariate logistic regression models. Additionally, the predictive value of RC for extubation failure was compared to that of the RSBI employed as a continuous variable using alternative multivariate logistic regression models.

Statistical analysis was performed using JMP version 16 (SAS Institute, Cary, North Carolina). Categorical

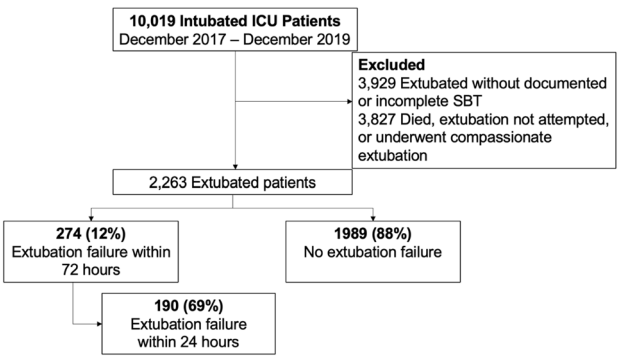

Fig. 1 Study population. *ICU* Intensive Care Unit; *SBT* Spontaneous Breathing Trial

variables are described as frequency (percentage). Normal or approximately normal variables are reported using the mean (± standard deviation), whereas skewed variables are reported with the median (interquartile range [IQR]). Categorical variables were compared using the Chi-square test or Fisher exact test. Normal variables were compared using a 2-sided Student *t* test and ordinal variables used the Kruskal–Wallis test. The Wilcoxon test was used for comparison of non-normally distributed data. All *p* values were 2-sided and a $p < 0.05$ was considered to indicate statistical significance.

Results

A total of 2263 adult patients were included in the final analysis (Fig. 1). The baseline characteristics of the study population are presented in Table 1. Apart from a predominance of men in the higher RC subset (72.3% vs 48.7%; *p* value < 0.01), the two groups of interest were balanced in terms of age, race, median body mass index (BMI), admission SOFA score, and days on the ventilator prior to the first extubation attempt. Similarly, the P/F ratio on the day of first extubation was comparable between the two subpopulations.

When considered as a continuous variable, median RSBI values were lower in the higher RC group (32 [IQR 26–39] vs 37 [IQR 31–47]; *p* value < 0.01). Only 24 patients in the overall population had an RSBI value of 105 or greater and all belonged to the lower RC group.

Extubation failure within 72 h was significantly more frequent in the lower RC group (13.6% vs 8.6%; *p* value < 0.01; Fig. 2). In either subset, most reintubations occurred in the first 24 h (149/216 in the lower RC group and 41/58 in the higher RC group). Inpatient deaths were also more frequent in the lower compliance group (11.5% vs 6.1%: *p* value < 0.01).

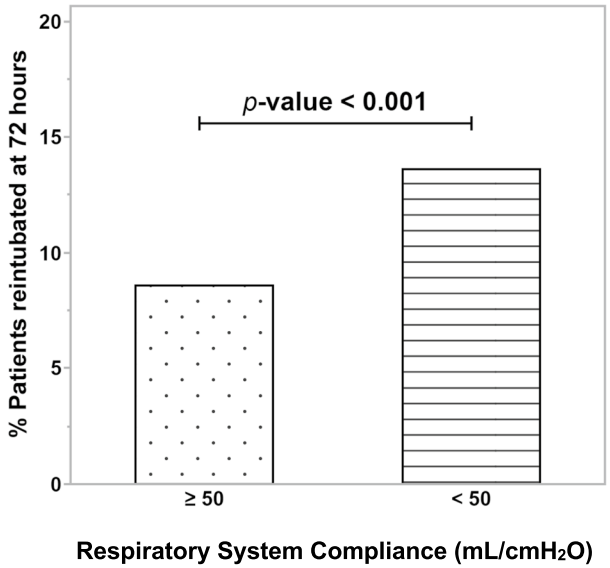

Fig. 2 Extubation failure at 72 h in patients with respiratory system compliance ≥ 50 and < 50 mL/cm H_2O

Table 1 Baseline characteristics of overall study population and stratified by lung compliance

	All patients (*N* = 2263)	Lung compliance < 50 mL/cm H_2O (*N* = 1587)	Lung compliance ≥ 50 mL/cm H_2O (*N* = 676)	*P*-value
Age (years)	68.5 ± 16.4	66.1 ± 16.7	65.0 ± 15.5	0.14
Male sex	1263 (55.8%)	773 (48.7%)	490 (72.3%)	< 0.01
Race				< 0.01
Caucasian	1653 (73.0%)	1114 (70.2%)	539 (79.7%)	
Black	462 (20.4%)	360 (22.7%)	102 (15.1%)	
Other	148 (6.5%)	113 (7.1%)	35 (5.2%)	
BMI (kg/m^2)	28.5 (23.9–34.4)	28.9 (24.0–34.7)	28.1 (23.6–33.3)	0.07
Admission SOFA score	5 (3–7)	5 (3–7)	4.5 (3–7)	0.05
P/F ratio on extubation day	286 (180–383)	285 (180–382)	295 (190–388)	0.18
RSBI on extubation day	36 (29–44)	37 (31–47)	32 (26–39)	< 0.01
Length of stay (days)	12 (7–20)	13 (7–21)	10 (7–16)	< 0.01
Ventilator days prior to first extubation	3 (2–5)	3 (2–6)	3 (2–5)	< 0.01
Extubation failures	387 (17.1%)	305 (19.2%)	82 (12.1%)	< 0.01
Within 24 h	190 (8.4%)	149 (9.4%)	41 (6.1%)	< 0.01
Within 72 h	274 (12.1%)	216 (13.6%)	58 (8.6%)	< 0.01
Inpatient deaths	223 (9.9%)	182 (11.5%)	41 (6.1%)	< 0.01

Age is presented as mean ± standard deviation. BMI, admission SOFA score, P/F ratio on extubation day, length of stay, and ventilator days are presented as median (interquartile range). Other numbers represent N (%). *BMI* body mass index; *RSBI* Rapid Shallow Breathing Index; *SOFA score* Sequential Organ Failure Assessment score

In a multivariate logistic regression model adjusting for age, sex, BMI, admission SOFA score, number of days on the ventilator, and the P/F ratio on the day of extubation, a calculated RC < 50 mL/cm H_2O was associated with higher odds of extubation failure at 24 h (adjusted odds ratio [aOR] 1.45; 95% confidence interval [95% CI] 1.00–2.10) and at 72 h (aOR 1.58; 95% CI 1.15–2.17) (Table 2). By contrast, when the RSBI replaced RC as a continuous variable, it displayed no significant association with extubation failure within 24 h (aOR 1.00 per 1-unit change; 95% CI 0.99–1.01) or within 72 h (aOR 1.00; 95% CI 0.99–1.01).

Discussion

In this study, we investigated the role of RC in patients who had a successful SBT. Our main findings include the following: (1) RC less than 50 mL/cm H_2O is associated with extubation failure at 72 h; (2) reintubations occur more often in the first 24 h; (3) RC less than 50 mL/cm H_2O is associated with a higher frequency of inpatient deaths. These findings were significant even after adjusting for age, sex, severity of disease, and number of days on the ventilator prior to extubation.

Extubation failure has been associated with post-extubation stridor, upper airway patency, positive fluid balance 24 h prior to extubation, excess bronchial secretions, inadequate cough strength, duration of mechanical ventilation > 72 h, RSBI greater than 105 breaths/min/L, and a prior failed weaning attempt [6, 12, 13]. Some studies have attributed this variation to the patient subpopulation, particularly those with chronic obstructive pulmonary disease or with a high asynchrony index [14, 15]. When comparing cause of respiratory failure in the compliance subsets, those patients with principal admission diagnoses of acute respiratory distress syndrome (ARDS), asthma, or COPD were more likely to have a RC less than 50 mL/cm H_2O (Table S1). Our findings suggest the addition of RC as another physiological discriminate to better predict extubation failure, even in those who had successful SBT with RSBI < 105.

The literature examining the role of static compliance in extubation readiness is limited. Okabe et al. concluded that there is an increased probability of extubation failure seen with compliance under 50–60 mL/cm H_2O [12]. While we concluded a similar threshold for extubation failure of less than 50 mL/cm H_2O, the former study was restricted to postoperative patients alone, whereas our study extended its inclusion to all mechanically ventilated adult critical care patients [12].

The role of static compliance as an index for pulmonary overdistension, which has been independently linked to extubation failure, is well established [16–18]. In patients with a reduced inspiratory capacity, an increase in tidal volume impinges on the upper plateau of the pressure–volume curve leading to the decrease in static compliance with clinical implications of increased pulmonary vascular resistance in ventilated regions and susceptibility to eventual collapse [16]. This inverse role in dynamic hyperinflation was later applied to weaning trials in COPD patients. Static compliance was found to not significantly differ from that of normal subjects except on the first day of mechanical ventilation, when subjects exhibited marked dynamic hyperinflation; however, this study was limited in its evaluation of the SBT, when these patients may exhibit marked dynamic hyperinflation [17]. This was further extrapolated in spontaneously breathing patients, when a prospective cohort of patients receiving mechanical ventilation demonstrated that the application of extrinsic PEEP led to an increase in the end-expiratory lung volume which significantly correlated with static compliance [18]. We concluded similar findings in our analysis of 304 patients (13.4%) with a pre-existing history of COPD. At time of SBT, this population subset had a median RC of 36 (IQR 28–50) with 72 patients (23.7%) requiring reintubation.

Table 2 Risk of extubation failure within 24 and 72 h

	aOR (95% CI) for extubation failure within 24 h	aOR (95% CI) for extubation failure within 72 h
Respiratory system compliance < 50 mL/cm H_2O	1.45 (1.00–2.10)	1.58 (1.15–2.17)
Age	1.00 (0.99–1.01)	1.01 (0.99–1.10)
Male sex	0.8 (0.59–1.10)	1.05 (0.80–1.38)
BMI	0.98 (0.96–1.00)	0.99 (0.97–1.01)
P/F ratio on day of extubation	1.00 (0.99–1.01)	0.98 (0.97–0.99
Ventilatory days prior to extubation	1.00 (0.99–1.01)	1.00 (0.99–1.01)
Admission SOFA score	1.02 (0.97–1.10)	1.02 (0.97–1.06)

Except for lung compliance and male sex, all other adjusted odds ratios are presented as values per 1-unit change. *aOR* adjusted odds ratio; *95% CI* 95% confidence interval; *BMI* body mass index; *SOFA score* Sequential Organ Failure Assessment score

Several studies have evaluated alternative cutoff RSBI thresholds in predicting extubation failure. *Frutos–Vivar* et al. reported a threshold of 57 breaths/min/mL increased the risk of reintubation from 11 to 18% [13]. Other studies have documented the significant differences in RSBI between reintubated and non-reintubated patients, but with varying medians [19–21]. No significant difference in sensitivity or specificity was noted in RBSI thresholds of 80 to 105 compared to less than 80 [22]. To our knowledge, the comparison of RC to RSBI as a predictive index has not been evaluated. Only 24 of the 2263 extubated patients (1.06%) had a RSBI value of greater than 105 breaths/min/mL, yet 274 (12%) failed extubation in our study. All patients who exceeded the RSBI threshold did, however, have a RC of less than 50 mL/cm H_2O.

Extubation failure alone is associated with increased mortality [1]. We found that a RC of less than 50 mL/cm H_2O was not only associated with extubation failure, but with an increased inpatient mortality of 11.9% vs 6.1%. Static compliance and its mortality prediction had not been previously defined, but rather suggested in relation to the mortality benefit cited with strategies to decrease driving pressure [23–25]. Driving pressure is measured in the absence of inspiratory effort and calculated by the following: plateau pressure–PEEP. When disassociated from this variable, individual changes in V_T and PEEP do not lead to mortality benefit [24]. We may have concluded similar findings by electing to measure static versus dynamic compliance.

Limitations

This study has several limitations. First, due to the retrospective design, selection bias may have been introduced pending availability of electronic health records. Such data points excluded due to availability of electronically extracted data included reason for intubation and use of non-invasive ventilatory support following extubation. Second, while a standardized ventilator weaning protocol was in place, adaptation, deviation, and variability of practice among providers may have also introduced bias. Such variability highlighted within the protocol included trial duration and range of CPAP and PSV. Also, while RC was calculated at completion of SBT after patients were returned to their prior ventilatory settings, we cannot account for variability in muscular activity at time of calculation. There was also a male predominance noted in the higher RC subset (72.3% vs 48.7%; *p* value); however, the multivariate logistic regression model adjusted for this variable when evaluating RC and its primary association. Finally, this study's inclusion period ended prior to the COVID-19 pandemic. We recommend future studies comparing RC in non-COVID to COVID patients.

Conclusion

Traditional protocolized weaning predictors and parameters remain insensitive in risk stratifying patients with acute respiratory failure for extubation success. We conclude that static RC, measured at the day of extubation, is a promising predictor for extubation failure. We recommend further validation studies in prospective cohorts.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00408-023-00625-7.

Author Contributions All authors contributed equally in manuscript preparation. GN, FI, and LA did all analysis and final interpretation.

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Declarations

Conflict of interest None of the authors report any potential conflicts of interest with the materials presented.

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