

Assessment of Respiratory Mechanics and Inspiratory Effort During Spontaneous Breathing Trials to Predict Extubation Failure in High-Risk Patients

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Abstract

Rationale: Conventional parameters to determine the success of spontaneous breathing trials (SBTs) may fail to detect impending respiratory distress.

Objectives: To assess whether SBT-induced changes in respiratory system compliance, inspiratory effort, and respiratory drive measured as occlusion pressure during the first 100 milliseconds (P0.1), all assessed noninvasively through airway occlusions, are associated with extubation outcomes.

Methods: We conducted a multicenter study on patients at high risk of extubation failure who successfully passed a 30-minute SBT on the basis of conventional parameters. The SBT was reproduced using a specific ventilator immediately before extubation to continuously monitor respiratory system compliance, inspiratory effort, and P0.1. Extubation failure was defined as reintubation within 72 hours.

Measurements and Main Results: Forty-six (19%) of 238 extubated patients required reintubation. No differences in V_T or respiratory rate were observed between successfully extubated

and reintubated patients at any time. In the success group, inspiratory effort and normalized compliance (i.e., scaled to predicted body weight) remained unchanged throughout the SBT. In the failure group, normalized compliance declined (1.0 [0.8–1.2] to 0.7 [0.6–0.9] ml/cm H₂O/kg; $P < 0.001$), whereas inspiratory effort increased (12 [10–15] to 18 [15–20] cm H₂O; $P < 0.001$) during the SBT. P0.1 increased in both groups but more markedly in reintubated patients (2 [1.5–2.4] to 3.2 [2.9–3.5] cm H₂O; $P < 0.001$). SBT-induced normalized compliance reduction less than or equal to -0.2 ml/cm H₂O/kg (less than or equal to -0.1 ; less than or equal to -0.2) and inspiratory effort increase > 2 cm H₂O (> 1 , > 3) were the most accurate predictors of extubation failure (area under the curve, 0.90 [0.84–0.93]; sensitivity, 80%; specificity, 83%; area under the curve, 0.94 [0.90–0.97]; sensitivity, 89%; specificity, 93%, respectively).

Conclusions: In high-risk patients, SBT-induced declines in respiratory system compliance and increases in inspiratory effort are associated with extubation failure.

Clinical trial registered with www.clinicaltrials.gov (NCT05295186).

Keywords: spontaneous breathing trial; extubation failure; lung mechanics; airway occlusion pressure; noninvasive monitoring

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At a Glance Commentary

Scientific Knowledge on the

Subject: Conventional criteria for assessing the success or failure of spontaneous breathing trials include gas exchange, standard hemodynamic parameters, V_T , and respiratory rate. These may overlook early, subtle signs of respiratory failure, particularly in patients at high risk.

What This Study Adds to the

Field: In this multicenter study conducted in patients at high risk for weaning failure who were extubated after a spontaneous breathing trial deemed successful by conventional criteria, a reduction in respiratory system compliance and an increase in inspiratory effort, both measured using noninvasively through airway occlusions, were strongly associated with subsequent extubation failure. Noninvasive evaluation of respiratory mechanics and inspiratory effort during spontaneous breathing trials may help to identify patients at greater risk of requiring reintubation.

A spontaneous breathing trial (SBT) is a well-established practice to identify patients eligible for extubation (1, 2). Various approaches have been proposed for conducting an SBT, without universal consensus on the optimal method (3). Conventional techniques, such as the T-piece trial or continuous positive airway pressure, provide a direct assessment of the patient's spontaneous respiratory capacity by abruptly reducing ventilatory support. Yet, these approaches can delay extubation, prolonging the duration of mechanical ventilation (4). In contrast, SBTs with low degrees of pressure support allow more patients to successfully complete the trial, thereby shortening the time to extubation (5, 6). Nevertheless, these "supportive" strategies may underestimate the work of breathing needed after extubation, exposing individuals who meet SBT success criteria to

the risk of reintubation, particularly those at high risk of weaning failure (7, 8).

To determine whether the SBT succeeds or fails, current guidelines recommend monitoring respiratory rate, V_T , hemodynamics, and gas exchange (9). However, these parameters may not reflect SBT effects on respiratory mechanics, inspiratory effort, and respiratory drive, which may more closely reflect respiratory distress (10, 11).

Techniques based on airway occlusions have been proposed to noninvasively assess respiratory mechanics and respiratory muscle workload during assisted ventilation (12). Specifically, during an end-inspiratory occlusion, plateau pressure measurement allows one to assess respiratory system compliance (13, 14); the negative deflection in airway pressure measured during the first breath during a sudden end-expiratory occlusion (ΔP_{OCC}) allows one to quantify the inspiratory effort (15); and the occlusion pressure during the first 100 milliseconds ($P_{0.1}$) reflects respiratory drive (16, 17). Whether systematic monitoring of these parameters during supportive SBTs provides predictive information on the risk of weaning failure is unknown.

In this multicenter study involving critically ill patients with one or more high-risk factors for extubation failure (18) and deemed ready for planned extubation, we aimed to determine whether SBT-induced changes in respiratory system compliance, inspiratory effort (ΔP_{OCC}), and respiratory drive ($P_{0.1}$) were associated with extubation outcomes.

Methods

Study Oversight

This prospective, multicenter, observational study was conducted in five general ICUs across four hospitals in Italy between September 2022 and April 2024 (additional details are provided in the data supplement). The study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committees of all participating centers (coordinating center: Bari University Hospital protocol 67994/22.29; ClinicalTrials.gov registration: NCT05295186). Written informed consent

was obtained from all enrolled patients or patients' next of kin, according to ethics committee recommendations.

Patient Population

Patients aged ≥ 18 years ready to be extubated according to prespecified criteria were screened for inclusion. Eligibility required the presence of at least one predefined high-risk factor for extubation failure, including age > 65 years or the presence of chronic cardiac or pulmonary disease (18). Readiness for extubation was defined as the ability to tolerate a 30-minute SBT with positive end-expiratory pressure (PEEP) of 5 cm H_2O and pressure support of 7 cm H_2O (3, 5). SBT success was defined by standard parameters (3) (details available in the data supplement). Patients were excluded if they had a tracheostomy, known neuromuscular disease, or declined to provide informed consent.

Study Protocol

After the success of the initial SBT in the pressure support mode, the decision to extubate the patient was taken; subsequently, patients were returned to their baseline ventilator settings for 1 hour to prevent fatigue from the screening phase (19). The SBT was then replicated under proportional assist ventilation with load-adjustable gain factors (PAV+). This helped standardize procedures across centers, because all data (except ΔP_{OCC}) were automatically collected through the noninvasive, breath-by-breath monitoring of the ventilator, allowing operator-independent measurement of respiratory mechanics (20). Briefly, patients were connected to a dedicated ventilator (Puritan Bennett 840, Medtronic) and ventilated for 30 minutes in PAV+ mode. The level of assistance was adjusted to match the same inspiratory pressure used during the initial SBT (7 cm H_2O), whereas PEEP and FI_{O_2} remained unchanged. At the end of this "study SBT," patients were reintubated in pressure support mode for 1 hour using baseline settings to avoid exhaustion (19). Afterward, all patients were extubated and received high-flow nasal cannula oxygen (18).

Data Collection

Demographics and relevant clinical characteristics were collected at study entry.

A data supplement for this article is available via the Supplements tab at the top of the online article.

Artificial Intelligence Disclaimer: OpenAI's ChatGPT was used for language editing. All authors reviewed and approved the final version of the manuscript and retain full responsibility for its content.

Need for reintubation and other relevant clinical outcomes were recorded at ICU discharge.

During the study SBT, respiratory rate, V_T , respiratory mechanics (including respiratory system compliance, airway resistance, and intrinsic PEEP) and the patient's work of breathing derived from the PAV+ algorithm (21) were recorded directly from ventilator screen. Airway plateau pressure and driving pressure were derived from compliance using standard equations (22). Respiratory system compliance was normalized to predicted body weight (C_{RS}/PBW), enabling more precise interindividual comparison (23). End-expiratory occlusion maneuvers were performed to measure ΔP_{OCC} (15) and $P_{0.1}$ (16). Rapid shallow breathing index was calculated as described elsewhere (24). All data were collected every 5 minutes throughout the SBT, yielding a total of six measurements. The SBT-induced changes in each parameter were calculated as the absolute difference between the values at 5 minutes and at the end of SBT. Arterial blood pressure and heart rate, as well as blood samples for arterial gas analysis, were collected at the beginning and at the end of the study SBT.

Endpoints

The original primary endpoint of the study was the difference in SBT-induced changes in work of breathing, assessed using PAV+ mode, between patients who subsequently required reintubation and those who were successfully extubated; changes in C_{RS}/PBW , ΔP_{OCC} , and $P_{0.1}$ were originally included as components of the primary outcome, being the key physiological components of the work of breathing. However, after study initiation, we became aware that PAV+ ventilators would have been withdrawn from the market and no longer would have been commercially available. This limited the feasibility and generalizability of work of breathing measurements. To preserve clinical relevance, after discussions among the investigators, the primary endpoint was redefined to focus on SBT-induced changes in C_{RS}/PBW , ΔP_{OCC} , and $P_{0.1}$ because these parameters are measurable noninvasively on all available ventilators. This change was recorded on www.clinicaltrials.gov and did not involve any modification of the study protocol, procedures, or data collection, because all parameters were recorded as originally planned. Work of breathing was

retained as a secondary endpoint. Secondly, we aimed to assess the discriminatory power of SBT-induced changes in C_{RS}/PBW , ΔP_{OCC} , and $P_{0.1}$ identifying patients in whom extubation failed. Extubation failure was defined as the development of acute respiratory failure requiring endotracheal reintubation within 72 hours after extubation (18). The decision to extubate was made by the attending physicians solely on the basis of the outcome of the initial SBT; the decision to reintubate patients because of postextubation respiratory failure was taken by treating clinicians, who were unaware of the study results. No rescue noninvasive ventilation was performed before reintubation (25).

Statistical Analysis

Normally distributed continuous variables are presented as mean and SD; nonnormally distributed variables are reported as median and interquartile range. Normality was assessed using the Shapiro-Wilk test. Group comparisons were performed using the chi-square test or the Mann-Whitney U test, as appropriate. Within-group comparisons between 5 and 30 minutes were conducted using the Wilcoxon signed-rank test. Time-by-group interaction was tested using aligned rank transformation ANOVA (26, 27).

Receiver operating characteristic curves with 95% confidence intervals (CIs) were generated to assess predictive ability for extubation failure. Optimal cutoffs were identified using the Youden index, and bootstrap-derived 95% CIs were calculated for each threshold (28). Kaplan-Meier analysis for time to reintubation was performed by stratifying patients according to receiver operating characteristic-derived cutoffs; curves were compared using the log-rank test. Differences across tertiles were evaluated using one-way ANOVA with the Tukey correction for pairwise comparisons. Nonparametric smoothing spline regression was used to model the relationship between each variable and time to reintubation, with R^2 values indicating model fit.

Sample size was calculated from preliminary analysis of the primary endpoints, assuming a significance level of $\alpha = 0.05$, power $(1 - \beta) = 0.80$, and intrasubject correlation of $r = 0.5$ (additional details are provided in the data supplement). All statistical tests were two-tailed, and P values < 0.05 were considered statistically significant. Analyses were performed using SAS version 9.4 (SAS Institute).

Results

Patients

Between June 2022 and January 2024, 408 patients were screened, and 251 were included in the study (Figure 1). After enrollment, 13 patients were excluded because of reintubation for urgent surgery. At the time of reintubation, none of these patients had signs of respiratory failure or gas exchange abnormalities. Among 238 analyzed patients, 46 (19%) required reintubation within 72 hours (extubation failure). No patient required reintubation between 72 hours and 7 days. Demographics and most relevant clinical characteristics of the population are displayed in Table 1. The number of enrolled patients per participating center is reported in the data supplement.

Primary Outcome

The main results of the study are displayed in Table 2 and Figure 2. During the SBT, the trends of C_{RS}/PBW and ΔP_{OCC} differed significantly between the extubation success and failure groups. In the extubation success group, C_{RS}/PBW and ΔP_{OCC} remained stable over the course of the SBT. In contrast, in the failure group, C_{RS}/PBW decreased by 0.3 (95% CI, -0.4 to -0.2 ml/cm H_2O /kg), from 1.0 (interquartile range, 0.8–1.2) to 0.7 (0.6–0.9) ml/cm H_2O /kg ($P < 0.001$). ΔP_{OCC} increased by 5 (4 to 6) cm H_2O , from 12 (10–15) to 18 (15–20) cm H_2O ($P < 0.001$). $P_{0.1}$ increased in both groups, by 0.7 (0.4–1.2) cm H_2O in the extubation success group and by 1.2 (0.8–1.9) cm H_2O in the extubation failure group. Airway resistance, intrinsic PEEP, V_T , respiratory rate, rapid shallow breathing index, gas exchange, and hemodynamics remained unchanged in both groups.

Secondary Outcomes

The discriminatory power of SBT-induced changes in study parameters to predict extubation failure is provided in Table 3 and in Figure E1 in the data supplement. Overall, the SBT-induced changes provided greater predictive accuracy than the absolute values recorded at the SBT end. The ΔP_{OCC} increase was the best predictor of the subsequent need for reintubation, with an optimal threshold of > 2 (> 1 , > 3) cm H_2O yielding an area under the curve (AUC) of 0.94 (0.90–0.97), with sensitivity of 89% and specificity of 93% ($P < 0.001$). A C_{RS}/PBW decrease less than or equal to -0.2 [less than

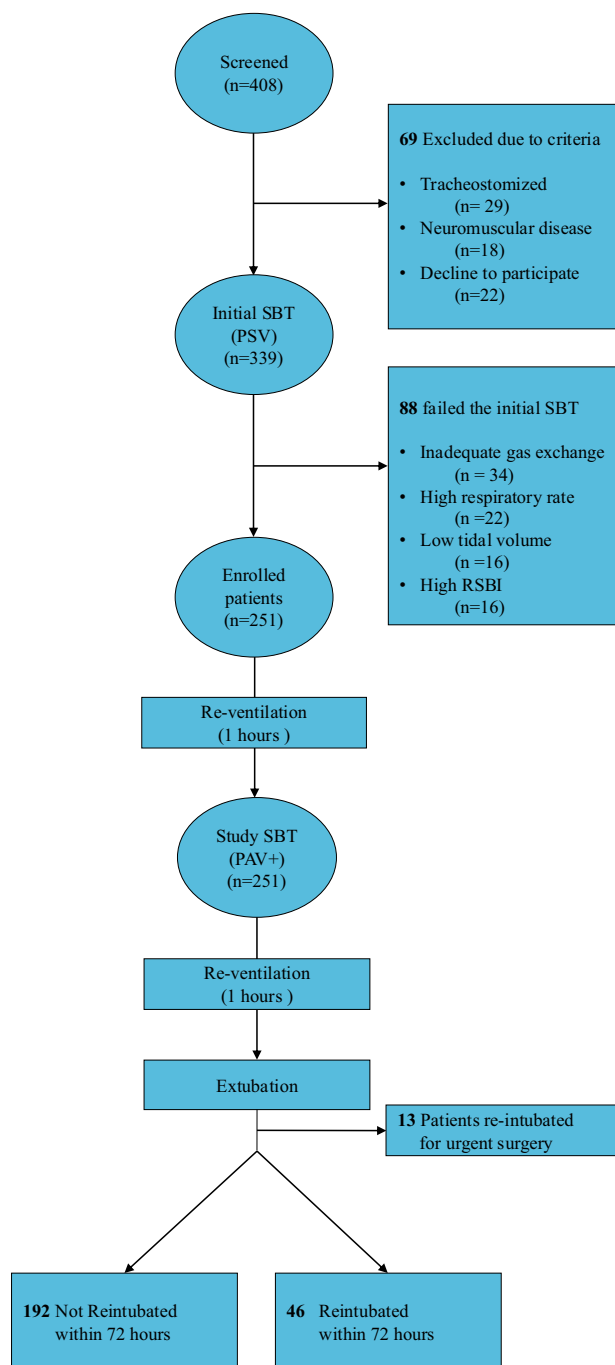


Figure 1. Flow diagram of patients' enrollment. PAV+ = proportional assist ventilation plus; PSV = pressure support ventilation; RSBI = the rapid shallow breathing index (i.e., the ratio of respiratory rate to $\dot{V}_T$); SBT = spontaneous breathing trial.

or equal to -0.1 , less than or equal to -0.2 ml/cm $\text{H}_2\text{O}/\text{kg}$ had an AUC of 0.90 (0.84–0.93), with sensitivity of 80% and specificity of 83%. An increase >0.8 (>0.6 , >1.5) cm H_2O in P0.1 had an AUC of 0.69 (0.62–0.74), with sensitivity of 72% and specificity of 60%. Figure 3 shows the time to

reintubation stratified by the best cutoffs for SBT-induced changes in C_{RS}/PBW , ΔP_{OCC} , and P0.1.

Exploratory Outcomes

First, patients in the failure group were stratified into tertiles on the basis of the

magnitude of SBT-induced changes in C_{RS}/PBW , ΔP_{OCC} , and P0.1, and time to reintubation was assessed across these tertiles (Figure 4). For C_{RS}/PBW , patients in the highest tertile (i.e., those who experienced the greatest reduction in respiratory system compliance during the SBT) were reintubated earlier than those in the lowest tertile (20 ± 12 h vs. 45 ± 14 h; $P < 0.001$). For ΔP_{OCC} , patients in the highest tertile (i.e., those exhibiting the largest increase in inspiratory effort) were reintubated earlier (12 ± 4 h) than those in the second (30 ± 9 h) and third (55 ± 12 h) tertiles, with all pairwise comparisons yielding $P < 0.001$. Reintubation timing did not significantly differ across P0.1 tertiles. Smoothing spline regression revealed a strong inverse relationship between SBT-induced changes in ΔP_{OCC} and time to reintubation ($R^2 = 0.89$) and a moderate association for C_{RS}/PBW ($R^2 = 0.46$), whereas no meaningful pattern was observed for P0.1 ($R^2 = 0.02$).

Second, we explored the relationship between SBT-induced changes in C_{RS}/PBW , ΔP_{OCC} , and work of breathing in both the extubation failure and success groups. In the failure group, a linear correlation was observed between SBT-induced declines in C_{RS}/PBW and increases in ΔP_{OCC} ($r = -0.71$; $P < 0.001$), whereas this correlation was weaker in the success group ($r = -0.48$; $P < 0.001$). A significant correlation was found between SBT-induced changes in ΔP_{OCC} and work of breathing in both the failure group ($r = 0.78$; $P < 0.001$) and the success group ($r = 0.86$; $P < 0.001$) (Figure E2).

Discussion

In this prospective, multicenter study in patients deemed at high risk of extubation failure, we show that evaluating compliance and ΔP_{OCC} during the SBT may aid in identifying patients with the highest likelihood of subsequent reintubation. In our cohort, a progressive reduction in C_{RS}/PBW less than or equal to -0.2 (less than or equal to -0.1 , less than or equal to -0.2) ml/cm $\text{H}_2\text{O}/\text{kg}$ and an increase in ΔP_{OCC} of >2 (>1 , >3) cm H_2O over the course of the SBT were the most accurate predictors of the subsequent need for reintubation. In contrast, SBT-induced changes in P0.1 had moderate predictive power, suggesting a more limited role of P0.1 than compliance and ΔP_{OCC} .

Table 1. Patient Demographics and Baseline Characteristics

	Extubation Success (n = 192)	Extubation Failure (n = 46)	P Value
Age, yr	64 [57–72]	63 [58–70]	0.851
Men, n (%)	115 (60)	27 (59)	0.882
APACHE II*			
At ICU admission	17 [13–21]	15 [13–20]	0.444
On day of extubation	13 [9–16]	13 [11–16]	0.085
Length of mechanical ventilation before extubation, d	5 [4–6]	4 [4–6]	0.690
Body mass index,† kg/m ²	29 [26–34]	29 [26–32]	0.673
Predicted body weight,‡ kg	60 [49–69]	62 [56–70]	0.100
Diagnosis at admission, n (%)			
Primary respiratory failure	113 (59)	24 (52)	0.456
Medical	44 (23)	10 (22)	0.915
Postoperative care	35 (18)	12 (26)	0.201
Comorbidities, n (%)			
Arterial hypertension	52 (27)	13 (28)	0.872
Neurologic disease	40 (21)	10 (22)	0.892
Diabetes mellitus	50 (26)	15 (33)	0.369
Renal disease	40 (21)	7 (15)	0.390
Liver disease	37 (19)	9 (20)	0.964
High-risk factors for reintubation, n (%)			
Age >65 yr	87 (45)	18 (39)	0.448
Heart failure as the primary indication for mechanical ventilation	39 (20)	10 (22)	0.830
Moderate to severe COPD	71 (37)	21 (45)	0.278
APACHE II on extubation day >12	96 (50)	27 (59)	0.289
Body mass index >30 kg/m ²	85 (44)	21 (46)	0.866
Inadequate cough reflex	48 (25)	12 (26)	0.879
Prolonged mechanical ventilation§	35 (18)	11 (24)	0.704
n > 2 comorbidities	124 (65)	29 (63)	0.764
Baseline ventilation, oxygenation, and hemodynamics			
PEEP, cm H ₂ O	7 [6–8]	7 [6–8]	0.980
Pressure support, cm H ₂ O	9 [8–10]	9 [8–10]	0.834
V _T /PBW, ml/kg	7.7 [7.2–8.5]	7.8 [7.3–8.5]	0.990
F _{IO₂}	0.35 [0.30–0.40]	0.35 [0.30–0.35]	0.270
Respiratory rate, breaths/min	21 [18–24]	21 [17–25]	0.733
Arterial pH	7.4 [7.38–7.42]	7.4 [7.35–7.42]	0.308
PaO ₂ , mm Hg	99 [89–106]	98 [81–108]	0.318
PaCO ₂ , mm Hg	41 [37–46]	42 [37–47]	0.446
Systolic arterial pressure, mm Hg	120 [109–129]	127 [115–132]	0.031
Diastolic arterial pressure, mm Hg	76 [70–82]	76 [65–84]	0.798
Heart rate, beats/min	79 [71–87]	80 [72–90]	0.523

Definition of abbreviations: APACHE II = Acute Physiology and Chronic Health Evaluation II; COPD = chronic obstructive pulmonary disease; PBW = predicted body weight; PEEP = positive-end expiratory pressure.

Results are expressed as median [IQR].

*APACHE II score was calculated from 17 variables. Scores range from 0 to 71 points, with higher scores indicating more severe disease.

†Calculated as weight in kilograms divided by height in meters squared.

‡Calculated as 50 (or 45.5 for women) + 0.91 × (height [cm] – 152.4).

§Mechanical ventilation ≥ 7 days.

||Comorbidities were categorized on the basis of Charlson comorbidity index.

Conventional monitoring during SBTs relies on respiratory rate, V_T, gas exchange, and clinical signs (1, 29, 30). In our study, the lack of significant differences in these parameters between the failure and success groups highlights their limitations, because they may not capture subtle changes in respiratory mechanics and inspiratory effort that precede overt signs of respiratory failure (31, 32). In their seminal paper, Jubran and Tobin demonstrated that in patients in whom the SBT fails, clinically evident respiratory distress is preceded by subtle

declines in lung elastic properties (10). In that study, patients in whom SBT failed exhibited a progressive deterioration in respiratory system compliance, leading to an increased elastic workload. In parallel, these patients showed a sustained rise in inspiratory effort and work of breathing, whereas the respiratory rate remained nearly stable. This pathophysiological sequence aligns well with our observations: In patients in whom extubation ultimately failed, we detected SBT-induced declines in compliance coupled with a consistent rise in work of

breathing because of ΔP_{OCC} increases, with stable V_T and respiratory rate. These findings suggest that an increase in inspiratory effort represents the first compensatory response aimed at preserving V_T in case of increases in elastic workload; tachypnea develops at later stages, when this becomes insufficient. This would reinforce the rationale for monitoring inspiratory effort throughout the SBT (11).

Although work of breathing is challenging to measure at the bedside in standard clinical practice (except when using the PAV+ algorithm), ΔP_{OCC} serves as a

Table 2. Differences between Extubation Success and Failure Groups in Respiratory Mechanics, Gas Exchange, and Hemodynamics at Beginning (5-Min Time Point) and End (30-Min Time Point) of Second Spontaneous Breathing Trial

	5 Min after SBT Start		End of SBT	
	Extubation Success	Extubation Failure	Extubation Success	Extubation Failure
PEEP, cm H ₂ O	5	5	5	5
Intrinsic PEEP, cm H ₂ O	1 [0–1]	1 [0–1]	1 [0–1]	1 [0–1]
Peak pressure, cm H ₂ O	12.1 [11.7–12.4]	12 [11.4–12.3]	12.1 [12.1–12.4]	12.2 [11.9–12.5]
FiO ₂	0.35 [0.30–0.40]	0.35 [0.30–0.35]	0.35 [0.30–0.40]	0.35 [0.30–0.35]
V _T /PBW, ml/kg	7.9 [7.3–8.5]	7.6 [7.1–8.4]	8 [7.6–8.5]	7.9 [7.5–8.5]
Respiratory rate, breaths/min	21 [19–23]	20 [18–23]	21 [19–24]	22 [16–25]
Rapid shallow breathing index, breaths/min/L	54 [46–62]	58 [42–68]	52 [42–61]	53 [36–81]
C _{RS} /PBW, ml/cm H ₂ O/kg	1.1 [0.9–1.3]	1.0 [0.8–1.2]	1.1 [0.9–1.3]	0.7 [0.6–0.9]*†
Airway resistance, cm H ₂ O/L × s ⁻¹	4.8 [4.7–4.9]	4.8 [4.7–5]	5.0 [4.0–6.4]	5.1 [4.2–6.7]
Work of breathing, J/s	0.6 [0.3–0.8]	0.6 [0.5–0.7]	0.6 [0.4–0.8]	1.1 [0.8–1.4]*†
Plateau pressure, cm H ₂ O	12 [11–13]	13 [12–14]	12 [11–13]	16 [14–19]*†
Driving pressure, cm H ₂ O	7 [6–8]	8 [7–9]	7 [6–8]	11 [9–14]*†
ΔP _{OCC} , cm H ₂ O	11 [9–13]	12 [10–15]	10 [9–13]	18 [15–20]*†
P0.1, cm H ₂ O	1.8 [1.5–2.2]	2 [1.5–2.4]	2.6 [2.4–2.8]†	3.2 [2.9–3.6]*†
Arterial pH	7.42 [7.39–7.45]	7.41 [7.34–7.44]	7.41 [7.38–7.43]	7.41 [7.39–7.48]
PaO ₂ , mm Hg	115 [90–133]	98 [86–114]	103 [95–110]	92 [93–108]
PaCO ₂ , mm Hg	43 [35–51]	47 [36–54]	43 [39–47]	42 [39–45]
Systolic arterial pressure, mm Hg	124 [111–136]	111 [108–133]	125 [113–136]	120 [108–134]
Diastolic arterial pressure, mm Hg	78 [71–85]	76 [72–84]	79 [72–86]	77 [73–85]
Heart rate, beats/min	75 [68–84]	72 [64–82]	74 [67–87]	73 [66–79]

Definition of abbreviations: ΔP_{OCC} = airway occlusion pressure; C_{RS}/PBW = respiratory system compliance normalized to predicted body weight; P0.1 = airway occlusion pressure measured the first 100 milliseconds of inspiration; PBW = predicted body weight; PEEP = positive end-expiratory pressure.

Results are expressed as median [IQR].

*Significantly different from the success group.

†Significantly different from the 5-minute time point in the same group.

noninvasive surrogate of its main component in case of a stable respiratory rate, as in our patients. Accordingly, our *post hoc* analysis confirms a strong correlation between the SBT-induced changes in work of breathing and ΔP_{OCC}. This may strengthen the clinical impact of our study, because, compared with work of breathing, ΔP_{OCC} is an easy-to-obtain metric available on most modern mechanical ventilators.

Several factors may have contributed to the decrease in respiratory system compliance observed during the SBT in patients who were subsequently reintubated. These include dynamic hyperinflation (33, 34), microatelectasis (35, 36), or subclinical pulmonary edema (37, 38). Notably, we found that the magnitude of SBT-induced changes in C_{RS}/PBW and ΔP_{OCC} were associated with the timing of reintubation. Interestingly, patients who exhibited more pronounced reduction in C_{RS}/PBW and greater increase in ΔP_{OCC} were reintubated earlier than those with less marked changes. These findings would indicate that changes in lung mechanics and inspiratory workload are dynamic processes, evolving before

overt clinical signs of respiratory failure. Previous studies highlighted the interplay between lung mechanics and inspiratory muscle workload (39–41). Doorduyn and colleagues reported that in patients in whom SBT failed, the contribution of expiratory muscles progressively increases during the trial: This potentially reduces end-expiratory lung volume and, consistently, respiratory system compliance (42).

In our study, respiratory system compliance was estimated using the PAV+ algorithm, which relies on end-inspiratory microairway occlusions (21). Although PAV+ ventilation allows a reliable, continuous, and noninvasive bedside assessment of respiratory mechanics, it is currently limited to a single ventilator model that is no longer commercially available. Respiratory system compliance, however, can be measured during assisted mechanical ventilation via end-inspiratory occlusions on many of the most recent ventilators (13), enhancing the reproducibility of our findings. This approach is well validated and widely accessible in clinical settings; however, it may pose technical challenges at the bedside,

particularly in patients exhibiting active expiration, which can compromise the accuracy of plateau pressure measurements (43). From the perspective of our results, evaluation of ΔP_{OCC} provides similar predictive power, and, if measured correctly, its reliability is less influenced by expiratory muscle activation.

In our population, P0.1 increased in both the success and failure groups over the course of the SBT, although values remained within a noncritical range. P0.1 aids bedside estimation of neural respiratory drive, reflecting the mismatch between neural drive and motor output, contributing to the mechanism of dyspnea (44, 45). Interestingly, we found that the upward trend was more pronounced in patients who were subsequently reintubated, particularly after 20 minutes of the trial. Notably, our protocol involved two sequential SBTs. Although a 1-hour reventilation period was implemented between trials to mitigate residual fatigue (19), we must acknowledge that repeating the SBT may have contributed to a progressive increase in neural drive in some individuals. Furthermore, it is plausible

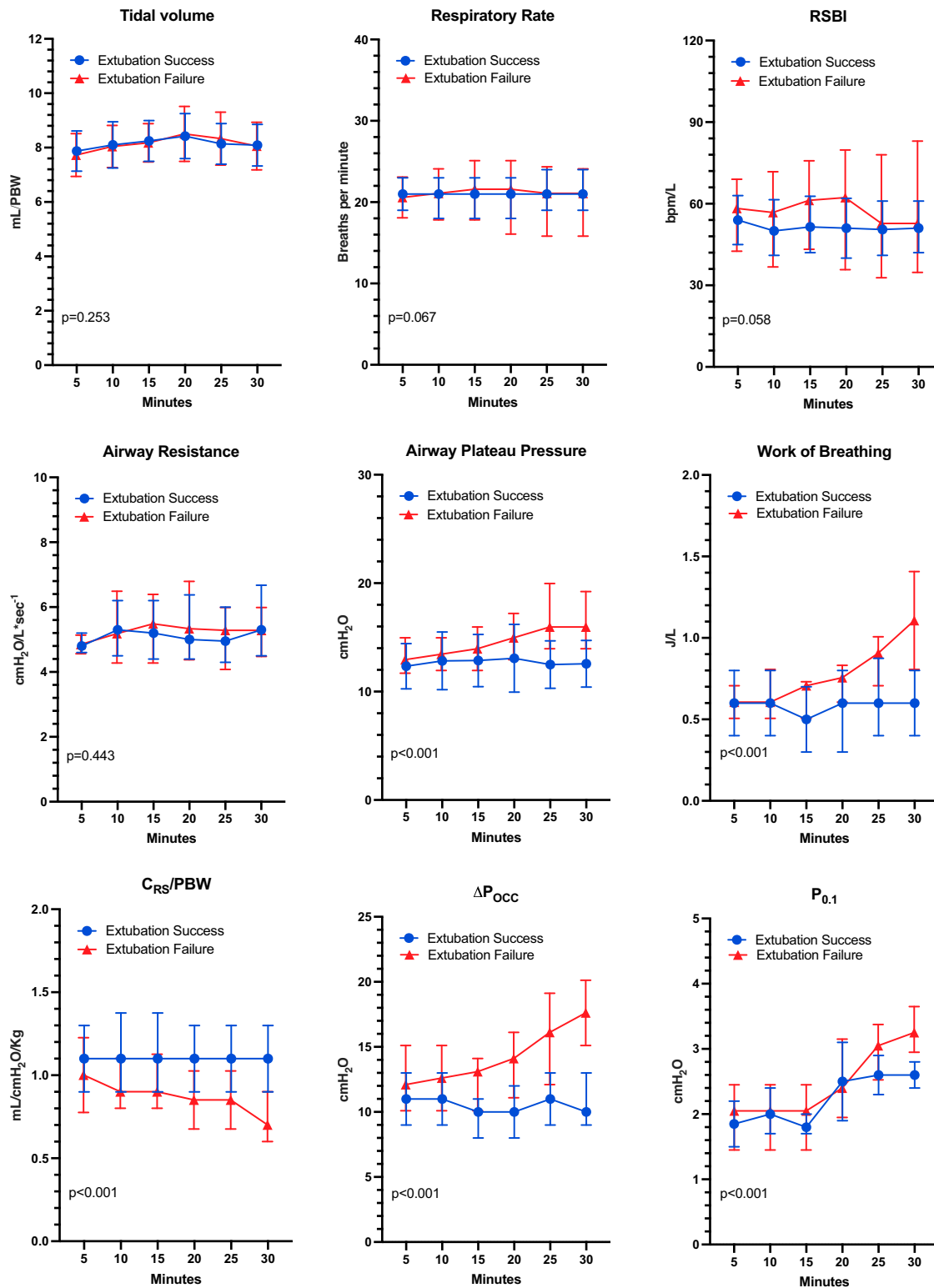


Figure 2. Trends of respiratory mechanics parameters recorded during the study spontaneous breathing trial. Each measure is reported as the median value and interquartile range, and measurements were taken every 5 minutes for a total of six time points. Patients in the extubation failure group are represented by red triangles, and those in the extubation success group are represented by blue circles. The P value reported in the figure refers to the time–group interaction. $P_{0.1}$, airway occlusion pressure measured for the first 100 milliseconds of inspiration; ΔP_{OCC} = airway occlusion pressure; RSBI = rapid shallow breathing index (i.e., the ratio of respiratory rate to V_T).

Table 3. Discriminatory Capacity of Respiratory Mechanics Measurements for Identification of Extubation Failure

Parameter	Area under ROC Curve		Youden Index		
	AUC [95% CI]	P Value	Threshold [95% CI]	Sensitivity	Specificity
Absolute values at end of SBT					
V _T /PBW, ml/kg	0.53 [0.46–0.59]	0.562	≤7.3 [≤7.0; ≤7.8]	24	87
Respiratory rate, breaths/min	0.54 [0.48–0.61]	0.405	≤17 [≤14; ≤24]	33	82
Rapid shallow breathing index, breaths/min/L	0.53 [0.47–0.60]	0.599	>68 [>35; >97]	41	83
C _{RS} /PBW, ml/cm H ₂ O/kg	0.88 [0.81–0.92]	<0.001	≤0.9 [≤1; ≤0.8]	89	76
Plateau pressure, cm H ₂ O	0.87 [0.83–0.91]	<0.001	>13 [>12; >15]	87	76
Driving pressure, cm H ₂ O	0.87 [0.83–0.91]	<0.001	>8 [>7; >10]	87	76
ΔP _{OCC} , cm H ₂ O	0.91 [0.86–0.94]	<0.001	>14 [>13; >15]	80	90
P0.1, cm H ₂ O	0.86 [0.81–0.90]	<0.001	>2.8 [>2.7; >3]	78	78
Changes in physiological variables throughout SBT					
V _T /PBW, ml/kg	0.54 [0.47–0.60]	0.464	>0.3 [>−1.9; >1.0]	54	57
Respiratory rate, breaths/min	0.51 [0.45–0.58]	0.804	≤6 [≤3; ≤8]	98	10
Rapid shallow breathing index, breaths/min/L	0.57 [0.51–0.67]	0.277	>2 [>−27; >10]	57	66
C _{RS} /PBW, ml/cm H ₂ O/kg	0.90 [0.84–0.93]	<0.001	≤−0.2 [≤−0.1; ≤−0.2]	80	83
Plateau pressure, cm H ₂ O	0.89 [0.84–0.92]	<0.001	>2 [>1; >2]	74	91
Driving pressure, cm H ₂ O	0.86 [0.84–0.92]	<0.001	>2 [>1; >2]	74	91
ΔP _{OCC} , cm H ₂ O	0.94 [0.90–0.97]	<0.001	>2 [>1; >3]	89	93
P0.1, cm H ₂ O	0.69 [0.62–0.75]	0.001	>0.8 [>0.6; >1.5]	72	60

Definition of abbreviations: ΔP_{OCC} = airway occlusion pressure; C_{RS} = compliance of respiratory system; P0.1 = airway occlusion pressure during first 100 milliseconds of inspiration; PBW = predicted body weight; V_T/PBW = V_T normalized to predicted body weight.

that extending the duration of the SBT beyond 30 minutes would have further amplified the differences between groups. Consistent with this, Delamaire and colleagues (46) reported persistently elevated P0.1 values during both the SBT and the subsequent reventilation phase in patients in whom extubation failed, indicating

sustained neuromechanical uncoupling despite the reintroduction of ventilatory support. However, in our failure cohort, the parallel increase in P0.1 and ΔP_{OCC}, together with the stability of respiratory rate and V_T, suggests that neural drive was well aligned with muscular effort. This balance indicates that respiratory muscle

performance was likely preserved throughout the SBT, allowing ventilatory demands to be met without the development of dyspnea.

In our study, high-flow oxygen therapy was systematically administered after extubation, and we observed a failure rate of 19%, which is consistent with recent

Kaplan-Meier Curves for Time to Reintubation

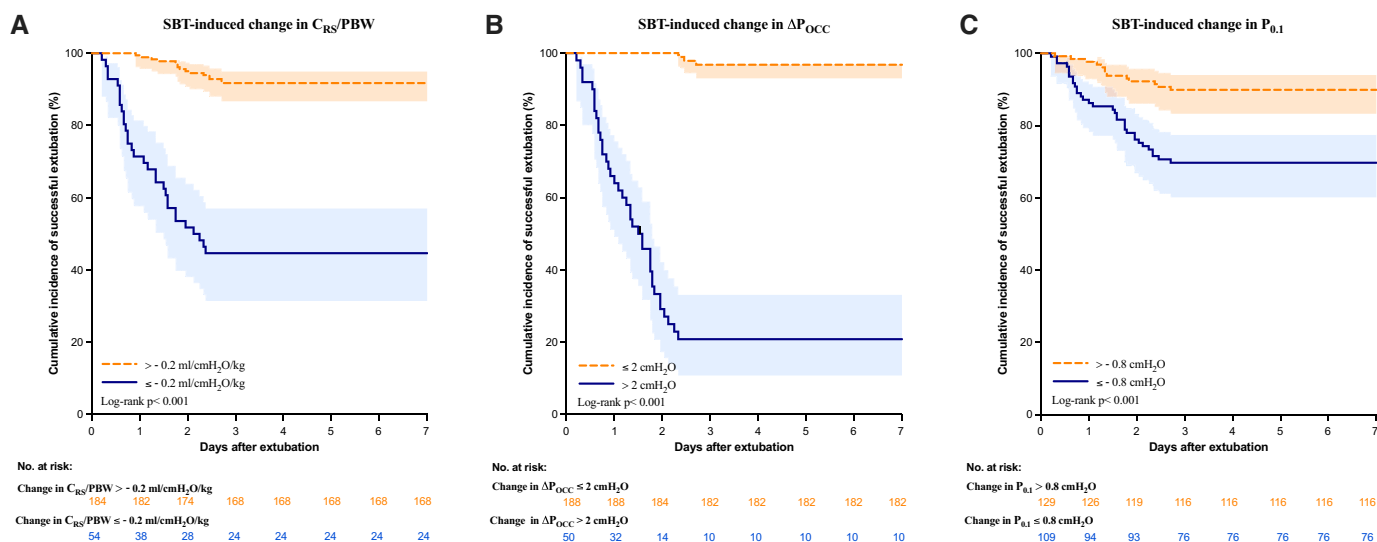


Figure 3. Kaplan-Meier analysis of time from extubation to reintubation. Patients were stratified according to the optimal cutoffs for the spontaneous breathing trial (SBT)-induced changes (i.e., absolute difference from the beginning to the end of the SBT) in compliance of respiratory system normalized to predicted body weight (A), airway occlusion pressure (ΔP_{OCC}) (B), and airway occlusion pressure measured for the first 100 milliseconds of inspiration (P0.1) (C).

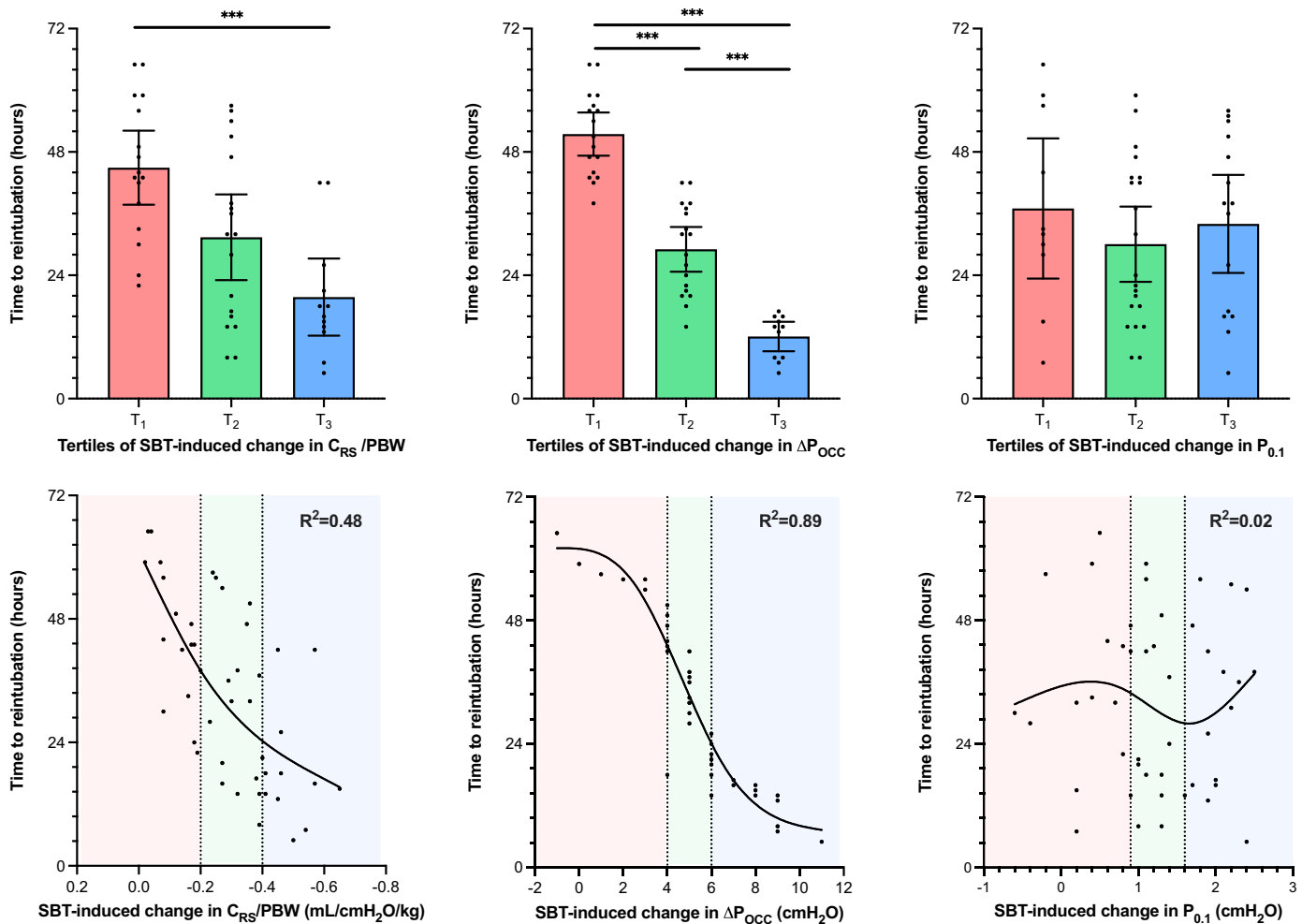


Figure 4. Upper panel: Time to reintubation among patients stratified into tertiles according to the magnitude of spontaneous breathing trial (SBT)-induced changes in respiratory system compliance (C_{RS}) normalized to predicted body weight (PBW) (left; T₁: $n = 17$; T₂: $n = 16$; T₃: $n = 13$), airway occlusion pressure (ΔP_{OCC}) (middle; T₁: $n = 17$; T₂: $n = 18$; T₃: $n = 11$), and airway occlusion pressure measured for the first 100 milliseconds of inspiration ($P_{0.1}$) (right; T₁: $n = 10$; T₂: $n = 21$; T₃: $n = 15$). Bar graphs display mean $\pm$ SD of time to reintubation for patients in the lowest (red), middle (green), and highest (blue) tertiles of change. (***) denotes statistical significance at $P < 0.001$ between tertiles. Lower panel: Smoothing spline regressions illustrating the relationship between SBT-induced changes and time to reintubation. Each dot represents a patient. Dashed lines mark the 33rd and 66th percentiles (SBT-induced changes in C_{RS}/PBW : -0.4 and -0.6 mL/cm H₂O/kg; SBT-induced changes in ΔP_{OCC} : 4 and 6 cm H₂O; SBT-induced changes in $P_{0.1}$: 0.9 and 1.6 cm H₂O). Colored areas represent the corresponding tertile ranges.

literature (18). Recent guidelines support the use of noninvasive ventilation to reduce the reintubation rate in high-risk patients (47). Because specific interventions (such as noninvasive ventilation and/or high-flow nasal oxygen) have been shown to improve outcomes in large cohorts of high-risk patients, this may lead to the indiscriminate application of postextubation interventions across all patients meeting high-risk criteria (47–49). This is partly because of the lack of a universally accepted definition of “high risk,” with studies adopting heterogeneous criteria (50). These criteria are based primarily on clinical history and comorbidities and do not account for patients’ physiological status at

the time of extubation (3). This may explain why randomized trials on postextubation respiratory support report relatively high numbers needed to treat (frequently exceeding 10) to prevent a single reintubation, suggesting that only a subset of high-risk patients derives meaningful clinical benefit (48, 49). Improving patient selection therefore seems critical, especially considering the cost and resource demands of postextubation strategies and the potential harm associated with inappropriate use of noninvasive ventilation after extubation (51). In this context, our data suggest that monitoring ΔP_{OCC} and respiratory system compliance during the SBT may provide valuable insights

into individual risk within the broader high-risk population. These variables reflect the underlying mechanisms of early respiratory failure and may help to identify patients at greatest risk of extubation failure. On the basis of our findings, it is physiologically plausible that patients who exhibit reduced compliance and increased ΔP_{OCC} during the SBT may benefit the most from noninvasive ventilation. Notably, noninvasive ventilation acts directly on these parameters (52): PEEP counteracts alveolar derecruitment and can improve compliance, whereas pressure support unloads inspiratory effort and preserves adequate V_T (53). From this perspective, the

absence of noninvasive ventilation use in our study represents both a limitation and a strength, because it allowed a clearer observation of the link between ΔP_{OCC} and compliance and extubation outcomes. This association might have been masked if noninvasive ventilation had been applied in all our extubated patients.

Clinical research has explored advanced monitoring techniques to monitor physiological changes induced by SBTs and extubation and to identify patients at highest risk of subsequent failure. Esophageal and gastric manometry (54), lung ultrasound (55), electrical impedance tomography (56), and diaphragmatic electrical activity (57) have shown promise. However, the requirement for sophisticated equipment and expertise limits their routine clinical applicability. Our results indicate that a noninvasive systematic monitoring of mechanics/effort during SBTs may help stratify the risk of extubation failure. Although impossible to demonstrate in the context of our study, and well beyond our purposes, our data suggest that integrating respiratory system compliance and ΔP_{OCC} into clinical decision making may support a more individualized and physiologically grounded approach to extubation and postextubation respiratory support. Further research is warranted to integrate these measurements into individualized interventional algorithms aimed at improving weaning outcomes while optimizing resource allocation.

Limitations

Our study has limitations. First, all patients underwent two consecutive SBTs: an initial screening SBT followed by a study SBT conducted in the PAV+ mode. As already discussed, it is possible that any stress or fatigue induced by the first trial could have influenced the subsequent “study” SBT. However, by including only patients who successfully passed a screening SBT, we were able to focus on subtle, subclinical differences that could herald the extubation failure. In addition, to mitigate the potential impact of the first trial, all patients were reventilated for 1 hour (19) using their baseline ventilator settings. Second, we used PAV+ during the study SBT to obtain reliable and noninvasive monitoring of respiratory mechanics and work of breathing parameters. The PAV+ algorithm has the advantage of performing precise micro-occlusions to identify the end of inspiration, ensuring consistent, continuous, and reliable measurement of respiratory system compliance while eliminating potential biases related to the clinician’s expertise in data collection (20). However, as acknowledged, this methodology is limited to a single ventilator model that is no longer commercially available, restricting its generalizability and consequently the reproducibility of the study and the clinical applicability of our results. Nevertheless, reliable measurement of ΔP_{OCC} and respiratory system compliance can be obtained in most ventilators through end-expiratory and end-inspiratory occlusions (13, 15), and P0.1 is available on

most ventilators, making our findings more broadly applicable. Third, we used a single breath-hold maneuver for assessing inspiratory effort (ΔP_{OCC}) and neural drive (P0.1), whereas previous studies averaged three consecutive occlusions to reduce variability. However, we reasoned that because by protocol we assessed ΔP_{OCC} and P0.1 every 5 minutes to capture temporal trends, multiple occlusions in such a short time frame could have interfered with the patient’s breathing pattern. This methodological difference may have introduced additional variability in the recorded values.

Conclusions

In patients at high risk of extubation failure, conventional parameters monitored during the SBT may not fully capture early signs of respiratory failure. In this study, SBT-induced reduction in respiratory system compliance and increases in ΔP_{OCC} were associated with extubation failure among patients who had succeeded the SBT on the basis of conventional criteria. Future research is warranted to integrate these measurements into interventional algorithms to improve weaning outcomes. ■

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