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Work of Breathing During Proportional Assist Ventilation as a Predictor of Extubation Failure

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BACKGROUND: Despite decades of research on predictors of extubation success, use of ventilatory support after extubation is common and 10–20% of patients require re-intubation. Proportional assist ventilation (PAV) mode automatically calculates estimated total work of breathing (total WOB). Here, we assessed the performance of total WOB to predict extubation failure in invasively ventilated subjects. METHODS: This prospective observational study was conducted in 6 adult ICUs at an academic medical center. We enrolled intubated subjects who successfully completed a spontaneous breathing trial, had a rapid shallow breathing index < 105 breaths/min/L, and were deemed ready for extubation by the primary team. Total WOB values were recorded at the end of a 30-min PAV trial. Extubation failure was defined as any respiratory support and/or re-intubation within 72 h of extubation. We compared total WOB scores between groups and performance of total WOB for predicting extubation failure with receiver operating characteristic curves. RESULTS: Of 61 subjects enrolled, 9.8% (n = 6) required re-intubation, and 50.8% (n = 31) required any respiratory support within 72 h of extubation. Median total WOB at 30 min on PAV was 0.9 J/L (interquartile range 0.7–1.3 J/L). Total WOB was significantly different between subjects who failed or were successfully extubated (median 1.1 J/L vs 0.7 J/L, P = .004). The area under the curve was 0.71 [95% CI 0.58–0.85] for predicting any requirement of respiratory support and 0.85 [95% CI 0.69–1.00] for predicting re-intubation alone within 72 h of extubation. Total WOB cutoff values maximizing sensitivity and specificity equally were 1.0 J/L for any respiratory support (positive predictive value [PPV] 70.0%, negative predictive value [NPV] 67.7%) and 1.3 J/L for re-intubation (PPV 26.3%, NPV 97.6%). CONCLUSIONS: The discriminative performance of a PAV-derived total WOB value to predict extubation failure was good, indicating total WOB may represent an adjunctive tool for assessing extubation readiness. However, these results should be interpreted as preliminary, with specific thresholds of PAV-derived total WOB requiring further investigation in a large multi-center study. *Key words: mechanical ventilation; weaning; noninvasive ventilation; endotracheal tube; rapid shallow breathing index; extubation.* [Respir Care 0;0(0):1–•. © 2023 Daedalus Enterprises]

Introduction

One of the biggest challenges in managing critically ill, intubated patients is the timing of extubation. Both premature extubation and delayed extubation are fraught with substantial consequences to the respiratory and cardiac systems, increased risk of infection, airway trauma, higher hospital costs, and increased mortality.[1,2] There is constant tension in the care of these patients to extubate as soon as they are physiologically capable, while at the same time avoiding the risks of premature liberation from mechanical ventilation. Despite decades of research attempting to identify predictors and strategies to promote extubation success, a significant portion of patients still requires rescue modes of noninvasive mechanical ventilation or re-intubation.[3]

Multiple indices have been proposed to predict extubation readiness with varying results. Single-value indices such as minute ventilation, peak inspiratory pressure, and the maximal inspiratory pressure intuitively perform less well than indices that incorporate several respiratory parameters.[1] More complex indices incorporate numerous respiratory mechanics parameters but are cumbersome to use and not universally available at the bedside.[4] To date, the most widely adopted index has been the rapid shallow breathing index (RSBI), which is easily applied at the bedside.[5,6] Current practice guidelines commonly support performing a spontaneous breathing trial (SBT) and measuring the RSBI to assess extubation readiness.[3,4,6] However, the accuracy of the RSBI and other proposed indices to predict extubation failure is overall modest.[7] Pooled results for the RSBI show that a positive result is minimally helpful in increasing the probability of successful weaning, whereas a negative result moderately increases the probability of weaning failure.[6,8] Furthermore, there is no evidence to date that the use of the RSBI improves clinical outcomes, such as duration of mechanical ventilation.[9] Despite widespread use of the RSBI, there remains room for improvement and an ongoing need for additional predictors of extubation failure.

Given numerous factors are responsible for extubation failure, indices that consider multiple physiologic parameters may better predict readiness for extubation. However, measurement of numerous physiologic parameters may not be practical nor timely. Proportional modes of ventilatory support provide a potential approach to capture a global assessment of respiratory mechanics. Proportional ventilation modes, such as proportional assist ventilation (PAV) and PAV with load-adjustable gain factors (PAV+), apply the equation of motion of the respiratory system and repeated physiological measurements to automatically calculate the patient's estimated work of breathing (WOB) and estimated total WOB.[10] No studies to date have evaluated the use of PAV-calculated total WOB to predict extubation outcomes. Thus, the purpose of this study was to assess the performance of a PAV-calculated total WOB to predict extubation failure in subjects who had already successfully passed an SBT.

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Drs Fazio and Lin contributed equally to this study.

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QUICK LOOK

Current knowledge

Despite decades of research on predictors of extubation success, use of ventilatory support after extubation is common, and approximately 10–20% of patients require re-intubation. Improving tools to assist clinicians in determining extubation readiness is important to maximize patient safety and improve outcomes of mechanically ventilated patients.

What this paper contributes to our knowledge

We analyzed the performance of an estimated total work of breathing (total WOB) value calculated on proportional assist ventilation (PAV) to predict extubation failure in subjects who had successfully passed a spontaneous breathing trial. The discriminative performance of a PAV-derived total WOB value to predict re-intubation was good, suggesting total WOB may represent an adjunctive tool for assessing extubation readiness.

Methods

Study Design

We conducted a prospective observational study in 6 adult ICUs between September 2016–January 2019, at the University of California, Davis Medical Center. The study was reviewed and approved by the local institutional review board (study number 752364), and informed consent was obtained from all subjects or their surrogates. This study was conducted in compliance with the Standards of Reporting of Observational Studies in Epidemiology (STROBE) guidelines[11] and the STROBE checklist (Supplemental information [SI] eTable A, see related supplementary materials at http://www.rcjournal.com).

Subjects

Eligible adult subjects were identified by daily conversations between the research staff and ICU team to determine which subjects were ready for extubation as determined by their primary ICU team. Subjects enrolled in the study must have had an SBT performed by the primary team (typically, CPAP with PEEP 5 cm H_2O for 30 min) with a measured RSBI < 105 breaths/min/L throughout the breathing trial. Additional inclusion criteria included an F_{IO_2} < 0.5, a Glasgow coma scale score > 10, ideal body weight > 25 kg, endotracheal tube inner diameter 6–10 mm, and hemodynamic stability off vasopressors at the time of extubation (See Fig. 1 and SI eFigure A, see related supplementary materials at http://www.rcjournal.com). Additionally, all

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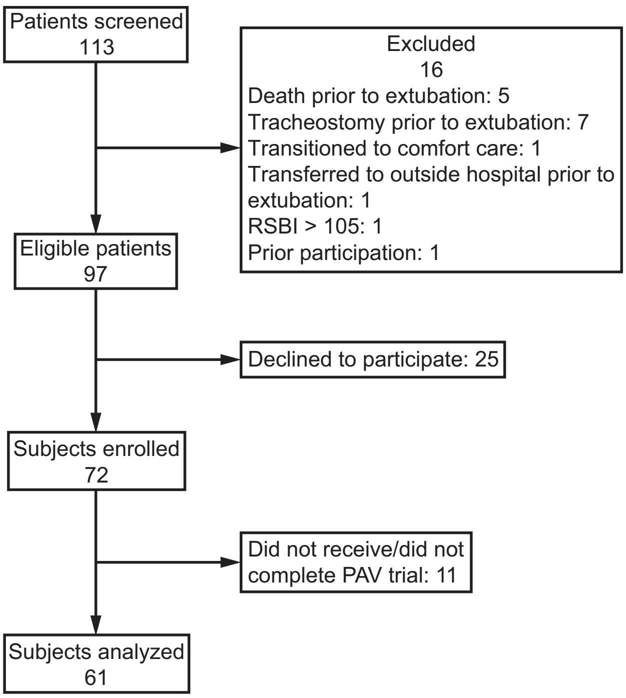

Fig. 1. Flow chart. RSBI = rapid shallow breathing index; PAV = proportional assist ventilation.

subjects were required to be on a Puritan Bennett 840 ventilator (PB 840) (Medtronic, Minneapolis, Minnesota) at the time of the study. Subjects were excluded if they were < 18 y old, were pregnant, were current prisoners, had a plan to transition to comfort-oriented care per the primary team, had a persistent bronchopleural fistula, were ventilated through a tracheostomy tube, or if they had a calculated RSBI > 105 breaths/min/L at the end of an SBT performed by the treating team. Recruitment was constrained by research staff availability as the study had limited departmental funding.

Procedures and Data Collection

After consent was obtained, research staff placed the subject on PAV mode on the mechanical ventilator for 30 min, and WOB measurements were recorded (Puritan Bennett PAV+ software, Medtronic). PAV+ software performs measurements of compliance and resistance and utilizes that information to calculate the patient-generated pressure (muscle pressure) and WOB using the equation of motion (flow, resistance, volume, and compliance all being measured breath to breath). While on PAV, research staff adjusted the percent support provided by the ventilator to ensure the subject was maintained in the normal WOB range recommended by the manufacturer. Therefore, for all subjects, we started with 50% ventilator support and adjusted support to keep the subject's WOB value within the designated normal range, or "green region," of 0.3–0.7 J/L, as determined by the ventilator's software (SI eFigure B, see related supplementary materials at http://www.rcjournal.com).

At 30 min, an instantaneous total WOB value was recorded, and the subject was placed back on their prior ventilator settings. We chose to measure total WOB at 30 min to ensure stability of the respiratory system after initiation of PAV mode and to ensure a steady-state level of percent support on the ventilator. Total WOB is defined as the total energy in J/L of tidal volume required to overcome airway resistance and respiratory system compliance. Patient WOB is defined as the amount of effort exerted by the patient and is a fraction of the total WOB. Even patients at the highest range of total WOB can be supported in the normal range for patient WOB by adjusting the ventilatory support provided. For example, patients with total WOB at 2.0 J/L on a percent support titrated to 80% would experience a respiratory load of approximately 0.4 J/L, well within a work load considered sustainable for an indefinite period for most individuals.

Timing of extubation, decision to extubate, and the extubation procedure were all performed by the primary health care team, who was blinded to total WOB values. No treatments were delayed by the real-time assessment of the total WOB measurement, including extubation (in our academic institution, decision to extubate often occurs after morning academic rounds, introducing natural delay from SBT to extubation).

Outcomes and Measurements

The primary a priori study outcome was extubation failure in subjects that had successfully passed an SBT. Extubation failure was defined a priori and based on literature as use of noninvasive ventilation (NIV), high-flow nasal cannula (HFNC), or re-intubation within 72 h of extubation.[1,12,13] Our secondary outcome was re-intubation within 72 h of extubation alone. All decisions regarding weaning and respiratory support provided, including re-intubation, were determined by the primary ICU treatment team, as this study was observational.

Each subject's electronic health record (EHR) was reviewed independently by 2 ICU researchers to confirm the presence of a failed or successful extubation. Disagreements were adjudicated by consensus. In addition to extubation outcomes, basic demographic information, comorbidities, hospitalization characteristics, vital signs, laboratory, respiratory, SBT, and mechanical ventilation–related data were extracted from the EHR.

Statistical Analysis

Continuous data were summarized with means and standard deviation (SD) when they were normally distributed or with medians and interquartile ranges (IQRs) when they were non-normally distributed; categorical data were

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summarized with proportions. The exposure of interest was total WOB measured 30 min after start of the PAV trial. Total WOB is calculated by the PB 840 in PAV+ mode as a continuous variable ranging from 0.1–2.0 J/L. Total WOB scores calculated by the ventilator as > 2.0 J/L were classified as 2.1 to denote a numerical but "out-of-range" value for statistical analysis. Total WOB scores were compared between groups using the Mann-Whitney U test. Assuming an extubation success rate of at least 70%,[3] using a Pearson chi-square test for proportion difference with normal approximation, with 0.8 power, and a type 1 error of 0.05, we estimated we would need to recruit 84 subjects (SAS Software, SAS Institute Inc, Cary, North Carolina).

We generated receiver operating characteristic (ROC) curves and calculated an area under the ROC curve, with 95% confidence interval (CI) to assess the ability of total WOB to correctly classify the presence of a failed or successful extubation. For each ROC analysis, we also calculated a Youden index to capture a total WOB cutoff point that balances sensitivity and specificity equally,[14] along with the positive predictive value (PPV) and negative predictive value (NPV).

Statistical analyses were performed using Stata, version 13.0 (StataCorp, College Station, Texas) and GraphPad Prism version 9.0 (GraphPad by Dotmatics, San Diego, California). All reported *P* values were 2 sided, and a *P* value < .05 was considered statistically significant.

Results

Participants

A total of 113 ICU patients on mechanical ventilation were screened for study participation, and 72 subjects were enrolled in the study. Sixty-one subjects completed the PAV trial, were followed for 72 h following extubation, and included in the analysis (Fig. 1). COVID restrictions on non-essential staff and our institution changing ventilator brands en masse lead to a decision to terminate the study before completion of targeted sample size. Participant and hospitalization characteristics, including comorbidities and ventilation-related information prior to extubation, are presented in Tables 1 and 2.

Extubation Failure

Overall, 50.8% ($n = 31$) of subjects failed extubation, defined as any use of NIV, HFNC, or re-intubation within 72 h of extubation, whereas 9.8% ($n = 6$) required re-intubation alone within 72 h of extubation. Of the entire cohort, 36.1% ($n = 22$) of subjects were extubated directly from mechanical ventilation to HFNC ($n = 12$) or NIV ($n = 10$). Median time to re-intubation was 32.3 h (IQR 19.6–44.6); no subjects died during the 72 h observation period following extubation. Reasons for re-intubation varied, including alveolar hemorrhage and acute respiratory distress ($n = 2$) (SI eTable B, see related supplementary materials at http://www.rcjournal.com).

Work of Breathing (WOB) Values

For the entire cohort, median total WOB at 30 min on PAV was 0.9 J/L (IQR 0.7–1.3 J/L). Median ventilator percent support provided during PAV was 50% (IQR 40–50%). PAV-derived total WOB values and ventilator percent support provided were significantly higher for subjects who failed extubation for any reason compared to those who were successfully extubated (median 1.1 J/L vs 0.7 J/L, $P = .004$) (Fig. 2) and (50% vs 45%, $P = .008$). Median total WOB and percent support provided by the ventilator for subjects who were reintubated were significantly higher than those who did not require re-intubation (1.65 J/L vs 0.8 J/L, $P = .005$) (62.5% vs 50%, $P = .042$).

Total WOB as a Predictor of Extubation Failure

The area under the curve was 0.71 [95% CI 0.58–0.85] for predicting requirement of any respiratory support (a priori extubation failure definition) and 0.85 [95% CI 0.69–1.00] for predicting re-intubation alone within 72 h of extubation from mechanical ventilation. The associated ROC curves for each extubation outcome are shown in Figure 3.

Using Youden index, the single total WOB value that maximized sensitivity and specificity equally for any respiratory support following extubation was 1.0 J/L (PPV 70.0%, NPV 67.7%) and was 1.3 J/L for re-intubation alone (PPV 26.3%, NPV 97.6%) (SI Table B). The sensitivity, specificity, and the likelihood ratios for total WOB scores at different cutoff points for each extubation outcome are presented in SI eTable C (See related supplementary materials at http://www.rcjournal.com).

Discussion

We conducted a small, observational study to examine the performance of PAV-calculated total WOB to predict extubation failure in subjects previously passing an SBT. Whereas all subjects in this study passed an SBT and had a RSBI < 105 breaths/min/L prior to study enrollment, 51% of subjects required some type of respiratory support following extubation, with 10% of subjects requiring re-intubation alone, which is consistent with the literature.[1,15] We found total WOB values differed significantly among subjects who had successful *versus* failed extubation. Discriminative performance was good (area under the curve = 0.85) for prediction of re-intubation alone. Re-intubation is one of the most clinically meaningful definitions of extubation failure given the independent association

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Table 1. Subject Characteristics

	Total Cohort ($n = 61$)	Successfully Extubated ($n = 30$)	Any Type of Respiratory Failure ($n = 31$)	Re-intubated ($n = 6$)
Demographics				
Age, y	59 (15)	56 (17)	61 (12)	63 (10)
Sex, male	27 (44.3)	13 (43.3)	14 (45.2)	3 (50.0)
BMI	30.0 (8.4)	28.7 (8.1)	31.1 (8.8)	33.8 (13.3)
Ethnicity				
Hispanic or Latino	8 (13.1)	7 (23.3)	1 (3.2)	0
Race				
White	34 (55.7)	18 (60.0)	16 (51.6)	2 (33.3)
Black	5 (8.2)	1 (3.3)	4 (12.9)	0
Pacific Islander or Native Hawaiian	3 (4.9)	1 (3.3)	2 (6.5)	1 (16.7)
American Indian or Alaskan Native	1 (1.6)	1 (3.3)	0	0
Asian	1 (2.0)	1 (3.3)	0	0
Multiracial	6 (9.8)	4 (13.3)	2 (6.5)	1 (16.7)
Other	11 (18.03)	4 (13.3)	7 (22.6)	2 (33.3)
ICU presentation				
Primary medical service				
Pulmonary critical care	54 (88.5)	25 (83.3)	29 (93.6)	4 (66.7)
Neurology	3 (4.9)	3 (10.0)	0	0
Surgery	3 (4.9)	2 (6.7)	1 (3.2)	1 (16.7)
Cardiology	1 (1.6)	0	1 (3.2)	1 (16.7)
Elixhauser comorbidity count	6.9 (3.5)	7.1 (3.3)	6.7 (3.7)	8.3 (4.6)
ICU admission SOFA score	8.8 (3.9)	8.3 (4.0)	9.3 (3.8)	11.8 (2.5)
Reasons for initial intubation				
Pneumonia/aspiration/pleural effusion	15 (24.6)	15 (16.7)	10 (32.3)	1 (16.7)
AMS/airway protection/CVA/seizure	20 (32.8)	13 (43.3)	7 (22.6)	2 (33.3)
Heart failure/volume overload	12 (19.7)	4 (13.3)	8 (25.8)	1 (16.7)
Obstructive lung disease (Asthma/COPD)	5 (8.2)	2 (6.7)	3 (9.7)	0
Interstitial lung disease	3 (4.9)	2 (6.7)	1 (3.2)	1 (16.7)
Diffuse alveolar hemorrhage	2 (3.3)	1 (3.3)	1 (3.2)	1 (16.7)
Gastrointestinal bleeds	2 (3.3)	1 (3.3)	1 (3.2)	0
Other	2 (3.3)	2 (6.7)	0	0
Hospitalization outcomes				
Mechanical ventilation time prior to index extubation, d	4.3 (2.0–8.0)	3.8 (1.6–8.0)	4.7 (2.3–7.1)	5.2 (3.3–5.9)
Total mechanical ventilation time, d	5.5 (3.0–10.0)	4.4 (1.6–9.2)	6.1 (4.1–12.1)	6.0 (5.5–7.1)
Total ICU length of stay, d	9.0 (6.0–14.0)	7.6 (4.0–13.0)	11.4 (6.0–15.0)	13.0 (10.0–14.0)
Hospital length of stay, d	15.8 (9.0–22.0)	14.3 (9.0–21.0)	16.3 (11.0–25.0)	21.1 (17.0–25.0)
Discharge disposition				
Death or hospice	7 (11.5)	3 (10.0)	4 (12.9)	1 (16.7)
Home	29 (47.5)	13 (43.3)	16 (51.6)	3 (50.0)
Acute care hospital transfer	5 (8.2)	1 (3.3)	4 (12.9)	2 (33.3)
Skilled nursing, long-term care, or rehab	19 (31.1)	12 (40.0)	7 (22.6)	0
Other	1 (1.64)	1 (3.33)	0	0

Data are presented as n (%), mean (SD), or median (interquartile range).
Any type of respiratory failure is defined as use of either noninvasive ventilation, high-flow nasal cannula, and/or re-intubation within 72 h of extubation.
BMI = body mass index
SOFA = Sequential Organ Failure Assessment
AMS = altered mental status
CVA = cerebrovascular accident

between re-intubation and poor subject outcomes found in previous studies.[1,16] However, discriminative performance was modest for predicting broader respiratory support requirements, perhaps reflecting the increasing use of HFNC modalities immediately following extubation in current critical care practice rather than association with total WOB.

Despite decades of research, reasons for extubation failure are highly variable,[4] and prior studies have identified

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Table 2. Readiness for Extubation Metrics Prior to Extubation*

	Total Cohort (n = 61)	Successfully Extubated (n = 30)	Any Type of Respiratory Failure (n = 31)	Reintubated (n = 6)
Passed SBT	61 (100)	30 (100)	31 (100)	6 (100)
RSBI	43 (23–59)	43 (21–59)	43 (30–59)	36 (23–47)
Minute ventilation	8.3 (6.8–10.1)	8.0 (6.4–10.4)	8.8 (7.2–10.1)	8.4 (6.2–10.8)
Peak inspiratory pressure	15 (13–16)	14 (14–16)	15 (13–17)	16 (13–18)
Mean airway pressure	8.0 (7.5–8.9)	8.3 (7.3–8.7)	8.0 (7.5–9.0)	8.8 (7.9–9.7)
PEEP	5 (5–5)	5 (5–5)	5 (5–5)	5 (5–5)
P_{aO_2}/F_{IO_2}	282 (223–378)	287 (227–362)	279 (223–387)	405 (280–480)
pH	7.44 (7.38–7.46)	7.43 (7.43–7.47)	7.44 (7.38–7.46)	7.38 (7.35–7.39)
P_{CO_2}, mm Hg	40 (35–49)	45 (40–50)	38.5 (34–42)	41 (35–49)
Breathing frequency, breaths/min	18 (14–21)	18.5 (14–21)	18 (13–20)	21.5 (15–25)
Heart rate, beats/min	87 (78–101)	87 (76–103)	87 (80–97)	88 (82–96)
Glasgow coma scale	11 (11–11)	11 (11–11)	11 (11–11)	11 (10–15)
Hemoglobin, g/dl	9.4 (8.2–10.8)	9.5 (8.3–10.8)	9.2 (8.0–11.1)	8.0 (7.8–10.1)
Mean arterial blood pressure, mm Hg	89 (79–99)	88 (75–99)	90 (83–99)	88 (87–90)
Temperature < 38.0 C	58 (95.1)	30 (100)	28 (90.3)	6 (100)
Temperature 38.0–38.3 C	3 (4.9)	0	3 (9.7)	0

Data are presented as n (%) or median (interquartile range).
Any type of respiratory failure is defined as use of either noninvasive ventilation, high-flow nasal cannula, and/or re-intubation within 72 h of extubation.
* Prior to extubation indicates the last recorded value documented in the electronic health record prior to documentation of extubation. Length of time between recorded value and extubation time varies depending on frequency of documentation or collection of lab based on individual care by treatment team.
SBT = spontaneous breathing trial
RSBI = rapid shallow breathing index

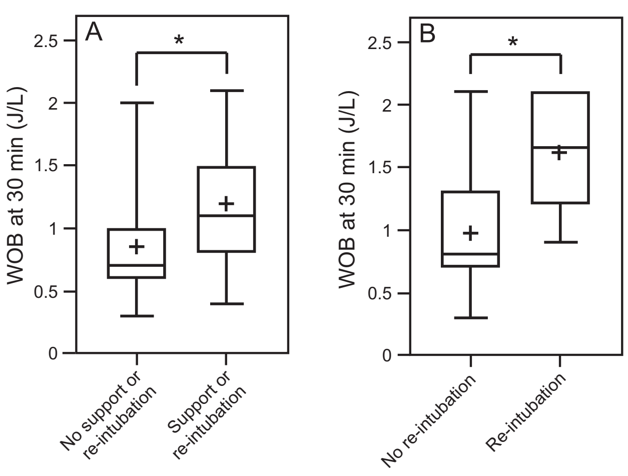

Fig. 2. Extubation failure outcomes and total work of breathing values measured at 30 min into proportional assist ventilation trial in J/L. WOB = work of breathing. J = joules; L = liter; + = mean.

numerous risk factors associated with failed extubation.[1,13] Several risk factors pertain to the nature of the patient's condition, including preexisting factors such as age > 65;[12] preexisting cardiac or pulmonary disease;[12,17] and aspects of acute illness that include impaired neurologic status,[18-20] Acute Physiology and Chronic Health Evaluation (APACHE) II score at time of extubation, anemia,[21] positive fluid balance, and elevated brain natriuretic peptide.[22,23] Other risk factors, such as ability to participate in airway hygiene, peak expiratory flow < 60 L/min,[24] and abundant endotracheal secretions,[20,21] pertain to a patient's respiratory function and time on mechanical ventilation. However, none of these risk factors, either alone or in combination, have proven sufficiently reliable for single predictor–based discrimination between patients who will extubate successfully or require re-intubation.

The RSBI has become the most used predictive tool based on its ease of calculation at the bedside and its intuitive interpretation.[5,8] However, its predictive performance can vary according to performance conditions, cutoff value used, and patient populations, such as those with COPD or neurosurgical injury.[25-28] Studies show the RSBI may be affected by conditions under which it is performed, with a 15–20% decrease in the RSBI when CPAP or low levels of pressure support are used instead of a T-piece, potentially resulting in misclassification.[29] Danaga et al[30] also found that the traditional RSBI cutoff of 105 breaths/min/L predicted only 20% of cases ready for extubation. Further, at least one randomized controlled trial that added the RSBI to a standard weaning protocol of daily SBTs found longer duration of weaning in the group that used RSBI, with no survival benefit.[9] Finally, a recent meta-analysis of 48 studies concluded the RSBI had good sensitivity (0.83) but poor specificity (0.58) for predicting extubation success.[7] Whereas, in our study, a total WOB > 1.0 J/L provided a sensitivity and specificity of 0.68, 0.70, respectively, for predicting extubation failure, a total WOB > 1.3 J/L provided a sensitivity and specificity of 0.83, 0.75, respectively, for predicting re-intubation.

Additional predictors of extubation outcome that show promise, but have not gained widespread clinical

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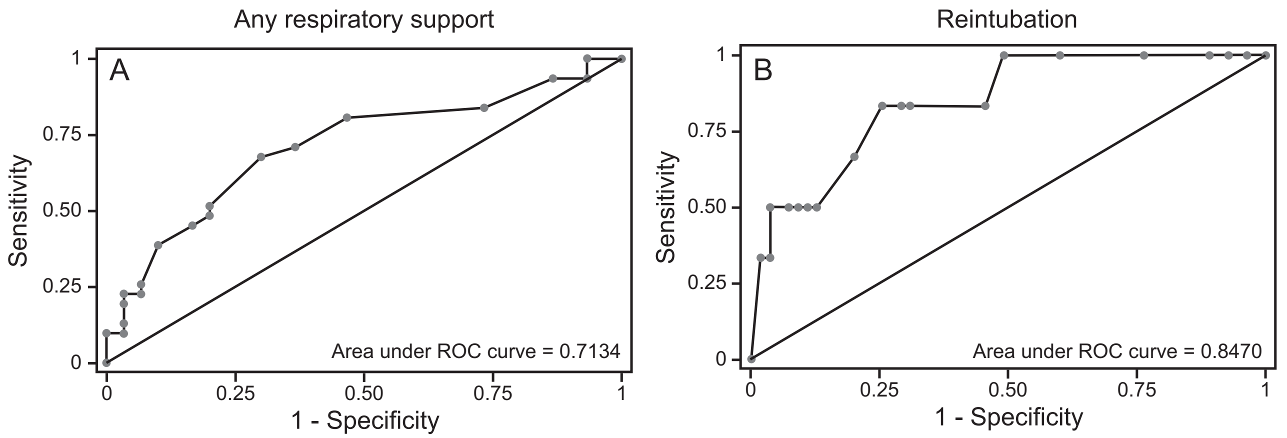

Fig. 3. Receiver operating characteristic curves for work of breathing values and extubation failure within 72 h of extubation from mechanical ventilation. ROC = receiver operating characteristic.

acceptance,[4] include peak expiratory flow as a surrogate for cough strength,[24] bedside measurements of functional residual capacity,[31] diaphragmatic function assessment by ultrasound,[32] central venous-to-arterial P_{CO2} difference/central venous oxygen saturation,[33] and a multiple-component extubation prediction score calculator.[33,34] More recently, machine learning (ML) approaches trained on large registry and patient-level data have shown promise with good to excellent predictive power but lack external validation and generalizability.[35-38] With advances in integration of ML models with EHR systems, in the near future, we will likely see more common deployment of ML models in clinical practice. At that point, selecting the right predictors/features in an ML model or an ensemble of models will be critical for realizing their full potential.

Accurate assessment of WOB in the ventilated patient traditionally requires an esophageal-pressure monitor and/or sensor devices inserted within the ventilator circuit to derive airway pressures;[39,40] however, the use of esophageal-pressure monitors and research devices in the clinical setting is currently limited.[41] The PAV+ ventilator mode noninvasively estimates the WOB through an automatic calculation of elastance and resistance and applying the respiratory system equation of motion. We would expect that other modes that adapt to patient inspiratory effort would have similar predictive value, like neurally adjusted ventilatory assist. In this observational study, we evaluated the ability of PAV-calculated total WOB to predict extubation failure and assessed whether the use of a specific threshold or threshold range could further support the decision to extubate as an additional physiological parameter. We determined the PAV-calculated total WOB range that provided optimal sensitivity and specificity for extubation failure in our subject cohort was between 1.0–1.3 J/L; however, these results should be interpreted as preliminary, with specific thresholds of PAV-derived total WOB requiring further investigation in a large multi-center study.

Consistent with our observations, Teixiera et al[39] found PAV had an area under the curve of 0.87 to predict extubation failure; but instead of absolute values, the authors chose to use a change in WOB, citing concerns with dead space and resistance measurements obscuring absolute measurement of WOB. In our analysis using PB 840s adjusted for tubing dead space and resistance before every use, we found a similar predictive ability of PAV using absolute thresholds. Banner et al[40] used PB 840s and indeed found ventilator-measured WOB had an improved predictive function compared to traditional predictors, but this was performed in a surgical population.

We suggest that the PAV-calculated total WOB provides an important adjunctive tool to determine extubation readiness and timing of extubation. In this study, a total WOB > 1.0 J/L provided a sensitivity, specificity, PPV, and negative-pressure ventilation of 68, 70, 70, and 68%, respectively, for predicting extubation failure. A total WOB > 1.3 J/L provided a sensitivity, specificity, PPV, and NPV of 83, 75, 26.3, and 97.6%, respectively, for predicting re-intubation (SI eTable C). Based on these results, we suggest that total WOB provides important adjunctive information to ultimately help clinicians determine extubation readiness. This, in addition to other physiological parameters such as an assessment of each patient's individual risk profile[42] and weaning difficulty,[3] may decrease re-intubation rates or the need for rescue therapies. The risks of extubation failure are not identical for all patients, as seen in the subjects who required re-intubation in our study. When considering the use of PAV-calculated total WOB in the decision to extubate, a different threshold may be necessary for different patient subgroups, depending on individual risks associated with extubation failure and delayed extubation.[43] Further research should examine modifiable pathophysiological causes for high total WOB in PAV mode, as well as different total WOB thresholds for different patient subgroups.

This study has some limitations. This was a small, single-center study of predominately medical ICU subjects using a single ventilator manufacturer; and therefore, results may not be generalizable. In addition, the small sample size precluded more vigorous multivariable analyses examining interactions of total WOB with previously described predictors and various factors associated with extubation failure. We also could not control for differences in individual health care provider judgment and preferences in the timing of extubation and selection of subsequent ventilation delivery device. Because not all PAV trials were performed immediately following an SBT (as SBTs were performed by the primary ICU treating team only), the subject's respiratory status may have changed in this period. We also did not record the SBT attempt number for the subject, which may be an important variable to consider in future studies. A priori, we defined extubation failure as any subject that required re-intubation, NIV, or HFNC within 72 h after extubation. However, over the course of the study, extubating subjects directly from mechanical ventilation to HFNC became more common, both at our institution and across medical centers.[1,22] In that regard, we defined re-intubation as its own failure category due to its association with mortality and poor patient outcomes. Relatedly, total WOB may only predict a subset of extubation failure types as there is a myriad of reasons for failure. Therefore, integration of multiple predictors, including total WOB, may result in better performing models than any one single indicator. However, utilization of total WOB as a value to consider for providers determining readiness to extubate is dependent on ventilators that provide this variable. Lastly, the accuracy of PAV-calculated total WOB needs further validation, especially as the underlying calculations are based on several assumptions that, if not entirely fulfilled, could affect reliability of the calculated score. However, a single-compartment experimental lung model study showed a strong linear correlation between PAV-calculated total WOB and the Campbell diagram total WOB ($r^2 = 0.93$).[44] Based on these limitations, a larger, multisite study is warranted to identify a total WOB threshold or threshold range with improved accuracy that would also generalize to a wider population and allow integration of multiple predictors.

Conclusions

Patients fail extubation for many quantifiable and non-quantifiable reasons. We suggest here that the addition of a PAV-calculated total WOB value for adults on mechanical ventilation who have passed an SBT with an RSBI < 105 breaths/min/L may provide important information for the clinician making decisions to extubate patients in a timely and safe manner. In the present study, we found that a total WOB cutoff value of 1.3 J/L measured on PAV prior to extubation was associated with a higher risk of re-intubation, though these results should be interpreted as preliminary due to their observational nature and further validation is necessary. Future research should assess total WOB as a predictor of extubation readiness to validate these findings in broader settings and in combination with additional predictors. Improving tools to assist clinicians in extubation readiness decisions is vital to maximize patient safety and improve outcomes of mechanically ventilated patients.

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