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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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 significantly greater among those who received 30 minutes of pressure support ventilation (82.3%) compared with those received 2 hours of T-piece ventilation (74%).

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

ABSTRACT

IMPORTANCE: Daily spontaneous breathing trial (SBT) 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 a spontaneous breathing trial (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 involving 1153 adults deemed ready for weaning after>24 hours of mechanical ventilation in 18 Spanish intensive care units (ICU) and conducted January 2016-April 2017 (follow-up until July 2017).

INTERVENTIONS: Patients were randomized to undergo a 2-hour T-piece SBT (n=578) or a 30-minute SBT with 8 cmH2O pressure support ventilation (PSV) (n=557).

MAIN OUTCOME AND MEASURES: Primary outcome was successful extubation (remaining free of mechanical ventilation 72h after first SBT). Secondary outcomes were reintubation among those extubated after SBT; ICU and hospital lengths of stay; hospital and 90-day mortality.

RESULTS: Among 1153 patients who were randomized (mean [SD] age, 62.2 [15.7]; 428 (37.1%) women) 1018 (88.3%) completed the trial. Successful extubation occurred in 473 patients (82.3%) in the PSV group and 428 patients (74.0%) in the T-piece group (difference 8.2% [95%CI: 3.4% - 13.0%]; p=0.001). Secondary outcomes in the PSV group vs T-piece group were reintubation 11.1% vs 11.9% (difference, -0.8% [95% CI, -4.8% to 3.2%]; p=0.63); median ICU length of stay 9 vs 10 days (difference, -0.3 days

[95% CI, -1.7 - 1.1 days]; p=0.69); median hospital length of stay 24 vs 24 days (difference, 1.3 days [95% CI, -2.2 - 4.9]; p=0.45); hospital mortality 10.4% vs 14.9% (difference, -4.4% [95%CI, -8.3% - -0.6%]; p=0.02); and 90-day mortality 13.2% vs 17.3% (difference, -4.1% [95%CI, -8.2% - 0.01%]; hazard ratio, 0.74 [95%CI, 0.55 - 0.99]; p=0.04).

CONCLUSIONS AND RELEVANCE: Among patients receiving mechanical ventilation, a spontaneous breathing trial 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 spontaneous breathing trials.

INTRODUCTION

Among patients receiving mechanical ventilation, rediness for extubation and liberation from ventilatory support is evaluated with spontaneous breathing trial (SBT)(1). Daily screening of respiratory function by spontaneous breathing trial (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 and pressure support ventilation (PSV), lasting between 30 minutes and 2 hours(5)(6)(7).There are no differences in the rate of successful extubation between 2-h PSV versus2-h T-piece(8), between T-piece for30 minutes versus 2 hours(9), or between PSV for 30 minutes versus 2 hours(10).Whereas shorter SBTs are better tolerated, there is no evidence that they result in higher successful extubation rate(9)(10). Some patients who failed a T-piece SBT 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 PSVSBTs 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, two weaning strategies were compared: an approach that is more demanding for

patients, T-piece SBT for 2 hours, versus an approach that is less demanding for patients, 8 cmH_2O PSV for 30 minutes.

METHODS

From January 2016 through April 2017, a multicenter randomized clinical trial was conducted in 18 Spanish ICUs. Each hospital's ethics committee approved the study, and all patients or their relatives provided written informed consent. Supplement 1 reports the study protocol.

Patients≥18 years old undergoing mechanical ventilation≥ 24 hours who fulfilled the weaning criteria were eligible. The weaning criteria were a) the resolution or improvement of the condition leading to intubation; b) hemodynamic stability, defined as systolic blood pressure (SBP) between 90 and 160 mmHg and heart rate <140 beats per minute without vasopressors or with low doses of vasopressors; c) Glasgow Coma Scale (GCS) score > 13; d) respiratory stability (oxygen saturation (SaO2) >90% with FiO2 ≤ 0.4, respiratory rate (RR) <35 breaths per minute, spontaneous tidal volume (Vt) >5 ml/kg, ratio of RR to Vt (f/Vt ratio) <100 breaths per minute/l, and maximal inspiratory pressure >15 cmH_2O); and e) non-copious 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 did a 2-hour T-piece SBT; patients randomized to undergo a less demanding SBT performed a 30-minute SBT with 8 cmH_2O PSV and zero PEEP; 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 1h 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 registered. Physicians were also recommended to register the Borg Dyspnea Scale (ranges from 0 to 10, where 0 means “nothing at all”, and 10 means “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 the ventilator.

Patients who did not tolerate the SBT were reconnected to the ventilator. Criteria for failure to tolerate the SBT were agitation, anxiety, low level of consciousness (GCS < 13), RR >35 breaths per minute and/or use of accessory muscles, SpO2 <90% with FiO2 > 0.5, HR > 140 beats per minute or >20% increase from baseline, SBP < 90 mmHg, or development of arrhythmia. Additional SBTs were not protocolized and mode and duration were left to the discretion of the attending team.

Respiratory failure within 72 hours of extubation was defined as the occurrence of at least one of the following: respiratory acidosis with pH < 7.32 and $PaCO_2$ > 45 mmHg, SaO_2 <90% with FiO_2 > 0.5, RR> 35 breaths per minute, low level of consciousness (GCS <13), severe agitation, or clinical signs of respiratory fatigue. Treatment of postextubation failure was not protocolized. When noninvasive ventilation was used, duration, maximum inspiratory and expiratory pressures, and maximum FiO_2 were recorded. When failure was treated with 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

Primary outcome

The primary outcome was successful extubation defined as remaining without invasive mechanical ventilation 72 hours after the first SBT.

Secondary outcomes

Secondary outcomes were the rate of reintubation among the patients who were extubated after the SBT; length of ICU and hospital stays; hospital, and 90-day mortality.

Exploratory outcomes

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

The post hoc outcomes were: ICU mortality, Borg Dyspnea Scale 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 alpha of 0.05 and a power of 80% was estimated at 540 patients in each group.

A pre-specified interim analysis was done when 500 patients were enrolled. The results showed a non-significant difference in primary outcome between groups. For this reason, the investigators decided to complete the estimated sample.

All patients were analyzed in the group allocated by randomization using the intention-to-treat principle, with no exclusion after randomization. Patients extubated out of protocol were analyzed as failed SBT. No participants were excluded from main or secondary analyses because of missing or incomplete data. Only reintubation was calculated among patients who completed the trial.

Categorical variables are presented as absolute and relative frequencies. Continuous variables are summarized as medians and interquartile range (25th and 75th percentiles) for non-normal distributions. The Mann-Whitney U was used for non-parametric continuous variables. To compare categorical variables, the chi-square test was used, except when expected

196 frequencies in contingency tables were less than five, in which case Fisher's exact test or the
197 Monte Carlo method was used.

198 Time-to-event outcomes were analyzed with Kaplan-Meier curves and compared by log-rank
199 test. For the time-to-event outcome "72-hour successful extubation", deaths occurring before
200 72 hours were introduced in the survival analysis as censored data. Event or censored times
201 for all patients were calculated from the time of randomization. Crude hazard ratios (HR) and
202 confidence interval (95% CI) were calculated using a univariable Cox proportional regression
203 model to estimate the effect size of allocation group. Proportionality of hazards was verified by
204 examining Schoenfeld residual plots.

205 A post-hoc random-effects multilevel logistic regression model was used to determine
206 variables associated with 72-hour successful extubation taking into account the effect of the
207 hospital. The patient characteristics that were associated with 72-hour successful extubation in
208 the bivariable analysis were introduced in the random-effects multilevel logistic regression
209 model as first-level variables and hospital as a second-level variable (random effect). Odds
210 ratios (OR) and median odds ratios (MOR) with 95% confidence intervals were used to
211 measure the association between each covariate and 72-hour successful extubation. The MOR
212 is a measure of the variation between the rates of 72-hour successful extubation at different
213 hospitals that is unexplained by the modeled risk factors; it is defined as the median of the set
214 of odds ratios that could be obtained by comparing two patients with identical patient-level
215 characteristics from two randomly chosen hospitals. Covariates were introduced in the
216 random-effects multilevel logistic regression model using a researcher-controlled backward
217 exclusion strategy. No tests for interaction were conducted for the subgroup analyses.

218 The following post hoc analyses were done on primary, secondary, exploratory and post hoc
219 outcomes: patients who were extubated out of protocol, a per protocol analysis and subgroup
220 analyses. The effect size was evaluated by computing the absolute risk difference with its 95%

CI for binary outcomes and difference in means with its 95% CI for continuous outcomes. Forest plots were used to display unadjusted risk ratios (95% CI) in the subgroup analysis by age, days of mechanical ventilation, APACHE II, COPD, medical, surgical, and trauma patients. The solid lines represent the 95% confidence interval.

A two-sided α-level of 0.05 was considered statistically significant. Data were analyzed using IBM SPSS Statistics version 22 (IBM Corporation®, Armonk, New York) and Stata version 14 (StataCorp LP®, College Station, Texas). Forest plots were elaborated using R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria).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 is a flow diagram of the patients in the study. In the study period, 2649 patients received mechanical ventilation for more than 24 hours in the participating ICUs; 1501 of these fulfilled the inclusion criteria, and 1153 were included in the study (578 patients randomized to undergo a 2-h SBT with a T-piece and 575 patients to undergo a 30-min SBT with 8 cmH_2O PSV). The two groups were similar in age, sex, APACHE II on admission, reason for ICU 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 T-piece (difference 8.2% [95%: 3.4% - 13%]) (Table 2).

The Kaplan-Meier curves showed a significantly difference, with a higher successful extubation rate in the PSV group (HR 1.54, [95% CI: 1.19 – 1.97]) (Figure 2).

Secondary outcomes

After the first SBT, 486 patients (92.5%) undergoing the 30-min PSV-SBT and 532 patients (84.1%) undergoing the 2-h T-piece SBT were extubated (difference 8.4% [95% CI: 4.7%- 12.1%]). 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% - -3.1%]) (Table 2). The ICU length of stay was 9 days (5 – 17) in the PSV group and 10 days (5 – 17) in the T-piece group (difference -0.3 [95% CI: -1.7 – 1.1]). The hospital length of stay was 24 days (15 – 40) in the PSV group and 24 days (15 – 39) in the T-piece group (difference 1.3 [95% CI: -2.2 – 4.9]). 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: -8.2% - -0.6%]) (Table 2).

Mortality at 90 days was significantly higher in the T-piece group than in the PSV group (difference -4.1% [95% CI: -8.2 – 0.01]; HR 0.74 [95% CI: 0.55 – 0.99]) (Supplement 3).

Exploratory outcomes

In the T-piece group, 58 patients required re-intubation, and in the PSV group, 59 patients required re-intubation. The time to reintubation was 23 hours (9 – 45) in the PSV group and 24.5 hours (9.8-44) in the T-piece group (difference 0.53 [95% CI: -7.2 –

8.25]). Reasons for reintubation were not significantly different in the two 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.

In 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% - 1.6%]) (Table 2).

Before randomization, physicians had to decide about 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% [-5.5% - 4.5%]). Of those 213 patients, only 117 (11.4%) were reintubated. Failure was treated by noninvasive ventilation in 91 (42.7%) patients, and 36 (39.6%) of these were finally reintubated. Failure was treated by high flow nasal cannula in 47 (22.1%) patients, and 20 (42.6%) of these were reintubated. The remaining 75 (35.2%) patients received standard oxygen, and 61 (81.3%) of these were reintubated.

Post hoc analysis:

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

The post hoc analysis showed that 29 patients (5%) in the PSV group and (6.6%) in T-piece group died in the ICU (difference -1.5% [95%CI: -4.5% - 1.1%]).

Multilevel logistic regression found a hospital-level random effect on successful extubation (MOR=1.56; p < 0.001). After adjusted for this random effect, the effect of the PSV persisted (adjusted OR 1.64 [95%CI: 1.23-2.20], p=0.001). 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<0.001) and COPD (adjusted OR 0.62 [95%CI: 0.44 – 0.87], p=0.006).Multilevel logistic regression did not find an effect of hospital on reintubation (MOR=1.19; p= 0.30). After adjusted for this random effect, reintubation in PSV group was not significantly different than in T-piece group (adjusted OR 0.92 [95%CI: 0.62-1.35], p=0.671). 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=0.03).

A total of 36 (3.1%) patients who failed the SBT were actually extubated, either because of physicians' decisions or self-extubation during the SBT. (Supplement 4). The results of the per protocol analysis were similar to those of intention-to-treat analysis (Supplement 5).

The primary and secondary outcomes were not significantly different in any of the subgroup analyses, except for surgical patients (Figure 3) (Supplement 6) (Supplement 7). The supplemental material reports the post hoc analyses about Borg Dyspnea Scale at the end of the SBT, patients' confidence in breathing without the ventilator, and data about blood gas analysis (Supplement 8) (Supplement 9) (Supplement 10)

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.

DISCUSSION

In this randomized trial of patients receiving mechanical ventilation, a 30-min PSV-SBT resulted in a significantly higher rate of successful extubation than a 2-h T-piece SBT without significantly increasing reintubation. The higher rate was realted 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, many physicians are concerned that some patients who breathe comfortably with low levels of PSV and/or PEEP 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 is somewhat exaggerated. The current study found that the T-piece SBT was worse tolerated than the PSV-SBT, although the work of breathing with the T-piece was supposedly similar to breathing spontaneously. In patients who successfully completed the SBT, the reintubation rate was not significantly different in the two

groups, and no imminent respiratory failure was observed after extubation from PSV. Moreover, the time to reintubation was around 24 hours in both groups, and the incidence of cardiac arrest was very low and even slightly higher in the T-piece group than in the PSV group.

Vallverdu et al.(16) showed that among patients who failed a 2-hour T-piece SBT, 64% did so 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 (11.6%) of patients who failed their 120-minute SBT after successfully completing the first 30minutes. Patients who failed after 30 minutes were older, more had cardiopulmonary disease, had spent more time under 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 outcome of these patients would have been if the SBT had been limited to 30 minutes. In the present study, the 30-min 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 two SBT approaches is that self-extubation during the SBT was more common in the T-piece group. Self-extubation was associated with significantly higher reintubation and mortality. Additionally, some physicians decided to extubate a few patients who failed the SBT; these patients more frequently developed postextubation respiratory failure and more frequently required reintubation.

Tolerance to SBTs in this trial may be compared with the studies done in the late 1990s by Esteban et al.(8)(9): patients' tolerance to T-piece SBTs in the present study was better than in their first trial (84% vs. 78%) and similar to in their second trial (84.6% vs. 84.1%). Moreover, tolerance to their 30-min T-piece SBT was worse than to the 30-min PSV in the present study (87.7% vs. 92.5%). However, the patients in Esteban's studies 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 2-h T-piece SBT and 2-h PSV-SBT, Matic et al. (18) found a higher rate of successful extubation with PSV than with 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 did the 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 two groups (about 11%), which is lower than the 17%in Esteban et al.'s first study (8)and similar to the 13% in their second study(9). Conversely, the reintubation rate was higher than in Perren et al.'s study(10)(9% for short SBTs and 4% for long SBTs), but their single-center design and small sample size preclude direct comparison.

Logistic regression analysis showed that the 30-min PSV-SBT was associated with successful extubation, whereas longer duration of mechanical ventilation before the

SBT and 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 will increase the risk of respiratory failure and reintubation is 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 failed SBT, APACHE II at admission, or hospital length of stay, which were not significantly different between the two groups.

LIMITATIONS

This study has several limitations. First, the prophylactic use of noninvasive ventilation and high flow nasal cannula after extubation was not protocolized. In some cases, these approaches were routinely employed 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 out-of-protocol, although few, could be expected to influence the main results, but the sensitivity analysis ruled out such bias (Supplemental 4).

Third, treatment allocation was not blinded for the investigators or attending physicians.

CONCLUSIONS

Among mechanically ventilated patients, 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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ARTICLE INFORMATION

Author Contributions:

Dr. Subira had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Subira and Fernandez.

Acquisition, analysis, or interpretation of data: Subira, Hernandez, Vazquez, Rodriguez, Gonzalez, Garcia, Rubio, Lopez, de la Torre, Keough, Arauzo, Hermosa, Sanchez, Tenza, Tizon, Laborda, Cabañes, Lacueva and Fernandez.

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Study supervision: Subira and Fernandez.

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491 **Table 1. Baseline patient characteristics.**

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	2-h T-piece (n=578)	30-min PSV (n=575)
Age, median (IQR), y	63 (53-73)	65 (52-75)
Sex, No. (%)		
Men	373 (64.5)	352 (61.2)
Women	205 (35.5)	223 (38.8)
APACHE II, median (IQR), points[a]	16 (11-22)	16 (11-22)
Comorbidity, No. (%)		
Cardiovascular disease	162 (28.0)	146 (25.4)
Diabetes mellitus[b]	147 (25.8)	123 (22.0)
COPD	118 (20.4)	110 (19.1)
Neurological disease	99 (17.1)	107 (18.6)
Cancer	94 (16.3)	87 (15.1)
Renal disease	68 (11.8)	76 (13.2)
Liver disease	63 (10.9)	64 (11.1)
Reason for admission, No. (%)		
Medical, non-respiratory	206 (35.6)	215 (37.4)
Medical, respiratory	190 (32.9)	189 (32.9)
Emergency surgery	113 (19.6)	105 (18.3)
Planned surgery	29 (5.0)	35 (6.1)
Trauma	40 (6.9)	31 (5)
Length of MV before SBT, median (IQR), d	4 (2-8)	4 (2-8)
Reconnection to ventilator before extubation, No. (%)[c]	158 (27.3)	145 (25.2)
Prophylactic NIV after extubation, No. (%)[c]	34 (5.9)	51 (8.9)
Prophylactic HFNC after extubation, No. (%)[c]	74 (12.8)	91 (15.8)

493 Abbreviations: APACHE, acute physiology and chronic health evaluation; PSV: pressure support
494 ventilation; COPD: Chronic obstructive pulmonary disease; MV: mechanical ventilation; SBT: spontaneous
495 breathing trial; NIV: noninvasive ventilation; HFNC: high flow nasal cannula; IQR, interquartile range.

496 [a]Data were missing for 8 patients in the 2-h T-piece group and 15 patients in the 30-min PSV group.

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

499 [c] Reconnection to ventilator and prophylactic NIV or HFNC was decided before randomization.

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Table 2. Primary, secondary, exploratory and post hoc outcomes[a] of patients who underwent a 2-h T-piece SBT or a 30-min PSV SBT.

	2-h T-piece (n = 578)	30-min PSV (n = 575)	Mean Difference[b], 30-min PSV minus 2-h T-piece (95% CI)	P Value
Primary outcome				
Successful extubation[c], No. (%)	428 (74.0)	473 (82.3)	8.2 (3.4 to 13.0)	0.001
Secondary outcomes				
Extubated after first SBT, No. (%)	486 (84.1)	532 (92.5)	8.4 (4.7 to 12.1)	<0.001
Reintubation within 72 h, No. (%)[d]	58 (11.9)	59 (11.1)	-0.8 (-4.8 to 3.1)	0.63
ICU length of stay, median (IQR), d	10 (5-17)	9 (5-17)	-0.3 (-1.7 to 1.1)	0.69
Hospital length of stay, median (IQR), d	24 (15-39)	24 (15-40)	1.3 (-2.2 to 4.9)	0.45
Hospital mortality, No. (%)	86 (14.9)	60 (10.4)	-4.4 (-8.3 to -0.6)	0.02
90-day mortality, No. (%)	100 (17.3)	76 (13.2)	-4.1 (-8.2 to 0.01)	0.04
Exploratory outcome				
Tracheostomy, No. (%)	50 (8.7)	41 (7.1)	-1.5 (-4.6 to 1.6)	0.38
Post hoc outcome				
ICU mortality, No. (%)	38 (6.6)	29 (5.0)	-1.5 (-4.2 to 1.1)	0.26

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

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

[b]Mean difference was defined across 30-min PSV and 2-h T-piece by absolute risk difference for binary outcomes (successful extubation, extubated after first SBT, reintubation within 72 h, mortality and tracheostomy) and difference in means for quantitative outcomes (length of stay).

[c]Remaining without mechanical ventilation 72 hours after the first SBT.

[d]Percentage calculated among patients extubated after first SBT.

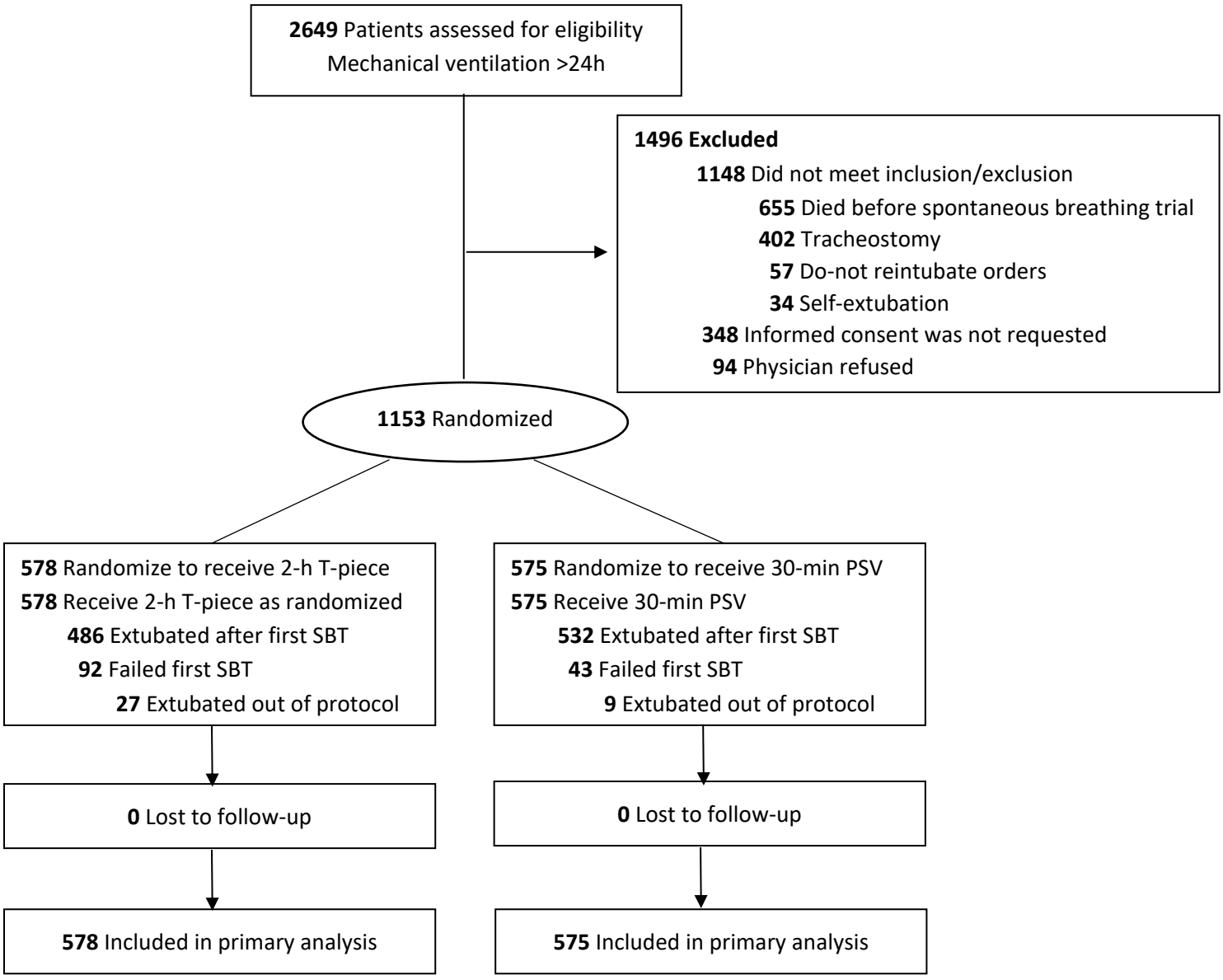
Table 3. Exploratory outcomes. Reasons for reintubation.

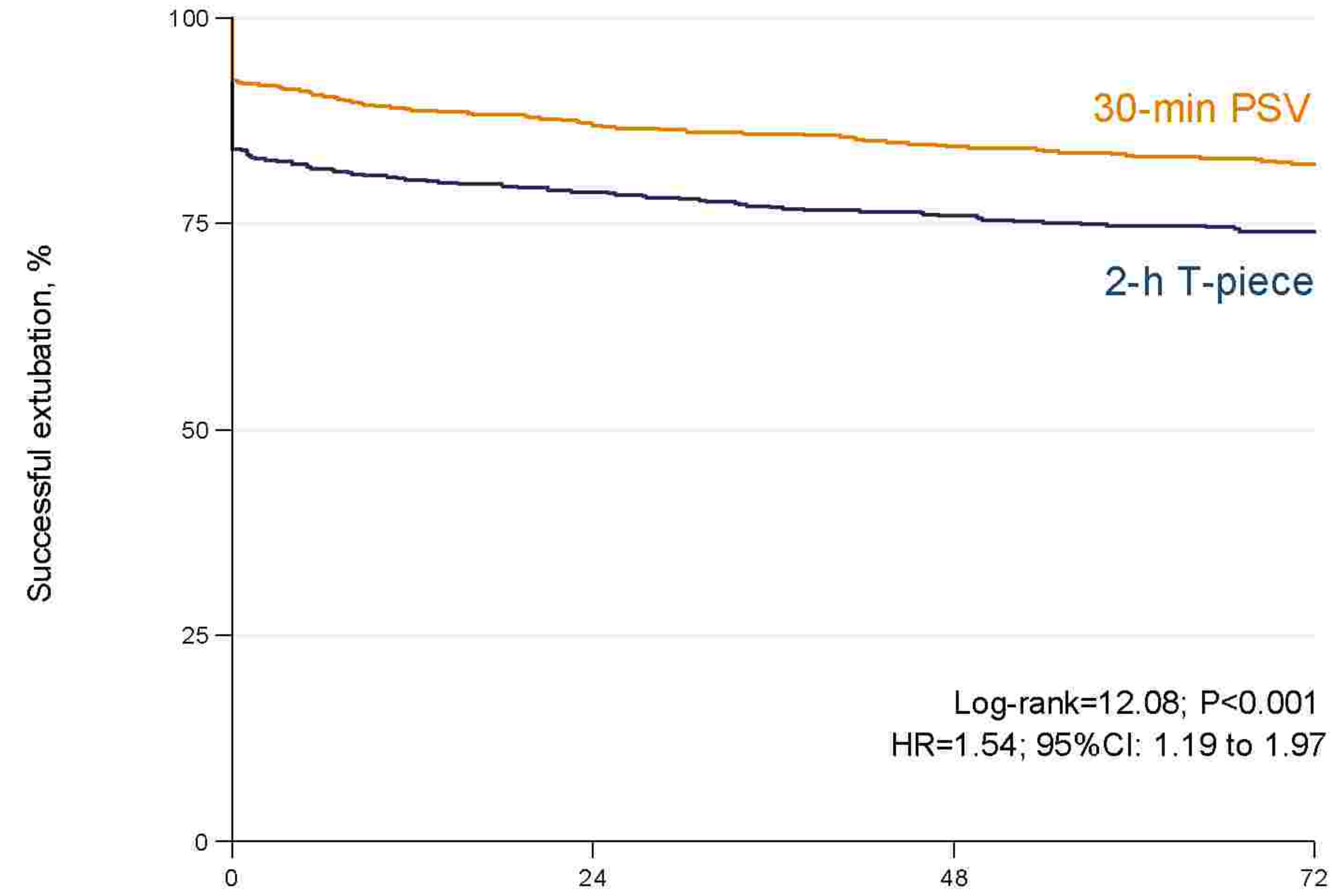
	2-h T-piece (n = 58)	30-min PSV (n = 59)	Mean Difference[a], 30-min PSV minus 2-h T-piece (95% CI)
Time to reintubation, median (IQR), h	24.5 (9.8-44.0)	23.0 (9.0-45.0)	0.53 (-7.2 to 8.2)
Reasons for reintubation[b]			
Excessive work of breathing	24 (41.4)	23 (39.0)	-2.4 (-20.2 to 15.4)
Difficulty managing secretions	18 (31.0)	19 (32.2)	1.2 (-15.7 to 18.0)
Refractory hypoxemia	11 (19.0)	14 (23.7)	4.8 (-10.1 to 19.6)
Level of consciousness	11 (19.0)	6 (10.2)	-8.7 (-21.5 to 3.9)
Airway obstruction	8 (13.8)	6 (10.2)	-3.6 (-15.4 to 8.1)
Surgery	4 (6.9)	4 (6.8)	-0.1 (-9.2 to 9.0)
Cardiac Arrest	3 (5.1)	1 (1.7)	-3.4 (-10.0 to 3.1)
Agitation	3 (5.2)	4 (6.8)	1.6 (-7.0 to 10.2)
Aspiration	3 (5.2)	1 (1.7)	-3.5 (-10.1 to 3.1)
Bradycardia < 50 bpm	1 (1.7)	0	-1.7 (-5.1 to 1.6)
Hemodynamic shock	1 (1.7)	1 (1.7)	-0.0 (-4.7 to 4.7)

[a]Mean difference was defined across 30-min PSV and 2-h T-piece by difference in means for quantitative outcomes (time to reintubation) and absolute risk difference for binary outcomes (reasons for reintubation).

[b]Could be more than one per patient.

Figure 1. Flow of patients.





No. of patients at risk

2-h T-piece	578	456	438	426
30-min PSV	575	501	484	472

Successful extubation (remaining without mechanical ventilation 72 hours after the first spontaneous breathing trial)

	2–hour T–piece	30–minutes PSV	RR (95% CI)
	n/N	n/N	
Age = 70 years	289/385	306/370	1.10 (1.02–1.19)
Age > 70 years	139/193	167/205	1.13 (1.01–1.26)
Mechanical ventilation = 4 days	249/326	263/304	1.13 (1.05–1.22)
Mechanical ventilation > 4 days	179/252	210/271	1.09 (0.99–1.21)
APACHE II = 20	296/404	329/410	1.10 (1.02–1.18)
APACHE II > 20	132/174	133/164	1.07 (0.96–1.20)
No COPD	351/460	387/465	1.09 (1.02–1.16)
COPD	77/118	86/110	1.20 (1.02–1.41)
Medical patients	283/396	329/404	1.14 (1.05–1.23)
Medical non–respiratory patients	154/206	182/215	1.13 (1.03–1.25)
Medical respiratory patients	129/190	147/189	1.15 (1.01–1.30)
Surgical patients	114/142	114/140	1.01 (0.91–1.14)
Planned surgical patients	23/29	33/35	1.19 (0.97–1.46)
Emergency surgical patients	91/113	81/105	0.96 (0.83–1.10)
Trauma patients	31/40	30/31	1.25 (1.04–1.49)