ORIGINAL ARTICLE

Spontaneous-Breathing Trials with Pressure-Support Ventilation or a T-Piece

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ABSTRACT

BACKGROUND

Spontaneous-breathing trials can be performed with the use of either pressure-support ventilation (PSV) or a T-piece. Whether PSV trials may result in a shorter time to tracheal extubation than T-piece trials, without resulting in a higher risk of reintubation, among patients who have a high risk of extubation failure is unknown.

METHODS

In this multicenter, open-label trial, we randomly assigned patients who had a high risk of extubation failure (i.e., were >65 years of age or had an underlying chronic cardiac or respiratory disease) to undergo spontaneous-breathing trials performed with the use of either PSV (with a pressure-support level of 8 cm of water and no positive end-expiratory pressure) or a T-piece. The primary outcome was the total time without exposure to invasive ventilation (reported as the number of ventilator-free days) at day 28 after the initial spontaneous-breathing trial. Secondary outcomes included extubation within 24 hours and extubation within 7 days after the initial spontaneous-breathing trial, as well as reintubation within 7 days after extubation.

RESULTS

A total of 969 patients (484 in the PSV group and 485 in the T-piece group) were included in the analysis. At day 28, the median number of ventilator-free days was 27 (interquartile range, 24 to 27) in the PSV group and 27 (interquartile range, 23 to 27) in the T-piece group (difference, 0 days; 95% confidence interval [CI], −0.5 to 1; P=0.31). Extubation was performed within 24 hours in 376 patients (77.7%) in the PSV group and in 350 patients (72.2%) in the T-piece group (difference, 5.5 percentage points; 95% CI, 0.01 to 10.9), and extubation was performed within 7 days in 473 patients (97.7%) and 458 patients (94.4%), respectively (difference, 3.3 percentage points; 95% CI, 0.8 to 5.9). Reintubation was performed in 72 of 481 patients (14.9%) in the PSV group and in 65 of 477 patients (13.6%) in the T-piece group (difference, 1.3 percentage points; 95% CI, −3.1 to 5.8). Cardiac or respiratory arrest was a reason for reintubation in 9 patients (3 in the PSV group and 6 in the T-piece group).

CONCLUSIONS

Among patients who had a high risk of extubation failure, spontaneous-breathing trials performed with PSV did not result in significantly more ventilator-free days at day 28 than spontaneous-breathing trials performed with a T-piece. (Supported by the French Ministry of Health; TIP-EX ClinicalTrials.gov number, NCT04227639.)

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In the intensive care unit (ICU), reducing the amount of time that patients are exposed to invasive mechanical ventilation is an important way to avoid complications. The early identification of patients who are able to breathe spontaneously on their own may hasten the time to tracheal extubation and reduce the duration of mechanical ventilation.[1,2] However, it is necessary to ensure that extubation is not associated with an increased risk of reintubation. The overall risk of reintubation in the ICU is approximately 10% but may exceed 20% among patients who have a high risk of extubation failure.[3]

To reduce the risk of reintubation, guidelines recommend systematically performing a spontaneous-breathing trial before extubation.[4] A spontaneous-breathing trial is a standard test performed to assess the patient for extubation readiness by establishing a condition that mimics the physiologic condition after extubation. Spontaneous-breathing trials can be performed with the use of a T-piece after the patient is disconnected from the ventilator or with the use of a low level of pressure-support ventilation (PSV). However, studies have suggested that the work of breathing needed during a PSV trial is markedly lower than that needed during a T-piece trial and also lower than that needed after extubation.[5] Consequently, although a PSV trial may potentially result in a shorter time to extubation, it may also result in a higher risk of reintubation because the work of breathing needed after extubation is underestimated, especially in patients who have a high risk of extubation failure.[6]

In a large clinical trial involving patients who had undergone intubation more than 24 hours earlier, the percentage of patients who underwent extubation after one spontaneous-breathing trial was higher with the use of PSV than with the use of a T-piece, and the percentage of patients who underwent reintubation did not differ significantly between the two groups.[7] However, these findings may not apply to patients who have a high risk of extubation failure. Therefore, this multicenter, randomized, controlled trial was conducted to determine whether PSV trials may result in a shorter time to extubation than T-piece trials, without resulting in a higher risk of reintubation, among patients who have a high risk of extubation failure.

Methods

Trial Design and Oversight

This multicenter, open-label, randomized, controlled trial was conducted in 31 ICUs in France. The trial was sponsored by the University Hospital of Poitiers, Poitiers, France. The trial protocol (available with the full text of this article at NEJM.org) that was used at all centers was approved by a central ethics committee and has been published previously.[8] The central ethics committee determined that an independent data and safety monitoring committee was not required because the two trial interventions are weaning strategies that are used routinely in clinical practice. Written informed consent was obtained from each patient or the next of kin before enrollment in the trial. All the authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

Trial Population

Adult patients were eligible for enrollment in the trial if they had undergone intubation more than 24 hours earlier, had a high risk of extubation failure, and were considered to be ready to undergo an initial spontaneous-breathing trial. Patients had a high risk of extubation failure if they were older than 65 years of age or had any underlying chronic cardiac or respiratory disease.[9,10] In accordance with recommendations from the International Consensus Conference on weaning,[11] patients were considered to be ready to undergo an initial spontaneous-breathing trial if they met all the following weaning criteria: a respiratory rate of 35 breaths per minute or lower; adequate oxygenation, defined as either an oxygen saturation of at least 90% (obtained during ventilation with a fraction of inspired oxygen [F_{IO_2}] of ≤40% and a positive end-expiratory pressure [PEEP] of ≤8 cm of water) or a ratio of partial pressure of arterial oxygen (Pa_{O_2}) (measured in mm Hg) to F_{IO_2} of at least 150 (obtained during ventilation with a PEEP of ≤8 cm of water); adequate cough; an awake state, defined as a score on the Richmond Agitation and Sedation Scale (RASS) of −2 to +1 (with scores ranging from −5 [most sedated] to +4 [most agitated])[12]; no use of continuous sedation; and no use of vasopressors (or use of minimal doses). Patients who had been admitted for traumatic brain injury, those

who had preexisting peripheral neuromuscular disease, and those who had a do-not-reintubate order at the time of the initial spontaneous-breathing trial were excluded. Details regarding the inclusion and exclusion criteria are provided in the Supplementary Appendix (available at NEJM.org).

RANDOMIZATION

Randomization was performed with the use of a central Web-based management system. The computer-generated random-assignment sequence was based on permuted blocks of four participants (unknown to investigators) and was stratified according to center. Patients were enrolled before the initial spontaneous-breathing trial and were randomly assigned in a 1:1 ratio to undergo spontaneous-breathing trials performed with the use of either PSV or a T-piece.

INTERVENTION

In patients who were randomly assigned to the PSV group, all spontaneous-breathing trials were to be performed with the use of PSV with a pressure-support level of 8 cm of water, an F_{IO_2} of 40% or lower, and no PEEP. In patients who were randomly assigned to the T-piece group, all spontaneous-breathing trials were to be performed with the use of a T-piece. The T-piece was connected to the end of the endotracheal tube after the tube had been disconnected from the ventilator, and additional oxygen was provided through the T-piece at a flow rate of up to 6 liters per minute, which corresponds to an F_{IO_2} of 40% or lower.[13] In both groups, spontaneous-breathing trials were to be performed for approximately 1 hour.

Failure of a spontaneous-breathing trial was defined, in accordance with the usual criteria,[11] as the occurrence of any of the following events during the trial: a respiratory rate higher than 35 breaths per minute; increased accessory-muscle activity; an oxygen saturation persistently lower than 90% while the patient was receiving oxygen with an F_{IO_2} of at least 40% or oxygen at a flow rate of at least 6 liters per minute; hemodynamic instability, defined as either a heart rate persistently higher than 140 beats per minute or a systolic blood pressure of less than 90 mg Hg or more than 180 mm Hg with signs of hypoperfusion; or depressed mental status or agitation. A spontaneous-breathing trial was considered to be successful if none of these events occurred during the trial. In both groups, when a spontaneous-breathing trial was successful, the recommendation was to perform extubation as soon as possible after the patient had been reconnected to the ventilator with the previous ventilator settings for approximately 1 hour, to avoid exhaustion.[14] When failure of a spontaneous-breathing trial occurred, spontaneous-breathing trials were to be performed on a daily basis with the use of the same strategy (either PSV or a T-piece), as long as weaning criteria were met, until a spontaneous-breathing trial was successful. The assessment for failure criteria was done by investigators, whereas the decision to perform extubation was made by treating clinicians.

All the patients were followed until day 28 after the initial spontaneous-breathing trial. After extubation, the prophylactic use of noninvasive ventilation (oxygen administered through a face mask) for at least 48 hours, as well as oxygen administered through a high-flow nasal cannula between sessions of noninvasive ventilation, was strongly encouraged in all patients.[10,15]

OUTCOMES

The primary outcome was the total time alive and without exposure to invasive mechanical ventilation (reported as the number of ventilator-free days) from the initial spontaneous-breathing trial (day 1) through day 28. This outcome was chosen because it accounts for both the time to extubation after the initial spontaneous-breathing trial (duration of weaning) and whether reintubation occurred (duration of additional mechanical ventilation).

Secondary outcomes included the following: the total time alive and without exposure to invasive or noninvasive mechanical ventilation at day 28; a successful initial spontaneous-breathing trial; the level of weaning difficulty, defined as simple weaning (extubation <24 hours after the initial spontaneous-breathing trial), difficult weaning (extubation 24 hours to 7 days after the initial spontaneous-breathing trial), or prolonged weaning (extubation >7 days after the initial spontaneous-breathing trial)[16]; the time to extubation after the initial spontaneous-breathing trial; extubation within 7 days after the initial spontaneous-breathing trial; extubation after one

spontaneous-breathing trial without reintubation within 72 hours; respiratory failure within 7 days after extubation; reintubation within 7 days after extubation; the length of the ICU stay; and death in the ICU, by day 28, and by day 90. Details regarding the criteria for the decision to perform reintubation and the criteria for respiratory failure after extubation are provided in the Supplementary Appendix.

STATISTICAL ANALYSIS

We calculated that a sample size of 900 patients would provide the trial with 80% power to show an absolute difference between the PSV group and the T-piece group in the duration of mechanical ventilation of −2 days (i.e., 2 more ventilator-free days in the PSV group than in the T-piece group) at a two-sided alpha level of 0.05. A description of the exact calculation of the sample size has been published previously.[8] However, a large number of patients were enrolled in the trial over a short period in the context of the coronavirus disease 2019 crisis. These circumstances caused some delays in trial monitoring and introduced the possibility that several patients would need to be excluded after enrollment, when each patient's inclusion and exclusion criteria were validated by a review committee whose members were unaware of the trial-group assignments. To account for such exclusions, the sample size was increased to 1000 patients at the recommendation of the ethics committee.

All the analyses were performed by the trial statistician according to a predefined statistical analysis plan, which is provided with the protocol. The analyses were performed on an intention-to-treat basis after inclusion and exclusion criteria were validated by the review committee. For the primary outcome, the number of ventilator-free days at day 28 was compared between the two trial groups with the use of the nonparametric Mann–Whitney U test. For the secondary outcomes regarding extubation, level of weaning difficulty (simple, difficult, or prolonged), respiratory failure after extubation, reintubation, and death, the percentage of patients was compared between the two groups with the use of the chi-square test. The time to extubation and the length of the ICU stay were compared between the two groups with the use of the nonparametric Mann–Whitney U test. Kaplan–Meier curves were plotted to assess the probability of extubation during the 7 days after the initial spontaneous-breathing trial and the probability of reintubation during the 7 days after extubation. The results are presented as absolute differences with 95% confidence intervals. Because of the potential for a type 1 error due to multiple comparisons, findings from analyses of secondary outcomes should be interpreted as exploratory. Missing data were sparse and were not replaced. A two-sided P value of less than 0.05 was considered to indicate statistical significance. SAS software, version 9.4 (SAS Institute), was used for all analyses.

RESULTS

TRIAL PARTICIPANTS

From January 2020 through June 2021, a total of 3975 patients in the 31 participating ICUs were considered to be ready to undergo an initial spontaneous-breathing trial. Of these patients, 1476 were eligible for inclusion in the trial, 983 underwent randomization, and 969 (484 in the PSV group and 485 in the T-piece group) were included in the analysis (Fig. 1). The characteristics of the patients at baseline were similar in the two trial groups, except for the higher percentage of women in the PSV group than in the T-piece group (Table 1). PSV trials were performed with a mean (±SD) pressure-support level of 8±1 cm of water, a mean PEEP of 0±1 cm of water, and a mean F_{IO_2} of 32±7%. T-piece trials were performed with additional oxygen administered at a mean flow rate of 4±4 liters per minute.

SPONTANEOUS-BREATHING TRIALS

All the patients underwent the initial spontaneous-breathing trial according to the trial-group assignment. Thereafter, 6 patients (1.2%) in the PSV group underwent at least one spontaneous-breathing trial performed with the use of a T-piece, and 10 patients (2.1%) in the T-piece group underwent at least one spontaneous-breathing trial performed with the use of PSV. Reasons for failure of the initial spontaneous-breathing trial are shown in Table S2 in the Supplementary Appendix.

PRIMARY AND SECONDARY OUTCOMES

At day 28, the median number of ventilator-free days was 27 (interquartile range, 24 to 27) in the PSV group and 27 (interquartile range, 23 to 27) in the T-piece group (difference, 0 days; 95%

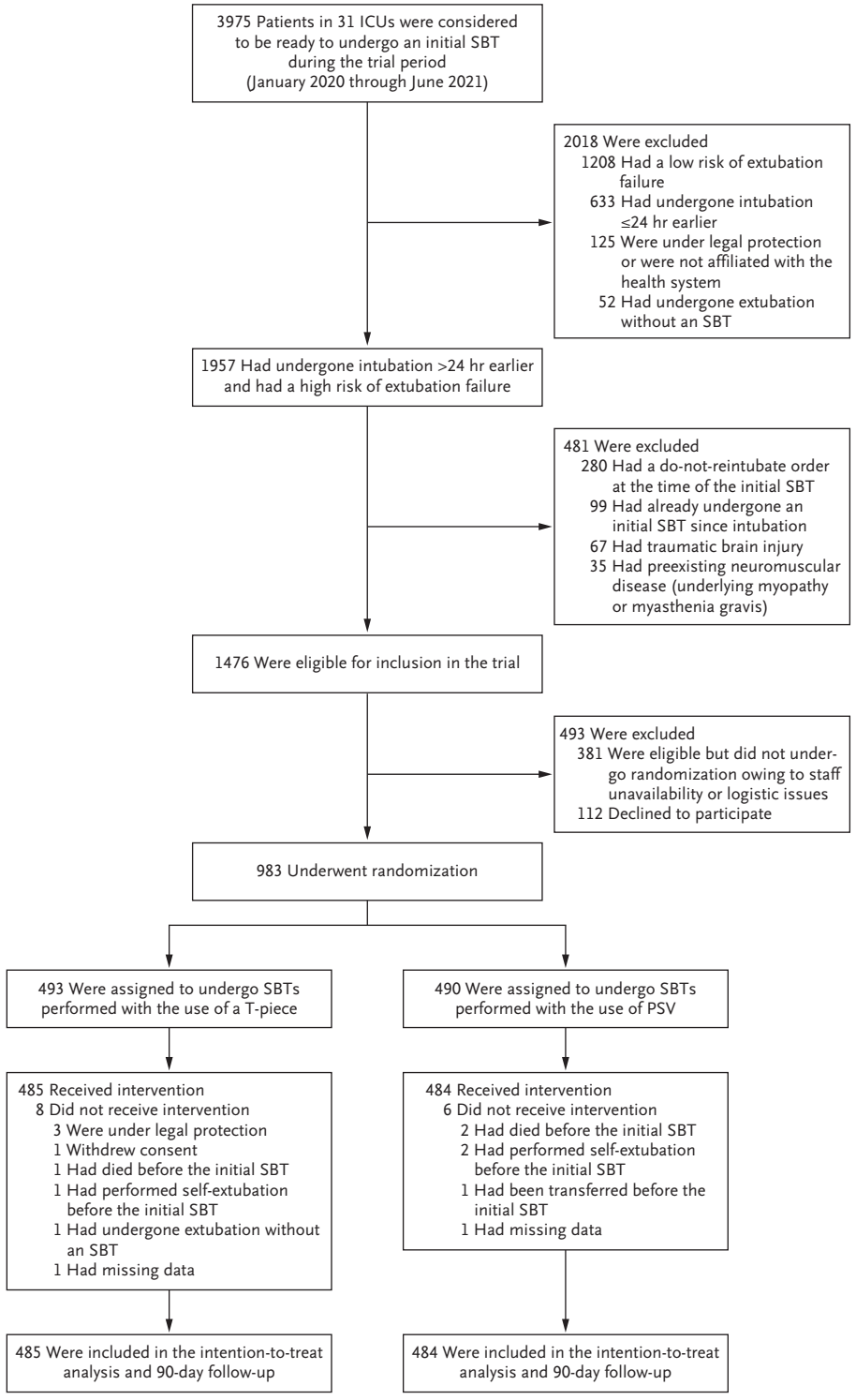

Figure 1. Enrollment, Randomization, Intervention, and Follow-up.

Patients who were under legal protection were minors, persons deprived of liberty by a judicial or administrative decision, or adults under any other legal protection. ICU denotes intensive care unit, PSV pressure-support ventilation, and SBT spontaneous-breathing trial.

Table 1. Characteristics of the Patients at Baseline.*

Variable	Pressure-Support Ventilation (N=484)	T-Piece (N=485)
At the time of admission		
Age — yr	69±9	68±9
Age >65 yr — no. (%)	356 (73.6)	335 (69.1)
Male sex — no. (%)	320 (66.1)	349 (72.0)
Body-mass index†	30±7	29±7
SAPS II‡	53±17	53±18
Underlying chronic cardiac disease — no. (%)		
Any	227 (46.9)	234 (48.2)
Ischemic heart disease	138 (28.5)	134 (27.6)
Left ventricular dysfunction	79 (16.3)	81 (16.7)
Atrial fibrillation	86 (17.8)	85 (17.5)
History of cardiogenic pulmonary edema	27 (5.6)	39 (8.0)
Underlying chronic respiratory disease — no. (%)		
Any	120 (24.8)	131 (27.0)
Chronic obstructive pulmonary disease	85 (17.6)	92 (19.0)
Obesity hypoventilation syndrome	26 (5.4)	28 (5.8)
Chronic restrictive pulmonary disease	27 (5.6)	27 (5.6)
Main reason for intubation — no. (%)		
Acute respiratory failure	283 (58.5)	287 (59.2)
Coma	74 (15.3)	63 (13.0)
Shock	23 (4.8)	33 (6.8)
Cardiac arrest	48 (9.9)	46 (9.5)
Surgery	42 (8.7)	39 (8.0)
Other reason	14 (2.9)	17 (3.5)
Covid-19 as main reason for admission — no. (%)	113 (23.3)	119 (24.5)
At the time of the initial spontaneous-breathing trial		
Median duration of mechanical ventilation (IQR) — days	6 (3–11)	6 (3–10)
SOFA score§	3.8±2.3	3.9±2.3
Median RASS score (IQR)¶	0 (0–0)	0 (0–0)
Use of vasopressors — no. (%)	44 (9.1)	58 (12.0)
Ventilator settings before the initial spontaneous-breathing trial		
Use of pressure-support ventilation — no. (%)	412 (85.1)	396 (81.6)
Pressure-support level — cm of water	9±3	9±3
Positive end-expiratory pressure — cm of water	6±2	7±2
Tidal volume — ml	482±128	482±131
Tidal volume — ml/kg	7.7±2.0	7.6±2.1
Respiratory rate — breaths/min	23±7	23±7
F_{IO_2} — %	33±9	33±8
Ratio of Pa_{O_2} (mm Hg) to F_{IO_2}	273±103	267±89
pH	7.45±0.06	7.45±0.06

Table 1. (Continued.)

Variable	Pressure-Support Ventilation (N=484)	T-Piece (N=485)
$Paco_2$ — mm Hg	38±7	39±7
Hypercapnia, with $Paco_2$ >45 mm Hg — no. (%)	64 (13.2)	74 (15.3)
Bicarbonate — mmol/liter	27±5	27±5
Lactate — mmol/liter	1.4±0.8	1.3±0.6

* Plus–minus values are means ±SD. The percentages may not total 100 because of rounding. Regarding the overall representativeness of the trial, the ethics committee does not allow the collection of information regarding characteristics of patients who are not included in a trial (i.e., patients who have not given consent); in addition, French law prohibits the collection of information regarding race or ethnic group. Additional information regarding representativeness is provided in Table S3. Covid-19 denotes coronavirus disease 2019, Fio_2 fraction of inspired oxygen, IQR interquartile range, $Paco_2$ partial pressure of arterial carbon dioxide, and Pao_2 partial pressure of arterial oxygen.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ The Simplified Acute Physiology Score (SAPS) II was calculated on the basis of 17 variables, information about previous health status, and information obtained at admission. Scores range from 0 to 163, with higher scores indicating more severe disease.
§ The Sequential Organ Failure Assessment (SOFA) score was obtained on the day of the initial spontaneous breathing trial. Scores range from 0 to 24, with higher scores indicating more severe organ failure.
¶ The Richmond Agitation and Sedation Scale (RASS) is a tool used to assess the depth of sedation on a scale of –5 to +4, with negative values indicating increased sedation, positive values indicating increased agitation, and a score of 0 indicating an alert and calm state.

confidence interval [CI], −0.5 to 1; P=0.31) (Table 2). The initial spontaneous-breathing trial was successful in 383 patients (79.1%) in the PSV group and in 348 patients (71.7%) in the T-piece group (difference, 7.4 percentage points; 95% CI, 2.0 to 12.8). Extubation was performed within 24 hours after the initial spontaneous-breathing trial (simple weaning) in 376 patients (77.7%) in the PSV group and in 350 patients (72.2%) in the T-piece group (difference, 5.5 percentage points; 95% CI, 0.01 to 10.9) (Fig. S1). Extubation was performed within 7 days after the initial spontaneous-breathing trial (simple or difficult weaning but not prolonged weaning) in 473 patients (97.7%) in the PSV group and in 458 patients (94.4%) in the T-piece group (difference, 3.3 percentage points; 95% CI, 0.8 to 5.9) (Fig. 2A). Among the patients with a successful initial spontaneous-breathing trial, the median time to extubation after the initial spontaneous-breathing trial was 2.8 hours (interquartile range, 2.0 to 4.2) in the PSV group and 2.7 hours (interquartile range, 2.0 to 3.7) in the T-piece group (difference, 0.1 hours; 95% CI, −0.1 to 0.3).

Of the 958 patients (481 in the PSV group and 477 in the T-piece group) with at least one extubation attempt in the ICU, 750 (78.3%) received prophylactic noninvasive ventilation and 388 (40.5%) received prophylactic oxygen administered through a high-flow nasal cannula after extubation (Table S1). Reintubation was performed within 7 days after extubation in 72 of 481 patients (14.9%) in the PSV group and in 65 of 477 patients (13.6%) in the T-piece group (difference, 1.3 percentage points; 95% CI, −3.1 to 5.8) (Fig. 2B). Data regarding other secondary outcomes are provided in Table 2.

SAFETY OUTCOMES

Data regarding adverse events and reasons for reintubation are provided in Table 3. Cardiac or respiratory arrest was a reason for reintubation in 9 patients (3 in the PSV group and 6 in the T-piece group).

DISCUSSION

In this multicenter, randomized, controlled trial involving 969 patients who had a high risk of extubation failure, the number of ventilator-free days at day 28 after the initial spontaneous-breathing trial did not differ significantly according to whether the spontaneous-breathing trial was performed with the use of PSV or with the use of a T-piece. Although the percentages of patients who underwent extubation within 24

Table 2. Primary and Secondary Outcomes.

Outcome	Pressure-Support Ventilation (N=484)	T-Piece (N=485)	Absolute Difference (95% CI)*	P Value
Primary outcome				
Median total time alive and without exposure to invasive ventilation at day 28 (IQR) — days	27 (24 to 27)	27 (23 to 27)	0 (–0.5 to 1)	0.31
Secondary outcomes				
Median total time alive and without exposure to invasive or noninvasive ventilation at day 28 (IQR) — days	25 (21 to 26)	25 (20 to 26)	0 (0 to 1)	—
Successful initial spontaneous-breathing trial — no. (%)	383 (79.1)	348 (71.7)	7.4 (2.0 to 12.8)	—
Level of weaning difficulty — no. (%)				—
Simple weaning: extubation <24 hr after the initial spontaneous-breathing trial	376 (77.7)	350 (72.2)	5.5 (0.01 to 10.9)	—
Difficult weaning: extubation 24 hr to 7 days after the initial spontaneous-breathing trial	97 (20.0)	108 (22.2)	–2.2 (–7.4 to 2.9)	—
Prolonged weaning: extubation >7 days after the initial spontaneous-breathing trial	11 (2.3)	27 (5.6)	–3.3 (–5.9 to –0.8)	—
Extubation ≤7 days after the initial spontaneous-breathing trial — no. (%)	473 (97.7)	458 (94.4)	3.3 (0.8 to 5.9)	—
Extubation after one spontaneous-breathing trial without reintubation within 72 hr — no. (%)	318 (65.7)	302 (62.3)	3.4 (–2.6 to 9.4)	—
Respiratory failure ≤7 days after extubation — no./total no. with at least one extubation attempt in the ICU (%)	92/481 (19.1)	75/477 (15.7)	3.4 (–1.4 to 8.2)	—
Reintubation ≤7 days after extubation — no./total no. with at least one extubation attempt in the ICU (%)	72/481 (14.9)	65/477 (13.6)	1.3 (–3.1 to 5.8)	—
Median length of the ICU stay (IQR) — days	12 (7 to 21)	11 (6 to 19)	1 (–1 to 2)	—
Death — no. (%)				
In the ICU	36 (7.4)	35 (7.2)	0.2 (–2.4 to 3.3)	—
By day 28	46 (9.5)	57 (11.7)	–2.2 (–6.2 to 1.7)	—
By day 90	80 (16.5)	91 (18.7)	–2.2 (–7.0 to 2.6)	—

* The absolute differences between percentages of patients are shown in percentage points. The 95% confidence intervals for the absolute differences between medians were estimated with the use of a 5000 bootstrap resampling technique.

hours and within 7 days after the initial spontaneous-breathing trial were higher in the PSV group than in the T-piece group, the percentage of patients who underwent reintubation within 7 days after extubation was similar in the two trial groups.

These findings are consistent with the results of previous clinical trials.[7,17-19] Although some previous studies have suggested that the work of breathing needed during PSV trials may be lower than that needed during T-piece trials,[5,20] our primary analysis showed no significant difference between these two strategies with respect to the number of ventilator-free days after the initial spontaneous-breathing trial.

Previous trials have used extubation after one spontaneous-breathing trial without reintubation within 48 hours or 72 hours as the primary outcome.[7,17,21] However, patients in whom the initial spontaneous-breathing trial failed were not monitored through extubation, so the findings apply only to patients who have simple weaning and not to patients who have difficult or prolonged weaning. Moreover, 48 hours and 72 hours may be premature time points for assessing reintubation, particularly when the patients have received prophylactic noninvasive ventilation, which is recommended for those who have a high risk of extubation failure and was provided in our trial.[15,22]

In the randomized clinical trial conducted by Subirà et al., which involved 1153 patients, the

percentage of patients who underwent extubation after one spontaneous-breathing trial was higher with the use of PSV than with the use of a T-piece, and the risk of reintubation did not differ significantly between the two groups.[7] In our trial, the percentage of patients who had undergone extubation after one spontaneous-breathing trial and had not undergone reintubation within 72 hours did not seem to differ substantially between the PSV group and the T-piece group. However, Subirà et al. compared a PSV trial performed for 30 minutes with a T-piece trial performed for 2 hours; this aspect of the trial design might explain the higher percentage of patients who had a successful initial spontaneous-breathing trial and the shorter time to extubation in the PSV group than in the T-piece group in their trial.

In addition, spontaneous-breathing trials performed with the use of PSV may underestimate the work of breathing needed after extubation and therefore may be associated with an increased risk of reintubation, particularly among patients who have a high risk of extubation failure.[6] Although previous large-scale clinical trials had shown that the risk of reintubation was no higher in the PSV group than in the T-piece group,[7,17] these findings needed to be confirmed among patients specifically identified as having a high risk of extubation failure. In our trial, the percentage of patients who underwent reintubation was less than 15% in both groups. These percentages are lower than those usually reported for patients at high risk,[23-25] which could be explained by the fact that nearly 80% of the patients received prophylactic noninvasive ventilation after extubation, an approach that has been shown to be effective in preventing reintubation.[10,15,22,26]

Our trial had some limitations. First, given the characteristics of the two strategies under evaluation, a double-blind trial design was not possible. However, the percentage of patients with difficult or prolonged weaning in our trial is consistent with percentages observed in previous studies (ranging from 20 to 30%),[16,27] which reinforces the external validity of our trial. Second, although the PSV strategy may have resulted in a shorter time to extubation than the T-piece strategy without resulting in a higher risk of reintubation, it did not increase the total time without exposure to invasive mechanical ventilation (i.e., it was not associated with a higher number of ventilator-free days). Thus, alternative outcome measures may be helpful in assessing these strategies for determining extu-

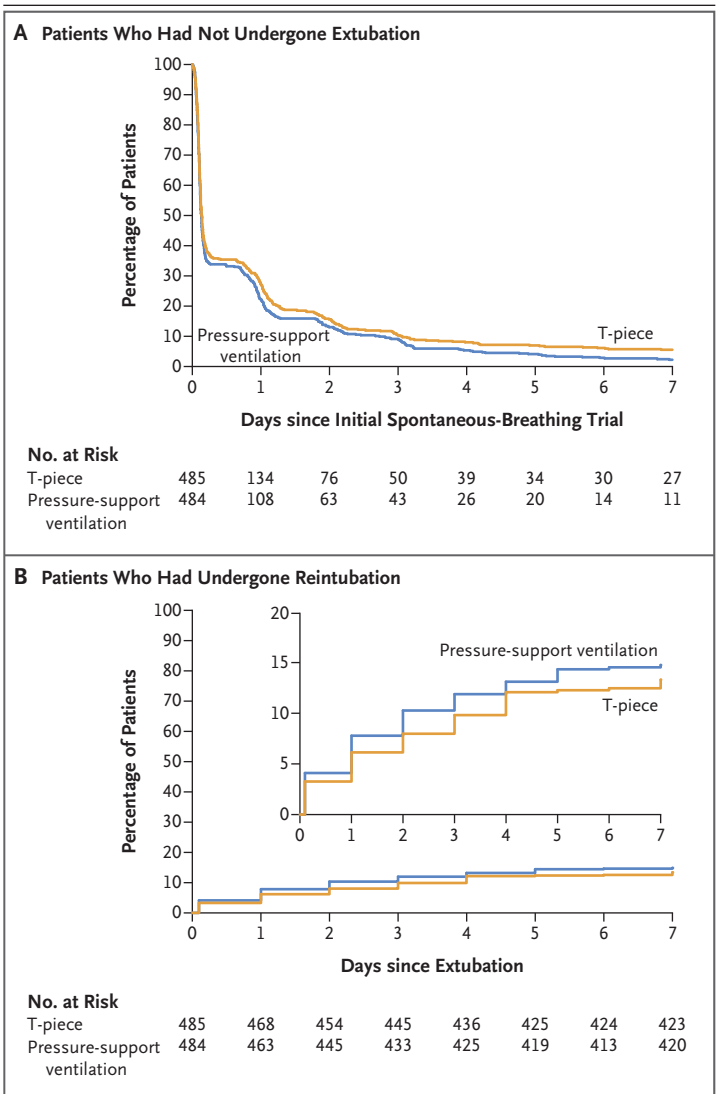

Figure 2. Kaplan–Meier Analysis of Time to Extubation and Risk of Reintubation after Spontaneous-Breathing Trials.

Panel A shows the probability that patients would undergo extubation during the 7 days after the initial spontaneous-breathing trial. Extubation was performed within 7 days in 473 patients (97.7%) in the pressure-support ventilation (PSV) group and in 458 patients (94.4%) in the T-piece group (difference, 3.3 percentage points; 95% confidence interval [CI], 0.8 to 5.9). Panel B shows the probability that patients with at least one extubation attempt in the intensive care unit would undergo reintubation during the 7 days after extubation. Reintubation was performed within 7 days in 72 of 481 patients (14.9%) in the PSV group and in 65 of 477 patients (13.6%) in the T-piece group (difference, 1.3 percentage points; 95% CI, −3.1 to 5.8). The inset shows the data on an enlarged y axis.

Table 3. Adverse Events and Reasons for Reintubation.

Event or Reason	Pressure-Support Ventilation (N=484)	T-Piece (N=485)	P Value
Death without an extubation attempt — no. of patients (%)	2 (0.4)	5 (1.0)	0.45
Adverse event after extubation — no. of patients (%)			
Upper-airway obstruction	25 (5.2)	22 (4.5)	0.65
Cardiogenic pulmonary edema	18 (3.7)	12 (2.5)	0.26
Cardiac arrest	3 (0.6)	6 (1.2)	0.31
Reintubation in the ICU — no. of patients (%)	78 (16.1)	71 (14.6)	0.52
Reason for reintubation — no. of patients/total no. (%)*			
Upper-airway obstruction	13/78 (16.7)	11/71 (15.5)	0.82
Cardiogenic pulmonary edema	8/78 (10.3)	6/71 (8.5)	0.69
Aspiration	5/78 (6.4)	8/71 (11.3)	0.31
Pneumonia	8/78 (10.3)	12/71 (16.9)	0.25
Atelectasis	10/78 (12.8)	4/71 (5.6)	0.13
Pleural effusion	3/78 (3.8)	1/71 (1.4)	0.62
Copious secretions	28/78 (35.9)	22/71 (31.0)	0.49
Ineffective cough	21/78 (26.9)	13/71 (18.3)	0.19
Weakness of respiratory muscles	17/78 (21.8)	14/71 (19.7)	0.72
Alveolar hypoventilation	6/78 (7.7)	5/71 (7.0)	0.86
Hypercapnic coma	7/78 (9.0)	0	0.01
Septic shock	5/78 (6.4)	4/71 (5.6)	0.99
Cardiogenic shock	1/78 (1.3)	1/71 (1.4)	0.99
Hemorrhagic shock	1/78 (1.3)	2/71 (2.8)	0.61
Indication for surgery	6/78 (7.7)	8/71 (11.3)	0.47
Cardiac or respiratory arrest	3/78 (3.8)	6/71 (8.5)	0.31

* Each patient may have had several reasons for reintubation.

bation readiness. Third, although the median RASS score at the time of the initial spontaneous-breathing trial indicates that the patients were alert and calm in both the PSV group and the T-piece group, specific information regarding sedation use was not collected in this trial. Finally, most patients received prophylactic noninvasive ventilation after extubation, and our results might not be generalizable to patients in ICUs in which this is not a routine practice.

Among patients who had a high risk of extubation failure, spontaneous-breathing trials performed with the use of PSV did not result in significantly more ventilator-free days at day 28 than spontaneous-breathing trials performed with the use of a T-piece.

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APPENDIX

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REFERENCES

1. Ely EW, Baker AM, Dunagan DP, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 1996;335:1864-9.

2. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet 2008;371:126-34.

3. Thille AW, Richard J-CM, Brochard L. The decision to extubate in the intensive care unit. Am J Respir Crit Care Med 2013; 187:1294-302.

4. Schmidt GA, Girard TD, Kress JP, et al. Official executive summary of an American Thoracic Society/American College of Chest Physicians clinical practice guideline: liberation from mechanical ventilation in critically ill adults. Am J Respir Crit Care Med 2017;195:115-9.

5. Sklar MC, Burns K, Rittayamai N, et al. Effort to breathe with various spontaneous breathing trial techniques: a physiologic meta-analysis. Am J Respir Crit Care Med 2017;195:1477-85.

6. Tobin MJ. Extubation and the myth of "minimal ventilator settings." Am J Respir Crit Care Med 2012;185:349-50.

7. Subirà C, Hernández G, Vázquez A, et al. 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. JAMA 2019;321:2175-82.

8. Thille AW, Coudroy R, Gacouin A, et al. T-piece versus pressure-support ventilation for spontaneous breathing trials before extubation in patients at high risk of reintubation: protocol for a multicentre, randomised controlled trial (TIP-EX). BMJ Open 2020;10(11):e042619.

9. Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L. Outcomes of extubation failure in medical intensive care unit patients. Crit Care Med 2011;39: 2612-8.

10. Thille AW, Muller G, Gacouin A, et al. Effect of postextubation high-flow nasal oxygen with noninvasive ventilation vs high-flow nasal oxygen alone on reintubation among patients at high risk of extubation failure: a randomized clinical trial. JAMA 2019;322:1465-75.

11. Boles J-M, Bion J, Connors A, et al. Weaning from mechanical ventilation. Eur Respir J 2007;29:1033-56.

12. Ely EW, Truman B, Shintani A, et al. Monitoring sedation status over time in ICU patients: reliability and validity of the Richmond Agitation-Sedation Scale (RASS). JAMA 2003;289:2983-91.

13. Coudroy R, Frat J-P, Girault C, Thille AW. Reliability of methods to estimate the fraction of inspired oxygen in patients with acute respiratory failure breathing through non-rebreather reservoir bag oxygen mask. Thorax 2020;75:805-7.

14. Fernandez MM, González-Castro A, Magret M, et al. Reconnection to mechanical ventilation for 1 h after a successful spontaneous breathing trial reduces reintubation in critically ill patients: a multicenter randomized controlled trial. Intensive Care Med 2017;43:1660-7.

15. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J 2017; 50(2):1602426.

16. Béduneau G, Pham T, Schortgen F, et al. Epidemiology of weaning outcome according to a new definition: the WIND Study. Am J Respir Crit Care Med 2017; 195:772-83.

17. Esteban A, Alía I, Gordo F, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. Am J Respir Crit Care Med 1997;156:459-65.

18. Matić I, Majerić-Kogler V. Comparison of pressure support and T-tube weaning from mechanical ventilation: randomized prospective study. Croat Med J 2004;45:162-6.

19. Ezingeard E, Diconne E, Guyomarc'h S, et al. Weaning from mechanical ventilation with pressure support in patients failing a T-tube trial of spontaneous breathing. Intensive Care Med 2006;32: 165-9.

20. Cabello B, Thille AW, Roche-Campo F, Brochard L, Gómez FJ, Mancebo J. Physiological comparison of three spontaneous breathing trials in difficult-to-wean patients. Intensive Care Med 2010; 36:1171-9.

21. Esteban A, Alía I, Tobin MJ, et al. Effect of spontaneous breathing trial duration on outcome of attempts to discontinue mechanical ventilation. Am J

Respir Crit Care Med 1999;159:512-8.
22. Oczkowski S, Ergan B, Bos L, et al. ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. Eur Respir J 2022;59(4):2101574.
23. Thille AW, Cortés-Puch I, Esteban A. Weaning from the ventilator and extubation in ICU. Curr Opin Crit Care 2013;19:57-64.
24. Hernández G, Vaquero C, Colinas L, et al. Effect of postextubation high-flow nasal cannula vs noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: a randomized clinical trial. JAMA 2016;316:1565-74.
25. Hernández G, Vaquero C, González P, et al. Effect of postextubation high-flow nasal cannula vs conventional oxygen therapy on reintubation in low-risk patients: a randomized clinical trial. JAMA 2016;315:1354-61.
26. Nava S, Gregoretti C, Fanfulla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. Crit Care Med 2005;33:2465-70.
27. Peñuelas O, Frutos-Vivar F, Fernández C, et al. Characteristics and outcomes of ventilated patients according to time to liberation from mechanical ventilation. Am J Respir Crit Care Med 2011;184:430-7.