EDITORIAL

Revisiting, Reframing, and Casting a New Light on Liberation From Mechanical Ventilation

Timothy D. Girard, MD, MSCI; Karen E. A. Burns, MD, FRCPC, MSc

Every year, more than 1 million patients throughout the world receive mechanical ventilation for acute respiratory failure. One of the most important decisions clinicians make in managing these critically ill patients is how to liberate them from invasive ventilation. Ventilator liberation poses an important dilemma for clinicians because premature or failed attempts at extubation, which typically necessitate reintubation, increase rates of ventilator-associated pneumonia, mortality, and other adverse outcomes.[1] Conversely, delaying extubation also increases a patient's risk of being oversedated and developing delirium or ventilator-associated events.[2]

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The current standard of care for managing patients with invasive ventilation involves daily screenings to identify patients who are ready to undergo a spontaneous breathing trial (SBT) to ascertain those ready to be separated from ventilator support.[3,4] Additionally, clinicians determine whether patients can be liberated from an endotracheal tube by assessing for extubation failure risk factors (eg, weak cough, heavy secretions, and depressed level of consciousness) before deciding to extubate patients who have had a successful SBT. Before the SBT became the standard assessment of ventilator liberation readiness, a series of investigations searched for the ideal predictor, but the "weaning parameters" examined were limited in their ability to predict successful extubation. Consequently, observing a still-intubated patient during a trial of unassisted breathing (ie, the SBT) remained the preferred approach. In 1995, Esteban et al[5] published a randomized trial that found that using daily SBTs hastened successful liberation compared with gradually titrating mandatory ventilation rate or inspiratory pressure. Shortly thereafter, Ely et al[6] showed that a respiratory therapy-driven SBT protocol resulted in earlier extubation than a physician-directed approach.

When conducting an SBT, a number of different techniques can be used. During a T-piece SBT, which was used by Esteban et al,[5] a patient receives supplemental oxygen but no ventilatory assistance. Alternatively, a patient may receive pressure support ventilation (PSV), during which a small amount of positive pressure (eg, 5-8 cm H_2O) assists inspiration. Additionally, the safety criteria used to determine when an SBT should be started can be either conservative or liberal, and SBTs can be conducted for variable durations. Thus, more than 2 decades after Esteban et al[5] and Ely et al[6] published trials ushering SBTs into routine use, new evidence to guide decision making about liberation from invasive ventilation in current practice is still warranted and needed.

In this issue of the *JAMA*, Subirà and colleagues[7] present the results of the largest randomized clinical trial ever conducted comparing alternative SBT techniques. The authors randomized 1153 mechanically ventilated adults in 18 Spanish intensive care units (ICUs) to 2 different SBT techniques: (1) a "highly demanding" 2-hour T-piece SBT or (2) a "less demanding" 30-minute PSV SBT with 8-cm H_2O inspiratory pressure and 0-cm H_2O positive end-expiratory pressure. By study design, participants in both groups who successfully completed an SBT were extubated because the trial eligibility criteria ensured that enrolled participants were good candidates for extubation. In this trial, participants in whom the initial SBT was unsuccessful were ventilated at the discretion of the ICU team, and subsequent SBTs were not directed by the trial protocol.

Subirà et al[7] found that participants in the 30-minute PSV SBT group were more likely than those in the 2-hour T-piece SBT group to have a successful initial SBT and therefore to be extubated. Thus, successful extubation (the primary outcome) occurred in 82.3% of patients in the PSV group and in 74.0% of participants in the T-piece group, an absolute increase of 8.2% (95% CI, 3.4%-13.0%). Additionally, although more participants in the less demanding SBT group had a successful initial SBT and were extubated, they did not experience a higher reintubation rate in the 72 hours after extubation. Moreover, those in the PSV SBT group were also significantly less likely to die in the hospital or during the 90 days after randomization—results that are difficult to explain given that the SBT techniques did not appear to affect other secondary outcomes. Nevertheless, these results are important because they provide evidence that, at least during an initial SBT, most patients can be tested for 30 minutes using 8-cm H_2O PSV.

Less demanding SBT techniques were previously studied in 2 multicenter randomized trials conducted in the late 1990s.[8,9] Similar to the trial by Subirà et al, these older investigations found no significant differences in reintubation rates when comparing 30-minute SBTs with 120-minute SBTs[9] and comparing SBTs conducted with 7-cm H_2O PSV vs T-piece SBTs.[8] Given these results, it is worth considering why many clinicians continue to rely on 120-minute SBTs and many still prefer to conduct T-piece SBTs.[4] Clinicians' tendency to be risk averse and delays in knowledge transfer may explain some of the variation in ventilator liberation practices, but limitations in the evidence are also

likely a contributing factor. No equivalence trials have been conducted comparing different SBT techniques, and questions remain regarding the quality and generalizability of the evidence. These new results reported by Subirà and colleagues[7] are therefore an important and welcome addition to the literature. At the same time, their trial raises a number of important questions.

First, when should SBTs be started during a patient's recovery from acute respiratory failure? Similar to previous trials,[5] a high percentage of participants in the trial by Subirà et al had a successful initial SBT, which leads to the question of whether some participants were ready to undergo an SBT and to be considered for extubation at an earlier time point. That only half of the patients who experience unplanned extubation require reintubation[10] suggests that recognizing the earliest time when patients are ready for extubation is a challenge for ICU clinicians.

Second, should a 30-minute PSV SBT be used regardless of a patient's characteristics and circumstances, or should patient-related factors influence how clinicians conduct SBTs? Even though Subirà et al enrolled a diverse group of participants in multiple centers, their protocol applied only to each participant's initial SBT. Consequently, the results of this trial cannot be generalized to patients in whom an initial SBT is unsuccessful, a group that may be more likely to have extubation failure after a successful 30-minute SBT.[11] Future trials of ventilator liberation techniques should continue to apply study interventions until patients achieve successful extubation (or another trial end point).

Third, does the use of related interventions—eg, computerized ventilator weaning[12] or extubation to noninvasive ventilation or high-flow nasal cannula oxygen therapy after a successful (or even a failed) SBT[13]—modify the effects or the implementation of different SBT techniques? The availability of noninvasive modes of support, for example, may encourage clinicians to extubate high-risk patients after a less demanding SBT. It is notable that in the trial by Subirà and colleagues, the use of prophylactic noninvasive ventilation or high-flow nasal cannula oxygen therapy after extubation was more common in the 30-minute PSV SBT group than in the 2-hour T-piece SBT group (25% vs 19%; $P = .01$).

Fourth, does the SBT technique affect long-term outcomes? If so, how? The effects of interventions on short-term outcomes are important and generally simple to ascertain in clinical trials. Long-term outcomes, however, including long-term survival and functional status, are equally or perhaps even more important to patients.[14] The trial by Subirà and colleagues[7] suggests that 90-day mortality may be reduced by using 30-minute PSV SBTs rather than more demanding SBTs. If this finding is true, identifying the mechanism(s) underlying this putative benefit will not only promote knowledge transfer but may also help in the identification of other interventions that favorably influence long-term outcomes.

Fifth, how should outcomes be defined and reported in ventilator liberation trials? Although successful extubation is an outcome valued by clinicians, patients, and patients' families,[14] there is no consensus regarding how to define, measure, and report this outcome. Are patients who are extubated to noninvasive ventilation, for example, successfully extubated? At what time point should investigators report successful extubation? Which study participants should be included in the denominator (all participants randomized to an intervention or only those who are extubated)? Which is more important, the proportion of participants successfully extubated or the time to successful extubation?

In summary, mechanical ventilation research in the ICU is challenging. With their publication in this issue of *JAMA*, Subirà and colleagues have addressed an important knowledge gap, advancing the science of ventilator liberation and revitalizing an important area of critical care research. Their results support the use of 30 minutes of PSV during an initial SBT for most patients. Yet much work remains to be done to improve the outcomes of mechanically ventilated ICU patients, a population that both is highly vulnerable and has great potential to respond to evidence-based care.[15]

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Effect of Pressure Support vs T-Piece Ventilation Strategies During Spontaneous Breathing Trials on Successful Extubation Among Patients Receiving Mechanical Ventilation
A Randomized Clinical Trial

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IMPORTANCE Daily spontaneous breathing trials (SBTs) are the best approach to determine whether patients are ready for disconnection from mechanical ventilation, but mode and duration of SBT remain controversial.

OBJECTIVE To evaluate the effect of an SBT consisting of 30 minutes of pressure support ventilation (an approach that is less demanding for patients) vs an SBT consisting of 2 hours of T-piece ventilation (an approach that is more demanding for patients) on rates of successful extubation.

DESIGN, SETTING, AND PARTICIPANTS Randomized clinical trial conducted from January 2016 to April 2017 among 1153 adults deemed ready for weaning after at least 24 hours of mechanical ventilation at 18 intensive care units in Spain. Follow-up ended in July 2017.

INTERVENTIONS Patients were randomized to undergo a 2-hour T-piece SBT (n = 578) or a 30-minute SBT with 8-cm H_2O pressure support ventilation (n = 557).

MAIN OUTCOME AND MEASURES The primary outcome was successful extubation (remaining free of mechanical ventilation 72 hours after first SBT). Secondary outcomes were reintubation among patients extubated after SBT; intensive care unit and hospital lengths of stay; and hospital and 90-day mortality.

RESULTS Among 1153 patients who were randomized (mean age, 62.2 [SD, 15.7] years; 428 [37.1%] women), 1018 (88.3%) completed the trial. Successful extubation occurred in 473 patients (82.3%) in the pressure support ventilation group and 428 patients (74.0%) in the T-piece group (difference, 8.2%; 95% CI, 3.4%-13.0%; *P* = .001). Among secondary outcomes, for the pressure support ventilation group vs the T-piece group, respectively, reintubation was 11.1% vs 11.9% (difference, −0.8%; 95% CI, −4.8% to 3.1%; *P* = .63), median intensive care unit length of stay was 9 days vs 10 days (mean difference, −0.3 days; 95% CI, −1.7 to 1.1 days; *P* = .69), median hospital length of stay was 24 days vs 24 days (mean difference, 1.3 days; 95% CI, −2.2 to 4.9 days; *P* = .45), hospital mortality was 10.4% vs 14.9% (difference, −4.4%; 95% CI, −8.3% to −0.6%; *P* = .02), and 90-day mortality was 13.2% vs 17.3% (difference, −4.1% [95% CI, −8.2% to 0.01%; *P* = .04]; hazard ratio, 0.74 [95% CI, 0.55-0.99]).

CONCLUSIONS AND RELEVANCE Among patients receiving mechanical ventilation, a spontaneous breathing trial consisting of 30 minutes of pressure support ventilation, compared with 2 hours of T-piece ventilation, led to significantly higher rates of successful extubation. These findings support the use of a shorter, less demanding ventilation strategy for spontaneous breathing trials.

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Visual Abstract

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Supplemental content

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Among patients receiving mechanical ventilation, readiness for extubation and liberation from ventilatory support is evaluated with a spontaneous breathing trial (SBT).[1] Daily screening of respiratory function by SBT is associated with a shorter duration of mechanical ventilation.[2] After a successful SBT and extubation, 10% to 25% of patients require reintubation, and reintubation is associated with higher mortality.[3,4]

The most common modes of SBT are T-piece ventilation and pressure support ventilation (PSV), lasting between 30 minutes and 2 hours.[5-7] There are no differences in the rate of successful extubation between 2-hour PSV and 2-hour T-piece ventilation,[8] between T-piece ventilation for 30 minutes vs 2 hours,[9] or between PSV for 30 minutes vs 2 hours.[10] Although shorter SBTs are better tolerated, there is no evidence that they result in higher successful extubation rates.[9,10] Some patients in whom a T-piece SBT failed might have been successfully extubated after a PSV SBT.[11]

A recent meta-analysis suggested that T-piece SBTs are the optimal method for evaluating weaning readiness.[12] Nevertheless, another meta-analysis found that PSV resulted in higher rates of successful extubation than T-piece SBTs.[13] Moreover, the latest American Thoracic Society guidelines for weaning recommend PSV SBTs with moderate-quality evidence.[14] Thus, further investigation is needed to determine the best approach for SBTs.

This study hypothesized that less demanding SBTs could result in a higher rate of successful extubation without increasing the reintubation rate. To test this hypothesis, 2 weaning strategies were compared: an approach that is more demanding for patients (T-piece SBT for 2 hours) vs an approach that is less demanding for patients (8-cm H_2O PSV for 30 minutes).

Key Points

Question What is the effect of a less demanding (30 minutes of pressure support ventilation) vs a more demanding (2 hours of T-piece ventilation) spontaneous breathing trial on rates of successful extubation?

Findings In this randomized clinical trial that included 1153 adults receiving mechanical ventilation, the proportion of patients successfully extubated was 82.3% among those who received 30 minutes of pressure support ventilation compared with 74% among those who received 2 hours of T-piece ventilation, a difference that was statistically significant.

Meaning These findings support the use of a shorter, less demanding strategy of 30 minutes of pressure support ventilation for spontaneous breathing trials.

Methods

From January 2016 through April 2017, a multicenter randomized clinical trial was conducted in 18 Spanish intensive care units. The ethics committee of each hospital approved the study, and all patients or their relatives provided written informed consent. The study protocol is available in Supplement 1.

Patients aged 18 years or older undergoing mechanical ventilation for at least 24 hours who fulfilled the weaning criteria were eligible. The weaning criteria were (1) the resolution or improvement of the condition leading to intubation; (2) hemodynamic stability, defined as systolic blood pressure between 90 and 160 mm Hg and heart rate less than 140/min without vasopressors or with low doses of vasopressors; (3) Glasgow Coma Scale score of 13 or greater; (4) respiratory stability (oxygen saturation >90% with fraction of inspired oxygen [Fio_2] ≤0.4, respiratory rate <35/min, spontaneous tidal volume >5 mL/kg, ratio of respiratory rate to tidal volume <100/min per liter, and maximal inspiratory pressure >15 cm H_2O); and (5) noncopious secretions (<3 aspirations in the last 8 hours). Patients with tracheostomies or do-not-reintubate orders were excluded.

Randomization

Patients were randomized in a 1:1 ratio to one of the two weaning strategies by means of tables of computer-generated random numbers in blinded blocks of 4 patients for each center. A central administrator who was not involved in the analyses used an opaque envelope to allocate patients to receive one of the two treatments. The intervention was not blinded for the investigators or attending physicians.

Interventions

Patients randomized to undergo a highly demanding SBT underwent a 2-hour T-piece SBT; patients randomized to undergo a less demanding SBT underwent a 30-minute SBT with 8-cm H_2O PSV and zero positive end-expiratory pressure; Fio_2 remained unchanged from the mechanical ventilation period leading up to the SBT.

Before randomization, attending physicians had to decide on the extubation strategy (whether to reconnect the patient to the ventilator for 1 hour before extubation and whether to administer noninvasive ventilation or high-flow nasal cannula after extubation).

Patients who successfully completed the SBT were extubated. Arterial blood gas analysis was not required, but when it was done, the results were recorded. Physicians were also recommended to record dyspnea using the Borg Dyspnea Scale (score range, 0-10; 0 indicates no dyspnea and 10 indicates maximal dyspnea) at the beginning and at the end of SBTs and to ask patients about their confidence in their ability to sustain breathing without a ventilator.

Patients who did not tolerate the SBT were reconnected to a ventilator. Criteria for failure to tolerate the SBT were agitation, anxiety, low level of consciousness (Glasgow Coma Scale score <13), respiratory rate higher than 35/min and/or use of accessory muscles, oxygen saturation by pulse oximetry less than 90% with Fio_2 higher than 0.5, heart rate higher than 140/min or greater than a 20% increase from baseline, systolic blood pressure lower than 90 mm Hg, or development of arrhythmia. Additional SBTs were not protocolized, and mode and duration were left to the discretion of attending teams.

Respiratory failure within 72 hours of extubation was defined as the occurrence of at least 1 of the following: respiratory acidosis with pH lower than 7.32 and $Paco_2$ higher than 45 mm Hg, oxygen saturation less than 90% with Fio_2 higher than 0.5, respiratory rate higher than 35/min, low level of consciousness (Glasgow Coma Scale score <13), severe agitation,

or clinical signs of respiratory fatigue. Treatment of postextubation respiratory failure was not protocolized. When noninvasive ventilation was used, duration, maximum inspiratory and expiratory pressures, and maximum Fio_2 were recorded. When respiratory failure was treated with a high-flow nasal cannula, duration, maximum flow, and maximum Fio_2 were recorded.

Patients needing reintubation within 72 hours were not randomized again for weaning, but the need for tracheostomy and the date of final liberation from mechanical ventilation were registered.

Outcomes

The primary outcome was successful extubation, defined as remaining free of invasive mechanical ventilation 72 hours after the first SBT.

Secondary outcomes were rate of reintubation among patients who were extubated after the SBT; intensive care unit and hospital lengths of stay; and hospital and 90-day mortality.

Exploratory outcomes were time to reintubation and reasons for reintubation, incidence of tracheostomy, and use of noninvasive ventilation and high-flow nasal cannula as prophylaxis against postextubation respiratory failure and to treat it.

Post hoc outcomes were intensive care unit mortality, Borg Dyspnea Scale score at the end of the SBT, patients' confidence in their ability to breathe without the ventilator, and arterial blood analysis after successful SBT.

Statistical Analysis

Based on previous studies,[8,9] a successful extubation rate of 75% and an absolute increase in successful extubation of 7% were expected. Thus, the required sample for an α=.05 and a power of 80% was estimated to be 540 patients in each group.

A prespecified interim analysis was performed when 500 patients were enrolled. The results showed a nonsignificant difference in primary outcome between groups. For this reason, the investigators decided to complete the estimated sample enrollment.

All patients were analyzed in the group to which they were randomized using the intention-to-treat principle, with no exclusion after randomization. Patients extubated outside of protocol were analyzed as having a failed SBT. No participants were excluded from main or secondary analyses because of missing or incomplete data. Reintubation was recorded only among patients who completed the trial.

Categorical variables are presented as absolute and relative frequencies. Continuous variables are summarized as medians and interquartile ranges (IQRs) for nonnormal distributions. The Mann-Whitney *U* was used for nonparametric continuous variables. To compare categorical variables, the χ^2 test was used, except when expected frequencies in contingency tables were less than 5, in which case the Fisher exact test or the Monte Carlo method was used.

Time-to-event outcomes were analyzed with Kaplan-Meier curves and compared by log-rank test. For the time-to-event outcome of 72-hour successful extubation, deaths occurring before 72 hours were introduced in the survival analysis as censored data. Event or censored times for all patients were calculated from the time of randomization. Crude hazard ratios and 95% confidence intervals were calculated using a univariable Cox proportional regression model to estimate the effect size of randomization group. Proportionality of hazards was verified by examining Schoenfeld residual plots.

A post hoc random-effects multilevel logistic regression model was used to determine variables associated with 72-hour successful extubation, taking into account the effect of hospital. Patient characteristics that were associated with 72-hour successful extubation in the bivariable analysis were introduced in the random-effects multilevel logistic regression model as first-level variables and hospital as a second-level variable (random effect). Odds ratios (ORs) and median ORs with 95% confidence intervals were used to measure the association between each covariate and 72-hour successful extubation. The median OR is a measure of the variation between rates of 72-hour successful extubation at different hospitals that is unexplained by the modeled risk factors; it is defined as the median of the set of ORs that could be obtained by comparing 2 patients with identical patient-level characteristics from 2 randomly chosen hospitals. Covariates were introduced in the random-effects multilevel logistic regression model using a researcher-controlled backward exclusion strategy.

Post hoc analyses were performed for primary, secondary, exploratory, and post hoc outcomes among the following populations: patients extubated after the first SBT, patients extubated outside of protocol, patients treated per protocol, and several subgroups defined by baseline demographic characteristics. Effect sizes were evaluated by computing absolute risk differences with 95% confidence intervals for binary outcomes and differences in means with 95% confidence intervals for continuous outcomes. Figures were plotted for unadjusted risk ratios and 95% confidence intervals in the subgroup analysis by age; days of mechanical ventilation; Acute Physiology and Chronic Health Evaluation (APACHE) II score; chronic obstructive pulmonary disease (COPD); and medical, surgical, or trauma admission. No tests for interaction were conducted for the subgroup analyses.

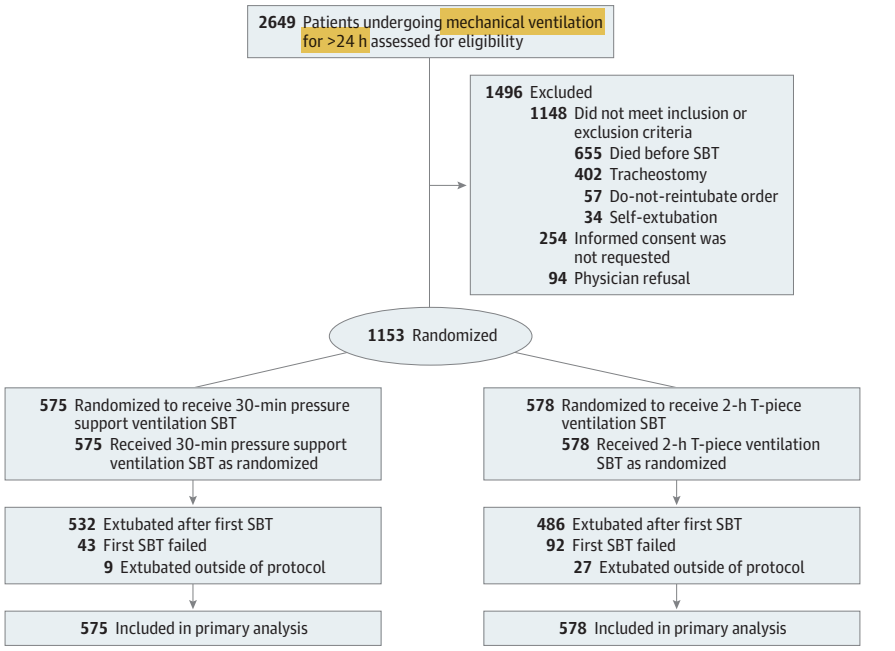
A 2-sided α=.05 was considered statistically significant. Data were analyzed using SPSS version 22 (IBM Corp) and Stata version 14 (StataCorp). Subgroup analysis graphs were generated using R version 3.5.2 (R Foundation for Statistical Computing). There was no adjustment for multiple comparisons. Therefore, the results of the subgroup analyses and the analyses for secondary and exploratory outcomes should be interpreted as exploratory.

Results

Study Participants

Figure 1 shows participant flow through the trial. During the study period, 2649 patients received mechanical ventilation for at least 24 hours in the participating intensive care units; 1501 of these fulfilled the inclusion criteria, and 1153 were included in the study; 578 patients were randomized to undergo a 2-hour T-piece SBT and 575 patients were randomized to undergo a 30-minute SBT with 8-cm H_2O PSV). The

Figure 1. Flow of Participants in a Trial of Pressure Support vs T-Piece Ventilation Strategies for SBTs



SBT indicates spontaneous breathing trial.

2 groups were similar in age, sex, APACHE II score on admission, reason for intensive care unit admission, and length of mechanical ventilation before the SBT (**Table 1**). No patients were lost to follow-up.

Primary Outcome

Successful extubation, defined as remaining free of mechanical ventilation 72 hours after the SBT, occurred in 473 patients (82.3%) in the PSV group and 428 patients (74%) in the T-piece group (difference, 8.2%; 95% CI, 3.4%-13%) (**Table 2**).

The Kaplan-Meier curves show a significant difference, with a higher successful extubation rate in the PSV group (hazard ratio, 1.54; 95% CI, 1.19-1.97; $P < .001$]) (**Figure 2**).

Secondary Outcomes

After the first SBT, 486 patients (92.5%) undergoing the 30-minute PSV SBT and 532 patients (84.1%) undergoing the 2-hour T-piece SBT were extubated (difference, 8.4%; 95% CI, 4.7%-12.1%; $P < .001$). Reintubation within 72 hours occurred in 59 patients (11.1%) in the PSV group and in 58 patients (11.9%) in the T-piece group (difference, −0.8%; 95% CI, −4.8% to −3.1%; $P = .63$) (Table 2). The median intensive care unit length of stay was 9 days (IQR, 5-17) in the PSV group and 10 days (IQR, 5-17) in the T-piece group (mean difference, −0.3 days; 95% CI, −1.7 to 1.1 days; $P = .69$). The median hospital length of stay was 24 days (IQR, 15-40) in the PSV group and 24 days (IQR, 15-39) in the T-piece group (mean difference, 1.3 days; 95% CI, −2.2 to 4.9 days; $P = .45$). Hospital mortality rates were 10.4% (n = 60) in the PSV group and 14.9% (n = 86) in the T-piece group (difference, −4.4%; 95% CI, −8.3% to −0.6%; $P = .02$) (Table 2).

Mortality at 90 days was significantly lower in the PSV group (13.2%) compared with the T-piece group (17.3%) (difference, −4.1% [95% CI, −8.2% to 0.01%; $P = .04$]; hazard ratio, 0.74 [95% CI, 0.55-0.99]) (eFigure 1 in Supplement 2).

Exploratory Outcomes

In the T-piece group, 58 patients required reintubation, and in the PSV group, 59 patients required reintubation. The median time to reintubation was 23 hours (IQR, 9-45 hours) in the PSV group and 24.5 hours (IQR, 9.8-44 hours) in the T-piece group (mean difference, 0.53 hours; 95% CI, −7.2 to 8.3 hours). Reasons for reintubation were not significantly different in the 2 groups; excessive work of breathing was the most common in both groups, followed by inability to clear secretions and hypoxemia (**Table 3**). Four patients (3 in the T-piece group and 1 in the PSV group) had cardiac arrest within 72 hours after extubation.

Among reintubated patients, tracheostomy was performed in 41 patients (7.1%) in the PSV group and in 50 patients (8.7%) in the T-piece group (difference, −1.5%; 95% CI, −4.6% to 1.6%) (Table 2).

Before randomization, physicians had to decide on an extubation strategy (standard oxygen, reconnection to the ventilator for a 1-hour rest after the SBT, and/or prophylactic noninvasive ventilation or high-flow nasal cannula after extubation). The use of each treatment was not significantly different in both groups (Table 1).

Postextubation respiratory failure occurred in 110 patients (20.7%) in the PSV group and in 103 patients (21.2%) in the T-piece group (difference, −0.5%; 95% CI, −5.5% to 4.5%). Among these 213 patients, 117 (11.4%) were reintubated. Respiratory failure was treated by noninvasive ventilation in 91 (42.7%) patients, and 36 (39.6%) of these patients were reintubated. Respiratory failure was treated by high-flow nasal cannula in 47 (22.1%) patients, and 20 (42.6%) of these patients were reintubated. The remaining 75 patients

(35.2%) received standard oxygen, and 61 (81.3%) of these patients were reintubated.

Post Hoc Analysis

In patients extubated after the first SBT, the 72-hour successful extubation rate was not significantly different between groups (eTable 1 in Supplement 2).

The post hoc analysis showed that 29 patients (5%) in the PSV group and 38 patients (6.6%) in the T-piece group died in the intensive care unit (difference, −1.5%; 95% CI, −4.5% to 1.1%).

Multilevel logistic regression found a hospital-level random effect on successful extubation (median OR, 1.56; $P < .001$). After adjustment for this random effect, the effect of the PSV persisted (adjusted OR, 1.64; 95% CI, 1.23-2.20; $P = .001$). Other patient characteristics independently associated with 72-hour successful extubation were length of mechanical ventilation before SBT (adjusted OR, 0.96; 95% CI, 0.94-0.98; $P < .001$) and COPD (adjusted OR, 0.62; 95% CI, 0.44-0.87; $P = .006$). Multilevel logistic regression did not find an association between hospital and risk of reintubation (median OR, 1.19; $P = .30$). After adjustment for this random effect, reintubation in the PSV group was not significantly different than in the T-piece group (adjusted OR, 0.92; 95% CI, 0.62-1.35; $P = .67$). The only variable independently associated with reintubation was length of mechanical ventilation before SBT (adjusted OR, 1.04; 95% CI, 1.01-1.07; $P = .03$).

A total of 36 patients (3.1%) in whom the SBT failed were extubated, either because of physician decision or self-extubation during the SBT (eTable 2 in Supplement 2). The results of the per-protocol analysis were similar to those of the intention-to-treat analysis (eAppendix and eTable 3 in Supplement 2).

Subgroup analyses were generally consistent with the overall study findings (**Figure 3**; eFigures 2 and 3 in Supplement 2). eTables 4, 5, and 6 in Supplement 2 report post hoc analyses of Borg Dyspnea Scale scores at the end of the SBT, patients' confidence in breathing without a ventilator, and blood gas analyses.

During the study, there were no severe adverse events attributable to the randomization group. The adverse events that occurred after extubation, such as difficulty managing secretions or excessive work of breathing, are inherent to critically ill patients.

Table 1. Baseline Participant Characteristics[a]

Characteristics	30-min PSV SBT (n = 575)	2-h T-Piece SBT (n = 578)
Age, median (IQR), y	65 (52-75)	63 (53-73)
Sex		
Men	352 (61.2)	373 (64.5)
Women	223 (38.8)	205 (35.5)
APACHE II score, median (IQR)[b]	16 (11-22)	16 (11-22)
Comorbidity		
Cardiovascular disease	146 (25.4)	162 (28.0)
Diabetes mellitus[c]	123 (22.0)	147 (25.8)
Chronic obstructive pulmonary disease	110 (19.1)	118 (20.4)
Neurological disease	107 (18.6)	99 (17.1)
Cancer	87 (15.1)	94 (16.3)
Renal disease	76 (13.2)	68 (11.8)
Liver disease	64 (11.1)	63 (10.9)
Reason for admission		
Medical, nonrespiratory	215 (37.4)	206 (35.6)
Medical, respiratory	189 (32.9)	190 (32.9)
Emergency surgery	105 (18.3)	113 (19.6)
Planned surgery	35 (6.1)	29 (5.0)
Trauma	31 (5)	40 (6.9)
Length of mechanical ventilation before SBT, median (IQR), d	4 (2-8)	4 (2-8)
Reconnection to ventilator before extubation[d]	145 (25.2)	158 (27.3)
Prophylactic noninvasive ventilation after extubation[d]	51 (8.9)	34 (5.9)
Prophylactic high-flow nasal cannula after extubation[d]	91 (15.8)	74 (12.8)

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; IQR, interquartile range; PSV, pressure support ventilation; SBT, spontaneous breathing trial.

[a] Data are expressed as No. (%) of participants unless otherwise indicated.

[b] Data were missing for 8 patients in the 2-hour T-piece SBT group and for 15 patients in the 30-minute PSV SBT group.

[c] The APACHE II score ranges from 0 to 71, with higher scores indicating higher mortality risk. A patient with a score of 16 has an estimated mortality risk of 25%.

[d] Attending physicians decided on the extubation strategy (reconnection to ventilator and prophylactic noninvasive ventilation or high-flow nasal cannula) prior to randomization.

Discussion

In this randomized trial of patients receiving mechanical ventilation, a 30-minute PSV-SBT resulted in a significantly higher rate of successful extubation than a 2-hour T-piece SBT without significantly increasing reintubation. The higher rate was related to more patients being extubated after the PSV-SBT, suggesting that a less demanding SBT better allows critically ill patients to demonstrated their ability to sustain breathing.

A recent meta-analysis concluded that breathing through a T piece requires the same amount of work as breathing after extubation, and the authors recommended that SBTs should be performed with T pieces because this approach better reflects the physiologic conditions after extubation.[12] Supported by anecdotal reports, physicians may be concerned that some patients who breathe comfortably with low levels of PSV and/or positive end-expiratory pressure could develop respiratory failure immediately after extubation, which might even be followed by cardiac arrest.[15] The results of this randomized trial designed to study extubation outcomes of opposing SBT strategies suggest that this concern may not be warranted. The current study found that the T-piece SBT was less well tolerated than the PSV SBT, although the work of breathing with the T piece may have been similar to breathing spontaneously. In patients who successfully completed the SBT, the reintubation rate was not significantly different in the 2 groups, and no imminent respiratory failure was observed after extubation from PSV. Moreover, the time to reintubation was about 24 hours in both groups, and the incidence of cardiac arrest was very low and even nominally higher in the T-piece group than in the PSV group.

Table 2. Primary, Secondary, Exploratory, and Post Hoc Outcomes of Patients Who Underwent a 2-Hour T-Piece SBT or a 30-Minute PSV SBT[a]

Outcomes	30-min PSV SBT (n = 575)	2-h T-Piece SBT (n = 578)	Difference, PSV SBT Minus T-Piece SBT (95% CI)[b]	*P* Value
Primary Outcome				
Successful extubation, No. (%)[c]	473 (82.3)	428 (74.0)	8.2 (3.4 to 13.0)	.001
Secondary Outcomes				
Extubation after first SBT, No. (%)	532 (92.5)	486 (84.1)	8.4 (4.7 to 12.1)	<.001
Reintubation within 72 h, No. (%)[d]	59 (11.1)	58 (11.9)	−0.8 (−4.8 to 3.1)	.63
ICU length of stay, median (IQR), d	9 (5-17)	10 (5-17)	−0.3 (−1.7 to 1.1)	.69
Hospital length of stay, median (IQR), d	24 (15-40)	24 (15-39)	1.3 (−2.2 to 4.9)	.45
Hospital mortality, No. (%)	60 (10.4)	86 (14.9)	−4.4 (−8.3 to −0.6)	.02
90-Day mortality, No. (%)	76 (13.2)	100 (17.3)	−4.1 (−8.2 to 0.01)	.04
Exploratory Outcome				
Tracheostomy, No. (%)	41 (7.1)	50 (8.7)	−1.5 (−4.6 to 1.6)	.38
Post Hoc Outcome				
ICU mortality, No. (%)	29 (5.0)	38 (6.6)	−1.5 (−4.2 to 1.1)	.26

Abbreviations: ICU, intensive care unit; IQR, interquartile range; PSV, pressure support ventilation; SBT, spontaneous breathing trial.

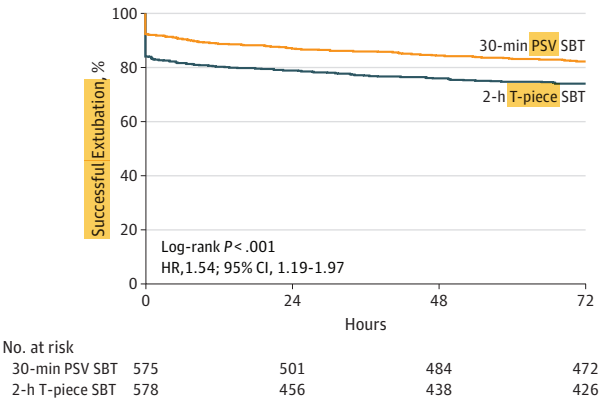
[a] No patients were lost to follow-up.

[b] Differences were calculated as absolute risk differences for successful extubation, extubated after first SBT, reintubation within 72 hours, mortality, and tracheostomy and as difference in means for length of stay.

[c] Defined as remaining free of mechanical ventilation for 72 hours after first SBT.

[d] Among patients extubated after first SBT.

Figure 2. Probability of Successful Extubation After First SBT in Each Group



PSV indicates pressure support ventilation; SBT, spontaneous breathing trial. Successful extubation was defined as remaining free of mechanical ventilation for 72 hours after first SBT.

Vallverdú et al[16] showed that among patients in whom a 2-hour T-piece SBT failed, 64% of failures occurred in the first 30 minutes, 12% between 30 and 60 minutes, and 24% between 60 minutes and 2 hours. In a recent observational study including 352 patients who underwent an SBT with PSV, Liang et al[17] sought to identify the characteristics of the 41 patients (11.6%) in whom a 120-minute SBT failed after successful completion of the first 30 minutes. Patients with SBT failures after 30 minutes were older, had more cardiopulmonary disease, had spent more time receiving mechanical ventilation before the SBT, and had undergone more previous SBTs. The authors suggested that patients with these characteristics might need a longer SBT to ensure that their ability to breathe is not overestimated. Nevertheless, it is unknown what the outcomes of these patients would have been if the SBT had been limited to 30 minutes.

In the present study, the 30-minute PSV SBT was enough to check patients' ability to breathe without increasing the rates of postextubation respiratory failure and reintubation.

Another finding related to tolerance of the 2 SBT approaches is that self-extubation during the SBT was more common in the T-piece group. Tolerance to SBTs in this trial may be compared with the studies in the late 1990s by Esteban et al[8,9]: patients' tolerance to T-piece SBTs in the present study was better than in the first trial by Esteban et al (84% vs 78%) and similar to their second trial (84.6% vs 84.1%). Moreover, tolerance to the 30-minute T-piece SBT in the second trial by Esteban et al was worse than tolerance to the 30-minute PSV in the present study (87.7% vs 92.5%). However, patients in the studies by Esteban et al received longer mechanical ventilation before the SBT, and this could contribute to worse tolerance and a higher reintubation rate.

In a single-center study comparing a 2-hour T-piece SBT and a 2-hour PSV SBT, Matić et al[18] found a higher rate of successful extubation with PSV than with a T piece (80% vs 73%), similar to the difference found in the present study despite a longer duration of the PSV SBT. This suggests that tolerance is not only about duration but also about the mode of SBT. Along the same lines, Ezingeard et al[11] found that some patients who did not tolerate a T-piece SBT went on to tolerate a PSV SBT and had a reintubation rate similar to patients who underwent a PSV SBT without having attempted a T-piece SBT. Taken together with these studies, the results of the present study suggest that a T-piece SBT is not the best way to check a patient's ability to breathe.

In this study, the reintubation rate was not significantly different between the 2 groups (about 11%), which is lower than the 17% in the first study by Esteban et al[8] and similar to the 13% in their second study.[9] Conversely, the reintubation rate was higher than in a study by Perren et al[10] (9% for short SBTs and 4% for long SBTs), but that study's single-center design and small sample size preclude direct comparison.

Table 3. Exploratory Outcomes: Reasons for Reintubation

Outcomes	30-min PSV SBT (n = 59)	2-h T-Piece SBT (n = 58)	Difference, PSV SBT Minus T-Piece SBT (95% CI)[a]
Time to reintubation, median (IQR), h	23.0 (9.0-45.0)	24.5 (9.8-44.0)	0.53 (−7.2 to 8.3)
Reasons for reintubation, No. (%)[b]			
Excessive work of breathing	23 (39.0)	24 (41.4)	−2.4 (−20.2 to 15.4)
Difficulty managing secretions	19 (32.2)	18 (31.0)	1.2 (−15.7 to 18.0)
Refractory hypoxemia	14 (23.7)	11 (19.0)	4.8 (−10.1 to 19.6)
Level of consciousness	6 (10.2)	11 (19.0)	−8.7 (−21.5 to 3.9)
Airway obstruction	6 (10.2)	8 (13.8)	−3.6 (−15.4 to 8.1)
Surgery	4 (6.8)	4 (6.9)	−0.1 (−9.2 to 9.0)
Cardiac arrest	1 (1.7)	3 (5.1)	−3.4 (−10.0 to 3.1)
Agitation	4 (6.8)	3 (5.2)	1.6 (−7.0 to 10.2)
Aspiration	1 (1.7)	3 (5.2)	−3.5 (−10.1 to 3.1)
Bradycardia (heart rate <50/min)	0	1 (1.7)	−1.7 (−5.1 to 1.6)
Hemodynamic shock	1 (1.7)	1 (1.7)	−0.0 (−4.7 to 4.7)

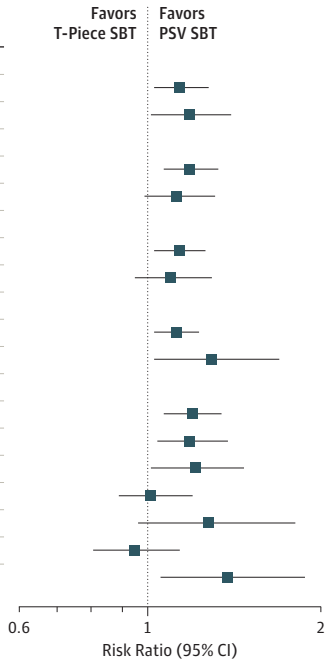
Abbreviations: IQR, interquartile range; PSV, pressure support ventilation; SBT, spontaneous breathing trial.

[a] Differences were calculated as absolute risk differences for reasons for reintubation and as difference in means for time to reintubation.

[b] Patients could have more than 1 reason for reintubation.

Figure 3. Unadjusted Risk Ratios for Successful Extubation After First SBT in Predefined Subgroups

	No./Total		
	30-min PSV SBT	2-h T-Piece SBT	Risk Ratio (95% CI)
Age, y			
≤70	306/370	289/385	1.10 (1.02-1.19)
>70	167/205	139/193	1.13 (1.01-1.26)
Length of mechanical ventilation, d			
≤4	263/304	249/326	1.13 (1.05-1.22)
>4	210/271	179/252	1.09 (0.99-1.21)
APACHE II score			
≤20	329/410	296/404	1.10 (1.02-1.18)
>20	133/164	132/174	1.07 (0.96-1.20)
COPD			
No	387/465	351/460	1.09 (1.02-1.16)
Yes	86/110	77/118	1.20 (1.02-1.41)
Patient admission type			
Medical	329/404	283/396	1.14 (1.05-1.23)
Nonrespiratory	182/215	154/206	1.13 (1.03-1.25)
Respiratory	147/189	129/190	1.15 (1.01-1.30)
Surgical	114/140	114/142	1.10 (0.91-1.14)
Planned	33/35	23/29	1.19 (0.97-1.46)
Emergency	81/105	91/113	0.96 (0.83-1.10)
Trauma	30/31	31/40	1.25 (1.04-1.49)



PSV indicates pressure support ventilation; SBT, spontaneous breathing trial; APACHE, Acute Physiology and Chronic Health Evaluation; COPD, chronic obstructive pulmonary disease. Successful extubation was defined as remaining free of mechanical ventilation for 72 hours after first SBT.

Logistic regression analysis showed that the 30-minute PSV SBT was associated with successful extubation, whereas longer duration of mechanical ventilation before the SBT as well as COPD were associated with extubation failure. However, only length of mechanical ventilation was significantly associated with reintubation. This result lends additional support to the idea that the concern that PSV SBTs increase risk of respiratory failure and reintubation may be exaggerated.

Hospital mortality and 90-day mortality were significantly higher in the T-piece group. This finding cannot be explained by the reintubation rate, days of mechanical ventilation after a failed SBT, APACHE II score at admission, or hospital length of stay, which were not significantly different between the 2 groups.

Limitations

This study has several limitations. First, prophylactic use of noninvasive ventilation and high-flow nasal cannula after extubation was not protocolized. In some cases, these approaches were routinely used based on recent studies, but in others, they were used only in patients with more comorbidities, such as heart failure or COPD, or more risk factors for

extubation failure. For this reason, it is impossible to draw conclusions about the use of noninvasive ventilation and high-flow nasal cannula for postextubation respiratory failure.

Second, patients extubated outside of protocol, although few, could be expected to influence the main results, but the sensitivity analysis ruled out such bias (eTable 2 in Supplement 2).

Third, investigators and attending physicians were not blinded to treatment randomization group.

Conclusions

Among mechanically ventilated patients, an SBT consisting of 30 minutes of PSV, compared with 2 hours of T-piece ventilation, led to significantly higher rates of successful extubation. These findings support the use of a shorter, less demanding ventilation strategy for SBTs.

ARTICLE INFORMATION

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