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Evolution of pattern of breathing during a spontaneous breathing trial predicts successful extubation

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Abstract *Purpose:* Rapid shallow breathing may occur at any time during spontaneous breathing trials (SBT), questioning the utility of a single determination of the rapid shallow breathing index (RSBI). We hypothesize that change in RSBI during SBT may more accurately predict successful extubation than a single determination. *Methods:* Prospective observational study. Seventy-two subjects were extubated. At 24 h, 63/72 remained extubated (Extubation Success), and 9 were re-intubated (Extubation Failure). Respiratory rate (RR), tidal volume (VT) and RSBI were measured every 30 min during 2-h T-piece SBT. Change in respiratory parameters was assessed as percent change from baseline. *Results:* Initial RSBI was similar in Extubation Success and Extubation Failure groups (77.0 ± 4.8, 77.0 ± 4.8, p = ns). Nevertheless, RSBI tended to remain unchanged or decreased in the Extubation Success group; in contrast RSBI tended to increase in the Extubation Failure group because of either increased RR and/or decreased VT ($p < 0.001$ for mean percent change RSBI over time), indicating worsening of the respiratory pattern. Quantitatively, only 7/63 subjects of the Extubation Success group demonstrated increased RSBI $\geq 20\%$ at any time during the SBT. In contrast, in the Extubation Failure group, RSBI increased in all subjects during the SBT, and eight of nine subjects demonstrated an increase greater than 20%. Thus, with a 2-h SBT the optimal threshold was a 20% increase (sensitivity = 89%, specificity = 89%). Similar results were obtained at 30 min (threshold = 5% increase). Percent change of RSBI predicted successful extubation even when initial values were ≥ 105. *Conclusion:* Percent change of RSBI during an SBT is a better predictor of successful extubation than a single determination of RSBI.

Keywords Weaning · Respiration · Artificial · Respiratory insufficiency · Respiration · Outcome assessment (health care)

Introduction

Prolonged mechanical ventilation is a risk for morbidity and mortality in critical ill patients [1]. Weaning failure is frequently associated with development of a rapid shallow breathing pattern [2–4]. Measurement of the rapid shallow breathing index (RSBI) is a simple bedside determination that may be utilized to identify this respiratory pattern classically thought to predict respiratory failure. However, despite being widely used and extensively studied, RSBI has variable sensitivity and specificity for predicting outcome following extubation [5–9].

Use of RSBI during a weaning protocol has failed to reduce the incidence of extubation failure, weaning time, or days on mechanical ventilation. Furthermore, use of RSBI has not been demonstrated to result in a survival benefit [10]. There are multiple potential explanations for these findings. First, patients may fail extubation without developing a rapid shallow breathing pattern during the weaning trial. Second, the threshold value that predicts extubation outcome may differ among individuals. Finally, other studies have demonstrated that respiratory failure may develop in a progressive nature during spontaneous breathing trials (SBT) as indicated by changes in esophageal pressure swings and/or minute ventilation recovery time [11, 12]. Therefore, a rapid and shallow breathing pattern suggestive of respiratory failure may develop at any time, questioning the utility of a single RSBI determination. Serial RSBI measurements have been investigated but have shown minimal or no improvement in the ability to predict successful extubation [13–16]. Although these studies evaluated RSBI at multiple time points, the change of RSBI in individual patients has not been assessed as a predictor of extubation outcome.

The present study evaluates the change in breathing pattern (evaluated as percent change in RSBI) during a 2-h SBT in individual subjects. We hypothesize that the change of RSBI, regardless of its initial value, may be a more accurate predictor of the overall capacity to tolerate extubation than RSBI determination at one point in time.

Materials and methods

Ninety-four subjects were prospectively recruited from the medical/surgical intensive care unit and cardiac care unit. Subjects were included if they met the following criteria as described by the Evidence-Based Medicine Task Force of the American College of Chest Physicians [17]: evidence for reversal of the underlying cause for respiratory failure; adequate oxygenation ($PaO_2/FIO_2 > 200$ mmHg; PEEP < 8 cmH$_2$O); pH ≥ 7.3; hemodynamic stability (absence of active myocardial ischemia, absence of vasopressor use or <5mcg/kg/min of dopamine or dobutamine, heart rate <140); absence of fever ($T < 38°C$); hemoglobin >8 or >10 g/dl in subjects with known coronary disease; and Glasgow coma scale >10. Exclusion criteria included: known upper airway obstruction, copious secretions with cough and "do not intubate/resuscitate" status. Subjects were 18 years of age or older, orally intubated (tube size ≥ 7.5 mm) and mechanically ventilated for more than 48 h. Assist-control ventilation (AC) was the preferred mode prior to initiation of the weaning trial. The decision to perform a weaning trial was made by the treating critical care physician.

SBT protocol

SBT was performed in a semi-seated position using a T-piece and supervised by a respiratory therapist. The T-piece was connected to a 200-ml reservoir of aerosol tubing on one port while the other port was connected via large-bore tubing to a high volume nebulizer (Airlife no. 002002, Cardinal Health Products). Oxygen flow was set at 15 l/min. The FIO$_2$ was set to the same value used during mechanical ventilation. Criteria for SBT tolerance were defined as described by the ACCP: hemodynamic stability (pulse <140/min, systolic blood pressure <200 and >90 mmHg); absence of significant arrhythmia (increased premature ventricular beats of >4 beats/min or new onset of sustained supra-ventricular rhythm); respiratory rate <35/min; adequate gas exchange (SpO$_2$ >88%; PO$_2$ >55 mmHg; pH ≥ 7.3; increase in PaCO$_2$ <10); no significant change in mental status; and absence of severe discomfort or signs of increased work of breathing [17]. Seventeen subjects failed at least one of the criteria during the SBT and were re-connected to the ventilator. The remaining subjects were maintained on T-piece for up to 2 h. If subjects tolerated the SBT, extubation was considered by the primary care team. Study investigators provided no input regarding the primary physician's decision to start a weaning trial, reconnect the subjects to mechanical ventilation, or extubate/reintubate the subject. The primary physician decided to extubate 17 subjects before completing the 2-h SBT. The duration of SBT was similar in those subjects who were successfully extubated as compared with those who subsequently required re-intubation.

Data collection

Electrocardiogram, blood pressure and SpO$_2$ were continuously monitored. Clinical and demographic characteristics, APACHE II score on admission, duration of mechanical ventilation and co-morbidities were recorded.

During the SBT, the respiratory pattern was measured by one investigator at 1, 30, 60, 90 and 120 min. Measurements were obtained for at least 60 s while the subjects breathed with a stable respiratory pattern. Minute ventilation was obtained using a calibrated Wright respirometer (Model Mark 20 Ferraris Respiratory, London, England) connected to the patient via an Adult Filtered Hygroscopic Condenser Humidifier (Airlife no. 003005, Cardinal Health). Respiratory rate was obtained by direct visualization, and tidal volume was derived allowing for calculation of RSBI. Measurements were not performed in subjects who were coughing, had copious secretions, were recently suctioned, or had a recent change in position. The primary care team was aware of the initial RSBI; however, the team was blinded to all subsequent values.

Change in respiratory pattern was assessed by the percent change of RSBI (relative to baseline) during the SBT. Two predefined parameters were evaluated: (1) maximum percent increase in RSBI at any time point during the 2-h SBT and (2) percent increase of RSBI assessed at 30 min.

Classification and analysis of outcomes

Subjects were classified into three groups based on ventilatory status 24 h after SBT. A 24-h period was used since all patients remained in the intensive care unit under the care of the critical care team for at least 24 h following extubation. The SBT-intolerant group included subjects who failed SBT before extubation and were reconnected to mechanical ventilation. The Extubation Failure group included subjects that required re-intubation within 24 h after extubation. The Extubation Success group included subjects that maintained spontaneous breathing >24 h after extubation.

Data are presented as mean ± SD unless otherwise indicated. Demographic and clinical variables were compared for the groups using analysis of variance with post hoc pairwise testing performed utilizing Tukey's HSD. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR) and negative LR were calculated for the Extubation Success versus Extubation Failure subjects, and the receiver-operating characteristic (ROC) curves were plotted for RR, VT, RSBI, percent change in RSBI at 30 min and maximum percent change in RSBI over the 2-h SBT.

A multivariate logistic regression model was used to identify factors that significantly predicted extubation success. In addition to RSBI, factors examined in the model included age, gender, days on ventilator, ventilator mode, endotracheal tube size, APACHE II score, hemoglobin concentration, fluid balance, Glasgow coma scale and past history of COPD, asthma, cardiac disease and diabetes. The backward elimination procedure was used to obtain the final model, and factors that showed no further significant improvement to the model fit were eliminated. Age and gender were forced into the final model.

The protocol was approved by the Institutional Review Board of Morristown Memorial Hospital where data were collected. Informed consent was waived due to the observational nature of this study.

Results

Ninety-four subjects were enrolled; three were excluded since RSBI could not be measured at the beginning of the SBT due to intractable cough, and two were excluded due to early intolerance precluding a second measurement of RSBI. Table 1 summarizes the clinical characteristics of the remaining 89 subjects. Seventeen of 89 did not tolerate spontaneous breathing and were not extubated (SBT Intolerant group). The remaining 72 subjects were extubated; 63 remained extubated for more than 24 h (Extubation Success group) and 9 required re-intubation (Extubation Failure group) after 9.1 ± 7.6 h. Of these nine subjects that failed extubation, seven developed respiratory failure that was attributed to the acute lung disease noted on presentation to the critical care unit, and two developed congestive heart failure. No subject was re-intubated due to upper airway obstruction, insufficient cough or impaired mental status, and none received continuous positive airway pressure or non-invasive ventilation. Demographic and clinical characteristics were similar between groups except for a lower prevalence of males in the SBT Intolerant group; there was no difference in gender between the Extubation Success and Extubation Failure group. There was a trend towards older age, higher APACHE II score, longer duration of mechanical ventilation and higher prevalence of COPD in the Extubation Failure as compared with the Extubation Success group. There were no significant differences between the groups in the indication for mechanical ventilation.

Respiratory data obtained at the onset of the SBT and at 30 min are presented in Table 1. At initiation of SBT, the SBT Intolerant group demonstrated higher RR and a trend towards higher RSBI compared to the other two groups. Mean values for RR, VT and RSBI at initiation of SBT were similar in the Extubation Success and Extubation Failure group. Of note, although mean values of RSBI were less than 105, rapid shallow breathing was present in 13/63 subjects (7 subjects with RSBI >125) in the Extubation Success group despite successful extubation. Furthermore, only 33% of subjects in the Extubation Failure group had rapid shallow breathing, but all failed extubation. Thus, the sensitivity and specificity of the initial RSBI to predict extubation outcome were 79 and 33%, respectively; sensitivity and specificity of RSBI were 76 and 33% when assessed at the last time point prior to extubation.

After 30 min of spontaneous breathing, the SBT Intolerant group showed a marked increase in the RSBI (mean 146.1 ± 88.6) associated with objective signs of respiratory distress, which prompted reinstitution of assisted ventilation. In contrast, there was no significant difference in the mean values for RR, VT or RSBI at 30 min between the Extubation Success and Extubation Failure groups.

Since the mean values for respiratory variables did not distinguish between the groups that tolerated the SBT, Fig. 1 analyzes the evolution of respiratory parameters in individual subjects during the SBT. The time course of RR and VT, expressed as percent change relative to

Table 1 Baseline characteristics and ventilatory data during SBT

	Extubation success (n = 63)	Extubation failure (n = 9)	SBT intolerant (n = 17)	p-value
Demographics				
Age	68 ± 17	75 ± 14	74 ± 10	0.23
Gender (male)	35 (55.6)	6 (66.7)	4 (23.5)	0.038
Medical history				
COPD	14 (22.2)	3 (33.3)	7 (41.2)	0.26
Asthma	1 (1.6)	0	0	0.81
Cardiac[a]	15 (23.8)	3 (33.3)	4 (23.5)	0.82
Diabetes mellitus	6 (9.5)	1 (11.1)	4 (23.5)	0.29
Indication for mechanical ventilation				
COPD exacerbation	8 (12.7)	2 (22.2)	5 (29.4)	0.24
Pneumonia	13 (20.6)	1 (11.1)	2 (11.8)	0.59
Sepsis	4 (6.3)	1 (11.1)	0	0.45
Heart failure	11 (17.5)	3 (33.3)	2 (11.8)	0.39
Postoperative	20 (31.7)	2 (22.2)	7 (41.2)	0.59
Trauma	2 (3.2)	0	0	0.65
Coma	2 (3.2)	0	0	0.65
Other	3 (4.8)	0	1 (5.9)	0.81
APACHE II score	17.4 ± 5.9	20.2 ± 3.8	18.2 ± 5.4	0.34
Glasgow	13.7 ± 1.7	13.3 ± 1.9	13.8 ± 1.0	0.74
Ventilator status at initiation of SBT				
Tube size ≥8 mm	36 (57)	5 (55.6)	8 (47.1)	0.75
Days on ventilator	5.5 ± 4.3	8.2 ± 4.6	5.7 ± 4.3	0.21
Assist control	51 (81)	7 (78.8)	11 (64.7)	0.36
Fluid balance				
Previous 24 h (l)	1.09 ± 2.17	1.16 ± 1.43	1.60 ± 3.28	0.68
Overall (l)	7.11 ± 9.70	7.78 ± 8.38	5.16 ± 6.87	0.69
Hemoglobin	11.0 ± 1.6	10.0 ± 1.4	10.8 ± 0.9	0.16
Ventilatory data during SBT				
Initial data				
RR_1	24.9 ± 7.5	20.8 ± 6.3	29.4 ± 10.9	0.031
VT_1	0.38 ± 0.17	0.40 ± 0.16	0.34 ± 0.12	0.70
$RSBI_1$ (range)	77.0 ± 38.1 (8–169)	73.1 ± 59.7 (22–195)	100.9 ± 61.5 (15–252)	0.14
$RSBI_1$ >105	13 (20.6)	3 (33.3)	7 (41.2)	0.20
$RSBI_1$ >125	7 (11.1)	2 (22.2)	6 (35.3)	0.05
Data at 30 min				
RR_{30}	25.2 ± 8.0	25.0 ± 7.4	36.5 ± 14.5	<0.01
VT_{30}	0.42 ± 0.17	0.39 ± 0.16	0.31 ± 0.13	0.05
$RSBI_{30}$	70.6 ± 37.5	83.2 ± 60.2	146.1 ± 88.6	<0.01

Data expressed as n (%) or mean ± standard deviation. p-values were obtained by ANOVA; post-hoc analysis showed significance between the SBT Intolerance group compared with both the Extubation Success and Extubation Failure groups

APACHE II Acute Physiology and Chronic Fealth Enquiry II, *COPD* chronic obstructive pulmonary disease, *RR* respiratory rate; *VT* tidal volume, *RSBI* Rapid Shallow Breathing Index

[a] Cardiac = history of congestive heart failure, a left ventricular ejection fraction of <35% or acute coronary syndrome

baseline, during the 2-h SBT is plotted in the Extubation Success and Extubation Failure groups. While RR was highly variable in the Extubation Success group, an increase in RR was seen in the majority of subjects in the Extubation Failure group ($p < 0.05$ for mean values at each time point, data not shown). Similarly, while VT tended to remain either unchanged or increased in the Extubation Success group, VT rarely increased and frequently decreased in the Extubation Failure group (p = ns for mean values at each time point, data not shown). However, the individual data demonstrate significant overlap for the time course of both RR (top panel) and VT (bottom panel) in the Extubation Success compared with the Extubation Failure group, and ROC analysis demonstrated that neither parameter could be used to reliably predict extubation outcome (area under the curve 0.76 and 0.78, respectively).

Figure 2 illustrates the evolution of RSBI, expressed as percent change relative to baseline, over the 2-h SBT. The top panel plots data for each individual and illustrates that RSBI remained unchanged or decreased in the Extubation Success group. Only 7/63 subjects of this group (12%) demonstrated an increase in RSBI ≥20% (see ROC analysis below) at one time point during the

Fig. 1 The time course of the RR and VT for each individual expressed as percent change relative to baseline was plotted. Significant overlap is seen in the success compared with the failure group. Seventeen subjects (15 in the success group and 2 in the failure group) were extubated before completing the 2-h SBT, as decided by the primary physician. The duration of SBT was similar in the success and failure groups
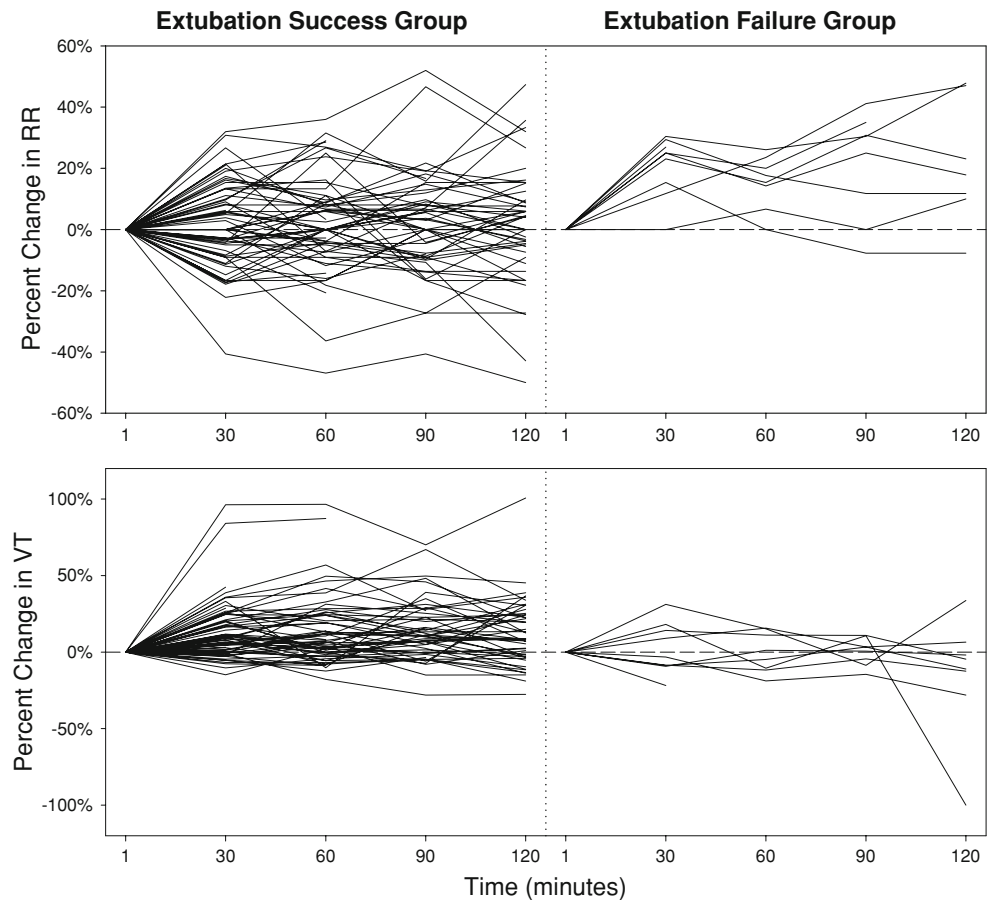
SBT. In contrast, in the Extubation Failure group RSBI increased in all subjects during the SBT, and eight of nine subjects (89%) demonstrated an increase greater than 20% for at least one time point. The bottom panel illustrates the mean percent change in RSBI for the Extubation Success and Extubation Failure groups. At 30 min, the Extubation Success group demonstrated a reduction of RSBI that averaged $-8.5 \pm 2.2\%$ (mean $\pm$ SE). In contrast, the Extubation Failure group demonstrated an increase in the RSBI at 30 min that averaged $21.8 \pm 8.8\%$ ($p < 0.001$). The divergence of the group means remained statistically different between the two groups throughout the SBT ($p < 0.001$).

Figure 3 plots the ROC curves that illustrate the ability of the initial RSBI and the maximum percent change in RSBI during the 2-h SBT to predict extubation outcome (area under the curve 0.41 and 0.93, respectively). The optimal threshold to predict successful extubation was a maximum increase in RSBI less than 20% at any time point during the SBT (sensitivity = 88.8%, specificity = 88.8%, PPV = 98%, NPV = 53%, positive LR = 8, negative LR = 0.125). Similar values for sensitivity and specificity were obtained for high-risk subgroups characterized by an initial RSBI >105 or $\geq$7 days of mechanical ventilation (Table 2). Multivariate

logistic regression analysis confirmed that percent change in RSBI was an independent predictor of extubation outcome after accounting for demographic and clinical variables and after adjustment for initial RSBI (odds ratio for <20% change in RSBI as prediction of extubation success = 60, CI = 6–566, $p < 0.001$).

The percent change in RSBI obtained at 30 min was evaluated to determine if a shorter SBT would provide sufficient data to predict extubation outcome. The optimal threshold to predict extubation outcome was a 5% increase in RSBI at 30 min with sensitivity and specificity of 83% and 78% (PPV = 96%, NPV = 38%, positive LR = 3.71, negative LR = 0.22, area under the ROC curve = 0.83).

Discussion

This study evaluated the evolution of pattern of breathing in a heterogeneous group of subjects in a combined medical and surgical ICU. The data demonstrated that in subjects who tolerated a SBT, the percent change of RSBI (increase <20% over a 2-h period) predicted successful extubation. Percent change of RSBI predicted extubation

Fig. 2 The evolution of RSBI, expressed as percent change relative to baseline. The *top panel* plots data for each individual; RSBI remained unchanged or decreased in the success group, whereas it increased in the failure group. A *reference line* at 20% change in RSBI is plotted to highlight these differences. The *bottom panel* illustrates the mean percent change in RSBI ($\pm$SE) for the success (*closed circle*) and failure groups (*open circle*). $*p < 0.001$
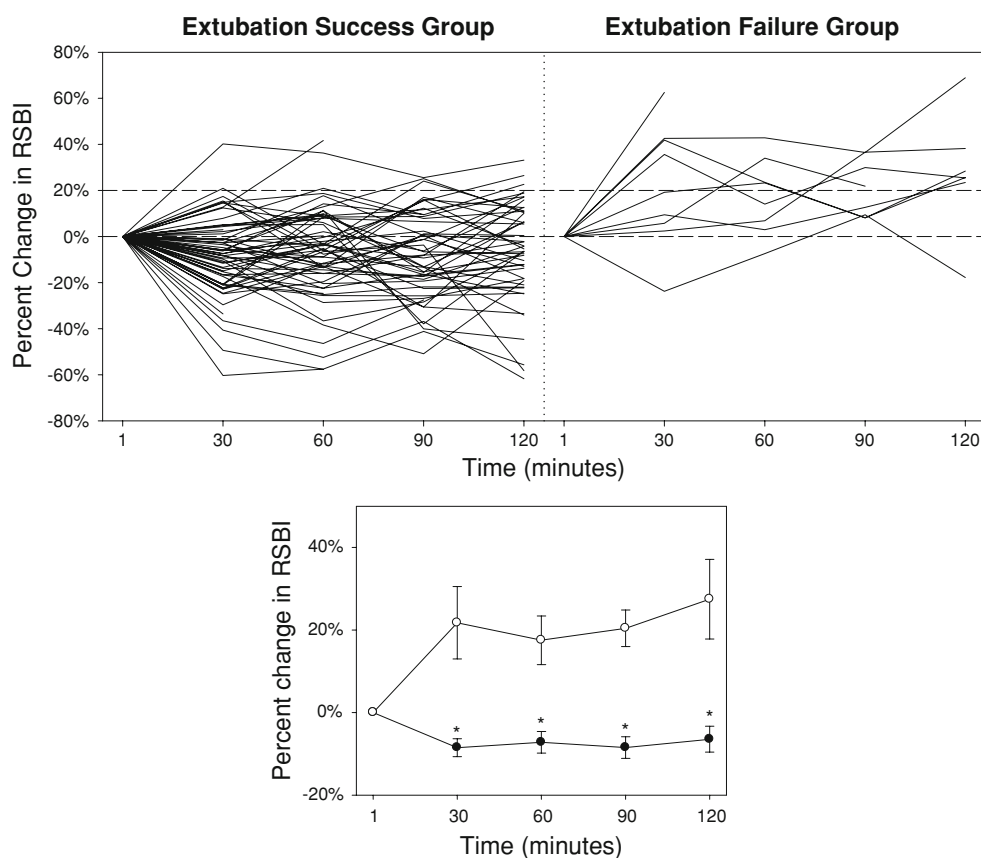
outcome independent of respiratory rate, tidal volume and RSBI. In addition, percent change of RSBI predicted extubation outcome even in subjects with absolute values for initial RSBI greater than 105. Thus, evolution of respiratory pattern during spontaneous breathing may be an accurate, non-invasive and simple determination that can be used in the critical care setting to evaluate extubation readiness.

Respiratory failure may develop in a progressive manner and at a rate that may be difficult to predict [12, 18–20]. Jubran et al. [11] demonstrated that progressive change in esophageal pressure was predictive of weaning outcome; however, similar results were not obtained when variability of RSBI was analyzed. Using different methodologies, others have demonstrated that variability of respiratory parameters may be predictive of weaning outcome [21, 22]. However, the above studies analyzed breath-by-breath variability, which includes transient changes. In the present study, RSBI was measured during 1-min periods of stable breathing, avoiding times when subjects had copious secretions, cough, recent suctioning or changes in position. Thus, this protocol was designed to avoid transient changes that may obscure the overall trend.

In this study, data obtained during the first 30 min of SBT indicated that an increase in RSBI of <5% from the initial value predicted extubation success. When the data were analyzed over the full 2 h, increased variability of RSBI was detected, and the optimal threshold for predicting extubation outcome was a 20% increase in RSBI. This higher threshold may reflect either progressive development of rapid shallow breathing or increased detection of variability when multiple measurements are performed. However, the high positive predictive value for data obtained at 30 min (96%) suggests that a 30-min SBT may be sufficient to predict successful extubation.

Conflicting results regarding the usefulness of a single determination of RSBI during the weaning process have been reported. In the present study, RSBI at any time point was not predictive of successful extubation. Prior studies have reported a wide range of predictive values for RSBI, which may reflect differences in methodology, classification of outcomes and patient populations [23–27]. Prior studies have measured RSBI during partially supported ventilation and/or with uncalibrated equipment (e.g., mechanical ventilator) [28–33]. In the present study a precise protocol to measure the RSBI was utilized; data were obtained using a calibrated Wright spirometer during a 1-min period of stable breathing. Prior studies have variably defined the term "failure" to indicate either failure to tolerate a trial of spontaneous breathing and/or

Initial RSBI

Approximate area under ROC curve = 0.41

Maximum percent change RSBI during SBT

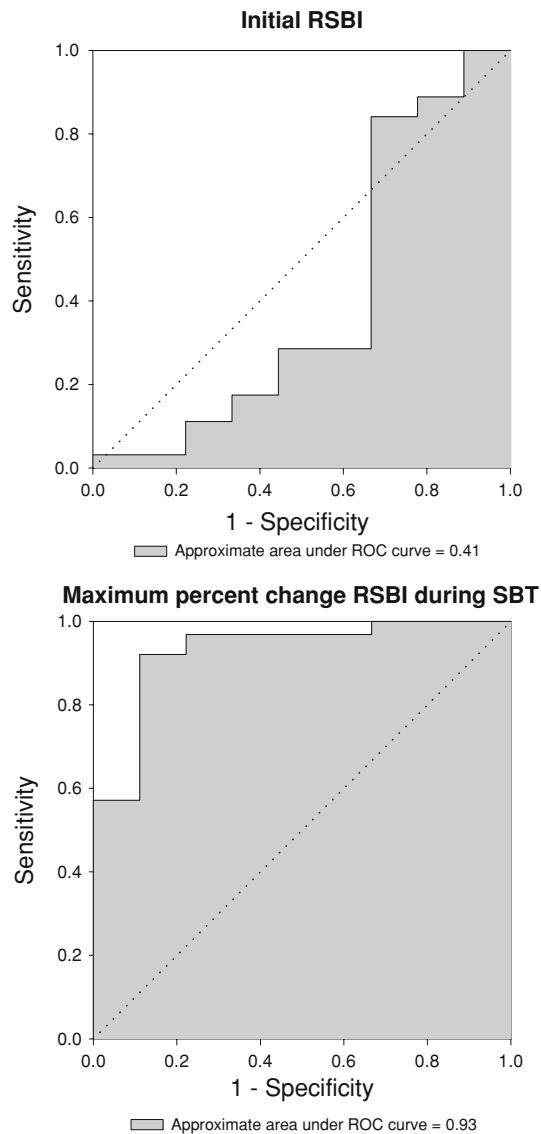Approximate area under ROC curve = 0.93

Fig. 3 The ROC curves that illustrate the ability of the initial RSBI and the maximum percent change in RSBI to predict extubation outcome was plotted. The optimal threshold to predict extubation outcome was a 20% increase in RSBI at any point during the SBT

failure to tolerate a trial of extubation. In the present study, failure to tolerate a trial of spontaneous breathing (SBT Intolerant group) was associated with development of rapid shallow breathing; in this group RSBI at 30 min was generally greater than 105. In contrast, the rapid shallow breathing index measured at any given time point did not predict the primary outcome of this study: prediction of extubation success versus subsequent requirement for re-intubation.

Several factors may have influenced the results of this study. Although the results suggest that the change in RSBI is capturing a physiological phenomenon associated with extubation failure, it is possible that the results were in part due to a selection bias. This selection bias might have occurred since the initial RSBI was not blinded, and the treating physician may not have performed an SBT if the RSBI was elevated. However, the percent of subjects with elevated RSBI was similar in all three groups, and 16 subjects with elevated initial RSBI were included because they were clinically stable, completed the SBT and were subsequently extubated. A further selection bias may be present since the SBT Intolerant group was reconnected to the ventilator and therefore was not included in the analysis of factors predicting extubation outcome. As a result, the number of patients that failed extubation was small compared with the group that was successfully extubated. However, the observed extubation failure rate of 12.5% is in accord with prior published data [34, 35]. These considerations suggest that the impact of a selection bias on the observed data was minimal.

This study had few subjects with characteristics associated with higher rates of extubation failure (e.g., prolonged intubation or prior failed weaning trials), which may limit applicability of the results to these high risk patients. Furthermore, the change in RSBI would not predict extubation outcome when changes in respiratory status occur following extubation due to mucus plugging, upper airway obstruction, aspiration and/or alteration of mental status. Finally, the exploratory nature of the present results requires prospective validation in a larger and more heterogeneous population.

Table 2 Predictive values of the percent change in RSBI at 30 min and the maximum percent change in RSBI during SBT for the Extubation Success and Extubation Failure groups

	Increase in RSBI at 30 min <5%		Maximum increase in RSBI during SBT <20%	
	Sensitivity	Specificity	Sensitivity	Specificity
Total ($n = 72$)	82.5	77.8	88.8	88.8
Patients with				
Initial RSBI ≤105 ($n = 56$)	80	83.3	88	100
Initial RSBI >105 ($n = 16$)	92.3	66.7	92.3	66.6
On the ventilator ≥7 days ($n = 26$)	90	83.3	85	100

Data are expressed as %

Whereas prior studies have evaluated individual values for RSBI as a predictor of weaning outcome, the present study extends prior observations by evaluating the dynamic changes of the breathing pattern as an index for the subsequent requirement for re-intubation. Respiratory failure occurs when there is an imbalance between mechanical work load and ventilatory output capacity, and may develop because of multiple different pathophysiologic derangements. Change in breathing pattern may be an expression of the increased effort needed to overcome different elements of respiratory mechanics (e.g., expiratory flow limitation, dynamic hyperinflation, dynamic lung compliance and/or respiratory muscle

dysfunction), or it may occur as an end product of load-capacity imbalance [18, 36]. Thus, the evolution of respiratory pattern, as assessed by change in RSBI, is a marker of the dynamic changes that occur during weaning that may improve the ability to predict extubation outcome. In addition, the change in RSBI can identify subjects who might be successfully extubated despite elevated initial values for RSBI.

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