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► **To cite this version:**

Arnaud Thille, Arnaud Gacouin, Rémi Coudroy, Stephan Ehrmann, Jean-Pierre Quenot, et al.. Spontaneous-Breathing Trials with Pressure-Support Ventilation or a T-Piece. *New England Journal of Medicine*, 2022, 387 (20), pp.1843-1854. 10.1056/NEJMoa2209041 . hal-03857047

HAL Id: hal-03857047

<https://hal.science/hal-03857047>

Submitted on 17 Nov 2022

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

A.W. Thille, A. Gacouin, R. Coudroy, S. Ehrmann, J.-P. Quenot, M.-A. Nay, C. Guitton, D. Contou, G. Labro, J. Reignier, G. Pradel, G. Beduneau, L. Dangers, C. Saccheri, G. Prat, G. Lacave, N. Sedillot, N. Terzi, B. La Combe, J.-P. Mira, A. Romen, M.-A. Azais, A. Rouzé, J. Devaquet, A. Delbove, M. Dres, J. Bourenne, A. Lautrette, J. de Keizer, S. Ragot, and J.-P. Frat, for the REVA Research Network*

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.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Thille can be contacted at aw.thille@gmail.com or at Médecine Intensive Réanimation, Centre Hospitalier Universitaire de Poitiers, 2 Rue la Milétrie, 86021 Poitiers CEDEX, France.

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.

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 [FiO_2] of $\leq 40\%$ and a positive end-expiratory pressure [PEEP] of ≤ 8 cm of water) or a ratio of partial pressure of arterial oxygen (PaO_2) (measured in mm Hg) to FiO_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 FIO_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 FIO_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 FIO_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 spontane-

ous-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 (\pm SD) pressure-support level of 8 ± 1 cm of water, a mean PEEP of 0 ± 1 cm of water, and a mean FI_{O_2} of $32\pm 7\%$. 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%

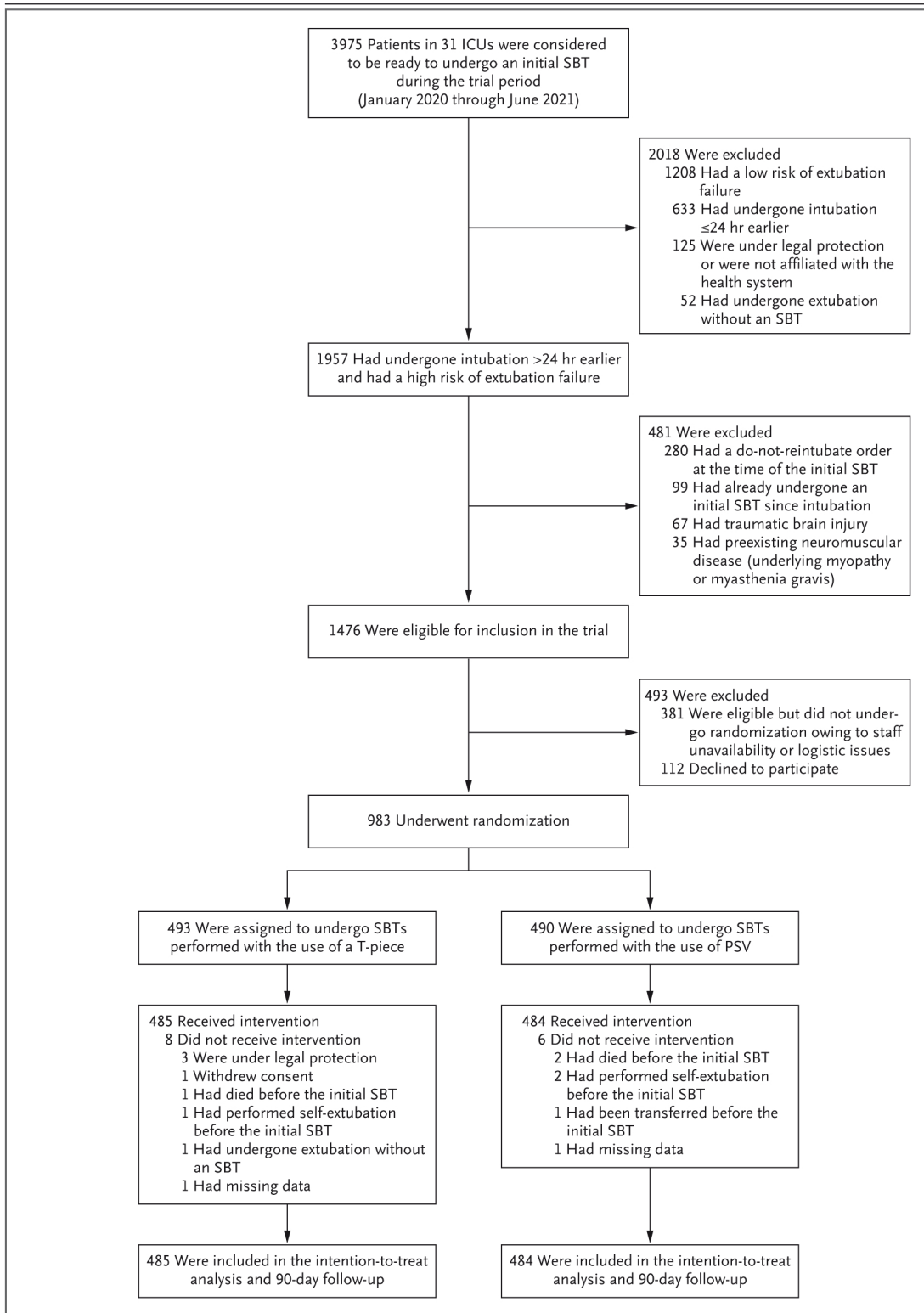


Figure 1. Enrollment, Randomization, Intervention, and Follow-up.

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
FiO ₂ — %	33±9	33±8
Ratio of Pao ₂ (mm Hg) to FiO 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, Fio₂ fraction of inspired oxygen, IQR interquartile range, Paco₂ partial pressure of arterial carbon dioxide, and Pao₂ 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

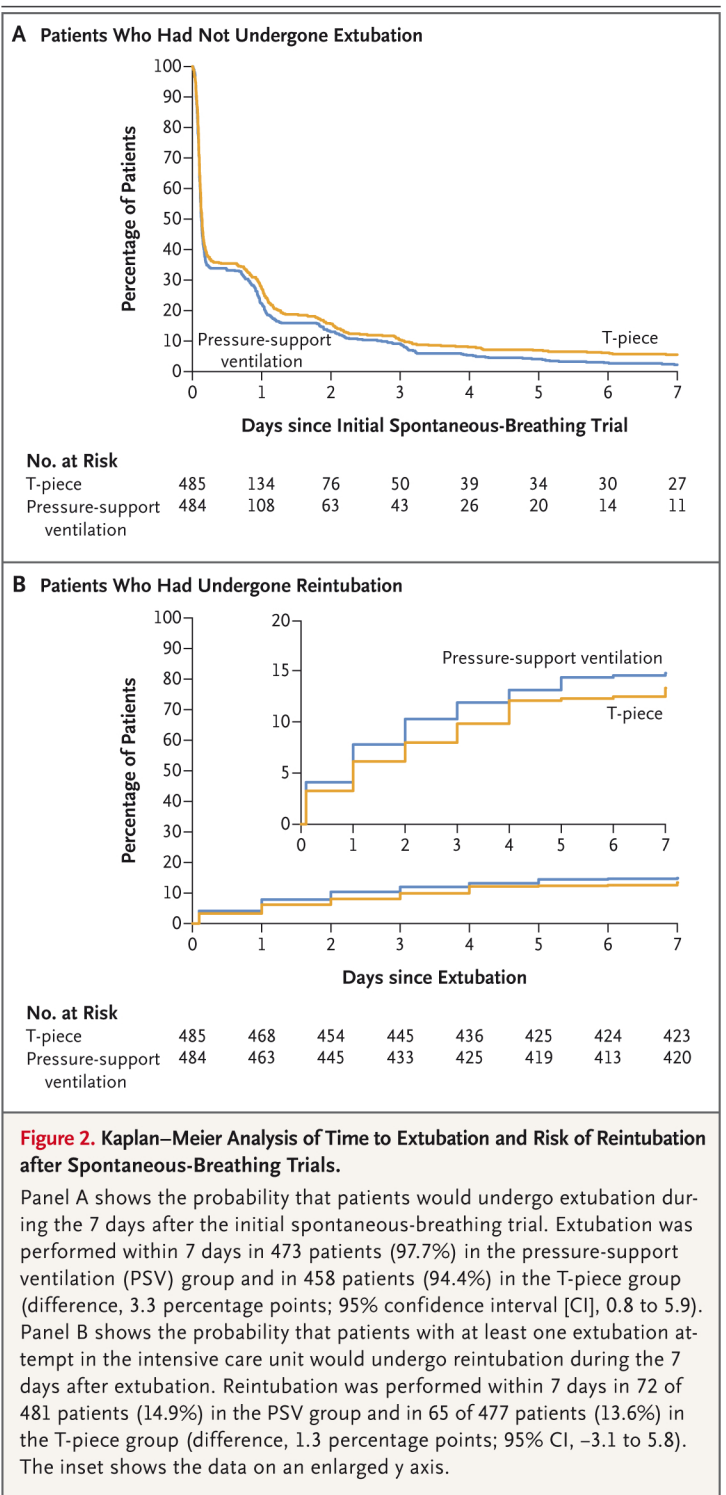
spontaneous-breathing trial without reintubation within 48 hours or 72 hours as the primary outcome.^{7,17,21} However, patients in whom the initial spontaneous-breathing trial failed were not monitored through extubation, so the findings apply only to patients who have simple weaning and not to patients 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-

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 per-

formed 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.

Supported by a grant (18-007) from the Programme Hospitalier de Recherche Clinique National 2018 of the French Ministry of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

We thank Jeffrey Arsham, an American translator who is employed by the University Hospital of Poitiers, for reviewing and editing an earlier draft of the manuscript.

APPENDIX

The authors' full names and academic degrees are as follows: Arnaud W. Thille, M.D., Ph.D., Arnaud Gacouin, M.D., Rémi Coudroy, M.D., Ph.D., Stephan Ehrmann, M.D., Ph.D., Jean-Pierre Quenot, M.D., Ph.D., Mai-Anh Nay, M.D., Christophe Guitton, M.D., Damien Contou, M.D., Guylaine Labro, M.D., Jean Reignier, M.D., Ph.D., Gael Pradel, M.D., Gaëtan Beduneau, M.D., Laurence Dangers, M.D., Clement Saccheri, M.D., Gwénaél Prat, M.D., Guillaume Lacave, M.D., Nicholas Sedillot, M.D., Nicolas Terzi, M.D., Ph.D., Béatrice La Combe, M.D., Jean-Paul Mira, M.D., Ph.D., Antoine Romen, M.D., Marie-Ange Azais, M.D., Anahita Rouzé, M.D., Jérôme Devaquet,

M.D., Agathe Delbove, M.D., Martin Dres, M.D., Ph.D., Jeremy Bourenne, M.D., Alexandre Lautrette, M.D., Ph.D., Joe de Keizer, Ph.D., Stéphanie Ragot, Pharm.D., Ph.D., and Jean-Pierre Frat, M.D., Ph.D.

The authors' affiliations are as follows: Centre Hospitalier Universitaire (CHU) de Poitiers, Médecine Intensive Réanimation (A.W.T., R.C., J.-P.F.), and Institut National de la Santé et de la Recherche Médicale (INSERM) Centre d'Investigation Clinique (CIC) 1402, Investigations of Sleep, Acute Lung Injury, and Ventilation (IS-ALIVE), Université de Poitiers (A.W.T., R.C., J.K., S.R., J.-P.F.), Poitiers, CHU de Rennes, Hôpital Pontchaillou, Service des Maladies Infectieuses et Réanimation Médicale, Rennes (A.G.), Centre Hospitalier Régional Universitaire de Tours, Médecine Intensive Réanimation, INSERM CIC 1415, Critical Research in Intensive Care and Sepsis-TriggerSep Research Network, and Centre d'Etude des Pathologies Respiratoires, INSERM U1100, Université de Tours, Tours (S.E.), CHU Dijon Bourgogne, Médecine Intensive Réanimation, INSERM CIC 1432, Université de Bourgogne Franche-Comté, Dijon (J.-P.Q.), Centre Hospitalier Régional d'Orléans, Médecine Intensive Réanimation, Orléans (M.-A.N.), Centre Hospitalier du Mans, Réanimation Médico-Chirurgicale, Le Mans (C.G.), Centre Hospitalier Victor Dupouy, Réanimation Polyvalente et Unité de Surveillance Continue, Argenteuil (D.C.), Groupe Hospitalier Régional Mulhouse Sud Alsace, site Emile Muller, Service de Réanimation Médicale, Mulhouse (G. Labro), CHU de Nantes, Médecine Intensive Réanimation, Nantes (J.R.), Centre Hospitalier Henri Mondor d'Aurillac, Service de Réanimation, Aurillac (G. Pradel), CHU de Rouen, Hôpital Charles Nicolle, Département de Réanimation Médicale, Normandie Université, Université de Rouen UR3830, Rouen (G.B.), CHU Félix Guyon, Service de Réanimation Polyvalente, Saint Denis de la Réunion (L.D.), CHU de Nice, Réanimation Médicale Archet 1, UR2CA-Unité de Recherche Clinique Côte d'Azur, Université Côte d'Azur, Nice (C.S.), CHU de Brest, Médecine Intensive Réanimation, Brest (G. Prat), Centre Hospitalier de Versailles, Service de Réanimation Médico-Chirurgicale, Le Chesnay (G. Lacave), Centre Hospitalier Fleuryat de Bourg-en-Bresse, Réanimation Polyvalente, Bourg-en-Bresse (N.S.), CHU Grenoble Alpes, Médecine Intensive Réanimation, INSERM U1042, HP2, Université Grenoble Alpes, Grenoble (N.T.), Centre Hospitalier Bretagne Sud, Réanimation Polyvalente, Lorient (B.L.C.), Assistance Publique-Hôpitaux de Paris (AP-HP), Groupe Hospitalier Paris Centre, Hôpital Cochin, Médecine Intensive Réanimation, Université Paris Cité, Institut Cochin, Centre National de la Recherche Scientifique (CNRS) Unité Mixte de Recherche (UMR) 8104, INSERM U1016 (J.-P.M.), and AP-HP, Groupe Hospitalier Universitaire AP-HP-Sorbonne Université, site Pitié-Salpêtrière, Service de Médecine Intensive-Réanimation, Département R3S (M.D.), Paris, Centre Hospitalier de Pau, Service de Réanimation, Pau (A. Romen), Centre Hospitalier Départemental de Vendée, Médecine Intensive Réanimation, La Roche Sur Yon (M.-A.A.), CHU de Lille, Médecine Intensive Réanimation, CNRS UMR 8576, INSERM U1285, Université de Lille, Lille (A. Rouzé), Hôpital Foch, Service de Réanimation Polyvalente, Suresnes (J.D.), Centre Hospitalier Bretagne Atlantique, Réanimation Polyvalente, Vannes (A.D.), Assistance Publique-Hôpitaux de Marseille, CHU La Timone 2, Médecine Intensive Réanimation, Réanimation des Urgences, Aix-Marseille Université, Marseille (J.B.), and Centre Jean Perrin, Unicancer, Service de Réanimation, Clermont-Ferrand (A.L.) — all in France.

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