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Pressure-support ventilation versus T-piece during spontaneous breathing trials before extubation among patients at high-risk of extubation failure: a post-hoc analysis of a clinical trial.

Short running title: Spontaneous breathing trials in at-risk patients

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Conflict of Interest Statement

Dr Thille reported receiving grants from the French Ministry of Health and personal fees and nonfinancial support from Fisher & Paykel Healthcare during the conduct of the study and personal fees from Maquet-Getinge, GE Healthcare, and Covidien outside the submitted work. Dr Sonnevile reported receiving grants from the French Ministry of Health, the European Society of Intensive Care Medicine, and the French Society of Intensive Care Medicine and personal fees from Baxter outside the submitted work. Dr Beloncle reported receiving personal fees from Lowenstein Medical and nonfinancial support from GE Healthcare, Getinge Group, and Covidien outside the submitted work. Dr Girault reported receiving grants, personal fees, and nonfinancial support from Fisher & Paykel Healthcare during the conduct of the study and grants and nonfinancial support from ResMed outside the submitted work. Dr Ricard reported receiving travel and accommodation expenses from Fisher & Paykel Healthcare outside the submitted work. Dr Ehrmann reported receiving grants, nonfinancial support, and other funding from Fisher & Paykel Healthcare during the conduct of the study; grants, personal fees, nonfinancial support, and other funding from Aerogen; grants from Hamilton; personal fees from La Diffusion Technique Française; and personal fees from Baxter outside the submitted work. Dr Terzi reported receiving personal fees from Boehringer Ingelheim and Pfizer outside the submitted work. Dr Demoule reported receiving personal fees from Medtronic, Baxter, Hamilton, and Getinge; grants, personal fees, and nonfinancial support from Philips and Lungpacer; personal fees and nonfinancial support from Fisher & Paykel Healthcare; and grants from the French Ministry of Health and Respinor outside the submitted work. Dr Frat reported receiving personal fees and nonfinancial support from Fisher & Paykel Healthcare during the conduct of the study and personal fees and nonfinancial support from SOS Oxygen outside the submitted work. No other disclosures were reported.

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Ethics approval

The study has been approved by the central ethics committee (Ethics Committee Ouest III, Poitiers, France) with the registration number 2016-A01078-43 (06 September 2016).

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ABSTRACT

Background: Spontaneous breathing trial (SBT) using T-piece remains the most frequently performed trial before extubation in ICUs.

Research question: We aimed at determining whether initial SBT using pressure-support ventilation (PSV) could increase successful extubation rates among patients at high-risk of extubation failure.

Study Design and Methods: Post-hoc analysis of a multicenter trial focusing on reintubation in patients at high-risk of extubation failure. The initial SBT was performed using PSV or T-piece according to the physician/center decision. The primary outcome was the proportion of patients successfully extubated 72h after initial SBT, *i.e.* extubated after initial SBT and not reintubated within the following 72 hours.

Results: Among the 641 patients included in the original study, initial SBT was performed using PSV (7.0 cm H₂O in median without positive end-expiratory pressure) in 243 patients (38%) and using T-piece in 398 patients (62%). The proportion of patients successfully extubated 72h after initial SBT was 67% (162/243) using PSV and 56% (223/398) using T-piece (absolute difference 10.6%, 95% CI 2.8 to 28.1; $p=0.0076$). The proportion of patients extubated after initial SBT was 77% (186/283) using PSV and 63% (249/398) using T-piece ($p=0.0002$), while reintubation rates within the following 72 hours did not significantly differ (13% vs. 10%, respectively; $p=0.4259$). Performing an initial SBT using PSV was independently associated with successful extubation (adjusted odds ratio 1.60, 95% CI 1.30 to 2.18; $p=0.0061$).

Interpretation: In patients at high-risk of extubation failure in the ICU, performing an initial SBT using PSV may hasten extubation without an increased risk of reintubation.

Key words: weaning; extubation; intensive care unit; mechanical ventilation.

Funding: French Ministry of Health

BACKGROUND

The decision of extubation is a critical time in ICUs because mortality is particularly high in case of extubation failure leading to reintubation.¹ The overall rate of reintubation after planned extubation is around 10% but may exceed 20% in patients at high-risk.^{1,2} To reduce that risk and in order to mimic the physiological conditions after extubation, guidelines recommend systematic performance of a spontaneous breathing trial (SBT) before extubation in all patients intubated at least 24h.³ To hasten extubation, guidelines suggest that the initial SBT be conducted using low levels of pressure-support ventilation (PSV trial), rather than T-piece disconnecting the patient from the ventilator (T-piece trial).³ The strength of this recommendation was only conditional given the moderate certainty of evidence. However, SBT using T-piece remains the most frequently trial performed before extubation of ICU patients in recent large cohort studies.^{4,5}

Regarding the work of breathing, while a T-piece trial accurately reflects the physiologic conditions occurring after extubation, a PSV trial is easier to pass with work of breathing significantly lower than during T-piece trial or that after extubation.⁶ Consequently, a PSV trial may potentially hasten extubation but increase the risk of reintubation.⁷ Up until now no study has demonstrated an increased risk of reintubation using PSV trial as compared to T-piece trial.

A large randomized controlled trial recently showed that the proportion of patients successfully extubated 72 hours after the initial SBT was higher using PSV than using T-piece.⁸ Reintubation rates did not differ, thereby suggesting that PSV may hasten extubation without an increased risk of reintubation. However, the high proportion of patients with simple weaning (*i.e.* extubated after the initial SBT) and the low reintubation rates suggest that most of the patients included in this study were at low-risk of extubation failure.^{9,10} Moreover, the strategy of oxygenation after extubation was not standardized and less than 10% of patients received prophylactic non-invasive ventilation.⁸ We recently conducted a randomized clinical trial showing that a combination of high-flow nasal oxygen alternating with non-invasive ventilation significantly decreased reintubation rates as compared to high-flow nasal oxygen alone.¹¹ This trial included only patients at high-risk of extubation failure with

high rates of difficult weaning and reintubation, while standardized oxygenation strategies have been applied immediately after extubation. In a post-hoc analysis of this trial, we aimed at determining whether initial SBT using PSV may hasten extubation without increased reintubation rates as compared with initial SBT using T-piece among patients at high-risk of extubation failure. Secondary objectives were to compare the two groups regarding weaning difficulty, duration of mechanical ventilation, post-extubation respiratory failure, length of stay and mortality.

METHODS

Study design and patients

The current study is a post-hoc analysis of a multicenter, randomized, controlled trial comparing the use of high-flow nasal oxygen alone versus high-flow nasal oxygen alternating with non-invasive ventilation immediately after extubation among patients at high-risk of reintubation in ICUs.¹¹ Patients intubated more than 24 hours could be included if they were at high-risk of extubation failure, *i.e.* older than 65 years, or having any underlying chronic cardiac or lung disease.^{12,13} Underlying chronic cardiac diseases included left ventricular dysfunction, whatever the cause defined by left ventricular ejection fraction $\leq 45\%$, history of cardiogenic pulmonary edema, documented ischemic heart disease or permanent atrial fibrillation. Underlying chronic lung diseases included chronic obstructive pulmonary disease, obesity-hypoventilation syndrome or restrictive pulmonary disease.

The original trial was approved by the central ethics committee. Written informed consent was obtained from all patients or next of kin before inclusion in the study. According to French law, this post-hoc analysis of the original study did not require further ethics approval.

Procedures

Weaning protocol was used in each center to rapidly identify patients able to breathe spontaneously in order to hasten extubation.^{14,15} SBT was performed each morning in all patients meeting all the

weaning criteria according to the international conference consensus on weaning,¹⁶ *i.e.* a respiratory rate ≤ 35 breaths per minute, adequate oxygenation defined as $SpO_2 \geq 90\%$ with $FiO_2 \leq 40\%$ or $PaO_2/FiO_2 \geq 150$ mm Hg with positive end-expiratory pressure (PEEP) ≤ 8 cmH₂O, adequate cough, patient awake with a Richmond Agitation-Sedation Scale between +1 and -2,¹⁷ and hemodynamic stability with no need for vasopressors.

According to each center and/or attending physician, SBT was performed from 30 minutes to 2 hours using either PSV with low levels of pressure-support or T-piece. Patients who underwent an initial SBT using T-piece were classified in the T-piece group and patients who underwent an initial SBT using PSV were classified in the PSV group.

SBT failure was defined according to the usual criteria of the international conference consensus on weaning,¹⁶ as development during the trial of any of the following events: respiratory rate > 35 breaths/min, increased accessory muscle activity, SpO_2 persistently below 90% (on $FiO_2 \geq 0.4$ or at least 6 L/min of oxygen), hemodynamic instability defined as heart rate persistently above 140 beats / min, or systolic blood pressure < 90 or > 180 mmHg, with appearance of cyanosis or mottling), depressed mental status or agitation.

Patients who successfully underwent SBT were extubated and then immediately treated with high-flow nasal oxygen alone or high-flow nasal oxygen alternating with non-invasive ventilation for at least 48h until complete recovery of respiratory status.

Outcomes

The primary outcome was the proportion of patients who were successfully extubated 72h after the initial SBT, *i.e.* extubated after the initial SBT and not reintubated within the following 72 hours.

Secondary outcomes included proportion of patients with simple, difficult or prolonged weaning, duration of mechanical ventilation prior to extubation, proportion of patients who developed post-extubation respiratory failure, proportion of patients who required reintubation within the 72h following extubation, at day 7 and up until ICU discharge, the length of stay in ICU and in hospital,

and mortality. Weaning difficulty was defined as following: simple weaning included patients extubated after the initial SBT, difficult weaning included patients who failed the initial SBT and were extubated within the 7 following days, and prolonged weaning included patients extubated more than 7 days after the initial SBT.^{5,16}

Patients were immediately reintubated if they had severe respiratory failure, hemodynamic failure defined by a vasopressor requirement to maintain mean arterial pressure of 65 mm Hg, altered consciousness (Glasgow coma scale < 12), cardiac or respiratory arrest. Severe respiratory failure leading to reintubation was defined by the presence of at least two criteria among the following: respiratory rate > 35 breaths per minute, clinical signs suggesting respiratory distress, respiratory acidosis defined as pH < 7.25 units and PaCO₂ > 45 mm Hg, hypoxemia defined as a need for FiO₂ ≥ 80% to maintain SpO₂ ≥ 92% or a PaO₂:FiO₂ < 100 mm Hg.

Statistical analysis

All the analyses were performed by the study statistician (SR). Proportions of patients successfully extubated 72h after the initial SBT were compared between the T-piece group and the PSV group by means of the χ^2 test. Successful extubation probabilities within the 72 hours following the initial SBT were described with Kaplan-Meier curves according to type of SBT and compared by log-rank test. Secondary outcomes were compared using χ^2 tests for categorical variables and Student's *t* test or Wilcoxon test for continuous variables. A multiple logistic regression analysis taking into account center as a random effect (using generalized linear mixed-effects model) was performed for the primary outcome with the use of a backward-selection procedure. Variables associated with successful extubation at 72 hours with a *p* value of less than 0.10 after univariable analysis were entered into the maximal model as fixed effects knowing that there was no missing data. The result was presented as odds ratio (OR) with 95% confidence interval (95CI) for fixed effects. A two-tailed *p* value of less than 0.05 was considered to be statistically significant. We used SAS software, version 9.4 (SAS Institute) and R version 3.6.2 for performing generalized linear mixed-effects models.

RESULTS

Among the 641 patients included in the original study, the initial SBT was performed using PSV in 243 patients (38%) and using T-piece in 398 patients (62%). Among the 30 participating centers, SBT was always performed using PSV in 6 centers (114 patients, 18%), always performed using T-piece in 11 centers (229 patients, 36%), and using as well PSV as T-piece in 13 centers (298 patients, 46%). The characteristics of the patients were similar in the two groups aside from a lower body-mass index in the PSV group (**Table 1**).

PSV trials were performed with a pressure-support level of 7.0 H₂O (IQR 7.0-7.0), a positive end-expiratory pressure level of 0 cm H₂O (IQR 0-0), and a FiO₂ of 30% (IQR 30-40) while T-piece trials were performed with an additional oxygen flow of 4 L/min (IQR 3-6). PSV trials were significantly longer than T-piece trials: 60 minutes (IQR 45-90) versus 50 (IQR 30-60); p<0.0001.

Primary Outcome

Successful extubation 72 hours after initial SBT occurred in 162 out of 243 patients (67%) in the PSV group and in 223 out of 398 patients (56%) in the T-piece group (absolute difference 10.6%, 95% CI 2.8 to 28.1; p=0.0076) (**Table 2**). Kaplan-Meier curves showed a higher successful extubation probability in the PSV group than in the T-piece group (p=0.0064 using log-rank test) (**Figure 1**).

After the initial SBT, 186 among the 243 patients (77%) undergoing a PSV trial were extubated versus 249 among the 398 patients (63%) undergoing a T-piece trial (absolute difference 13.9%, 95% CI 6.6 to 20.9; p=0.0002) (**Table 2**). Among patients extubated after the initial SBT, reintubation rates within 72 hours following extubation were 13% (24/186) after a PSV trial and 10% after a T-piece trial (26/249) (absolute difference 2.5%, 95% CI -3.6 to 8.9; p=0.4259).

Secondary Outcomes

The proportion of patients with difficult or prolonged weaning was lower using PSV than using T-piece: 24% (n=57) vs. 37% (n=149), $p=0.0004$ (**Table 2 and Figure 2**). Among patients who failed the initial SBT, SBT was switched within the following days and was performed using T-piece trial in 5.3% of patients (3/57) in the PSV group, and using PSV trial in 4.7% of cases (7/149) in the T-piece group. Among all patients, median duration of mechanical ventilation prior to extubation was shorter in the PSV group than in the T-piece group: 5 days (IQR 3-8) vs. 6 (IQR 3-11), $p=0.0014$. The proportion of patients who developed post-extubation respiratory failure was 22% (n=53) in the PSV group and 26% (n=105) in the T-piece group (absolute difference -4.6%, 95% CI -11.1 to 2.4; $p=0.1926$). Reintubation rates at 72h did not differ between groups: 13% (n=31) in the PSV group and 12% (n=46) in the T-piece group (absolute difference 1.2%, 95% CI -3.9 to 6.7, $p=0.6504$). Median length of stay in ICU was 11 days in the PSV group (IQR 7-19) and 12 days (IQR 8-20) in the T-piece group ($p=0.1082$). In-ICU mortality rates were 6% (n=15) in the PSV group and 8% (n=32) in the T-piece group (absolute difference -1.9%; 95% CI -5.8 to 2.5%; $p=0.3789$).

Factors associated with successful extubation

The proportion of patients successfully extubated 72 hours after initial SBT was lower in the 11 centers always performing T-piece trials (116 out of 229 patients, 51%) as compared with the 6 centers always performing PSV trials (74 out of 114 patients, 65%) and with the 13 centers performing as well T-piece as PSV trials (195 out of 298 patients, 65%); $p=0.0014$ (**Figure 3**).

After univariable analysis, the existence of any underlying chronic lung disease, acute respiratory failure as the main reason for intubation, and initial SBT using T-piece were three factors associated with not being successfully extubated 72 hours after initial SBT (**Table 3**).

After multivariable logistic regression including the three variable above-mentioned and taking into account center as a random effect, acute respiratory failure as the main reason for intubation (adjusted OR 1.80 (95%CI 1.29 to 2.52); $p=0.0005$) and type of SBT remained two risk factors of not being successfully extubated 72 hours after initial SBT. The probability of successful intubation 72

hours after the initial SBT was 1.58 times higher (95%CI 1.02 to 2.43; p=0.03) when performing initial SBT using PSV than when using T-piece.

DISCUSSION

In this post-hoc analysis of a large randomized controlled trial including 641 patients at high-risk of extubation failure, initial SBT using PSV was associated with a significantly higher rate of successful extubation at 72 hours as compared with initial SBT using T-piece. The proportion of patients extubated after the initial SBT was significantly higher using PSV than using T-piece and reintubation rates did not differ between the 2 groups, showing that SBT using PSV may hasten extubation without increasing the risk of reintubation.

SBT performed using low levels of PSV is a trial easier to pass with work of breathing significantly lower than during a T-piece trial,^{6,18} and it has been shown that some patients were able to pass a PSV trial immediately after failing a T-piece trial.^{18,19} Thus, due to lower respiratory muscle effort PSV trials may hasten extubation as compared to T-piece trials. In accordance with physiological data, a previous multicenter randomized clinical trial showed that the proportion of patients who failed the initial SBT was lower using PSV than using T-piece.²⁰ However, the proportion of patients successfully extubated within the following 48 hours was not significantly different between the two groups. By pooling all previous trials, a meta-analysis suggested that patients undergoing PSV trials may be more likely to pass the initial SBT and to be extubated successfully compared to those undergoing T-piece trials.²¹ More recently, Subirà et al. showed in a large-scale randomized clinical trial including 1153 patients that the proportion of patients successfully extubated 72 hours after the initial SBT was higher with a PSV trial than with a T-piece trial.⁸ The proportion of patients who passed the initial SBT was higher using PSV than using T-piece and reintubation rates did not differ. These findings suggest that PSV trial may hasten extubation without an increased risk of reintubation. However, the proportion of patients extubated after the initial SBT (simple weaning) was unusually high, *i.e.* more than 80-90% whereas rates are generally closer to 60-70%.⁴ Moreover, reintubation rates were

relatively low (11%), meaning that the population consisted mainly in patients at low-risk of extubation failure.⁹ Clinical trials in which such patients predominate may be underpowered to demonstrate the safety of SBT using PSV in patients at high-risk of reintubation. Indeed, a PSV trial may potentially hasten extubation while increasing the risk of reintubation by underestimating the work of breathing needed to breathe without ventilator assistance, as was reported by Tobin in a comment on the myth of “minimal ventilator settings”.⁷

The recent study by Subirà and colleagues supported the use of a short and less demanding ventilation strategy for SBT.⁸ The authors compared a short SBT using PSV for 30 minutes versus a prolonged SBT using T-piece for 2 hours. In line with this study, our results show that initial SBT using PSV may hasten extubation without an increased risk of reintubation, even in patients at high-risk of extubation failure. However, in our study PSV trials were not shorter than T-piece trials, suggesting that it is more the type of trial than its duration that could influence SBT success and the subsequent time to extubation. These findings are also in keeping with a previous multicentre randomized controlled trial showing that there was no difference in successful extubation rate between trials lasting 30 minutes and those lasting 2 hours.²²

Clinical implications

An ideal weaning readiness test would exhibit perfect accuracy in predicting the tolerance of unassisted spontaneous breathing after extubation. In a meta-analysis pooling all studies examining patient effort according to type of SBT, a T-piece trial seemed to accurately reflect the physiologic conditions occurring after extubation. In contrast, SBT using PSV were easier to pass, with work of breathing significantly lower than during a T-piece trial or than after extubation. Our study found no difference in terms of reintubation or post-extubation respiratory failure, whatever the type of SBT. Although a PSV trial may underestimate work of breathing after extubation, we believe that PSV trials may hasten extubation by facilitating a clinician's decision. The decision to extubate is difficult for clinicians and a highly demanding ventilation strategy for SBT could unduly delay extubation in

patients able to spontaneously breathe without the ventilator. Whereas SBT using T-piece is still the most frequently performed trial before extubation in ICUs,^{4,5} SBT using PSV seems to be the most efficient trial in terms of hastening extubation and could be applied in all ICU patients.

Limitations

The main limitation of this study is the post-hoc nature of the analysis. However, all patients included in the original trial were retained in the analysis and the characteristics of patients were similar in the two analyzed groups. The original study showed that application of non-invasive ventilation immediately after extubation significantly decreased reintubation rates in patients at high-risk of extubation failure.¹¹ Although the strategy of oxygenation after extubation could have an influence on reintubation rates, the proportion of patients who received non-invasive ventilation after extubation was exactly the same in the 2 groups, thereby mitigating potential selection bias. Another limitation is that the physician could have chosen the type of SBT according to the patient. However, the proportion of patients successfully extubated 72h after initial SBT remained significantly higher in centers always performing PSV trials as compared with centers always performing T-piece trials, thereby reducing the potential impact of this bias. Obviously, these results do not warrant definitive conclusions on the most efficient weaning strategy and our findings need to be confirmed in a randomized controlled trial specifically focusing on patients at high-risk of reintubation. When comparing our results with those in the literature, the primary outcome was the same as in previous RCTs.^{8,20} However, our primary outcome focused only on patients with simple weaning, *i.e.* patients extubated after the initial SBT, thereby limiting application of these findings to simple weaning and not taking into account patients with weaning difficulties.

CONCLUSIONS

In this post-hoc analysis from a large RCT, execution of an initial SBT using PSV in ICU patients at high-risk of extubation failure significantly increased the proportion of patients successfully

extubated within the following 72 hours as compared with T-piece. SBT using PSV may hasten extubation without an increased risk of reintubation. Another large prospective RCT is needed to confirm these findings in this population at high-risk of reintubation before being in a position to apply this weaning strategy to all ICU patients.

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Author's contribution: Pr. Arnaud W. Thille 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. AWT designed the study and wrote the manuscript. SR provided substantial contributions to the conception and design of the study, and performed statistical analysis. All authors contributed to drafting of the work, revising it critically for important intellectual content and approved the final version of the manuscript. All authors give their agreement to be accountable for all aspects of the work, and ensure the accuracy and integrity of any part of the work.

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Table 1: Patient characteristics according to initial spontaneous breathing trial (SBT): pressure-support ventilation (PSV) vs. T-piece.

	PSV (n=243)	T-piece (n=398)	P value
Characteristics of the patients at admission			
Age, years	69 (10)	70 (10)	0.4509
Male sex	161 (66%)	264 (66%)	0.9841
Body-mass index, kg/m ²	27 (6)	29 (7)	0.0198
SAPS II at admission, points	55 (18)	55 (19)	0.9922
Underlying chronic cardiac disease	111 (46%)	195 (49%)	0.4148
Underlying chronic lung disease	83 (34%)	130 (33%)	0.6970
Main reason for intubation			0.8205
Acute respiratory failure	126 (52%)	199 (50%)	
Coma	41 (17%)	71 (18%)	
Shock	22 (9%)	45 (11%)	
Cardiac arrest	27 (11%)	34 (9%)	
Surgery	22 (9%)	41 (10%)	
Other reason	5 (2%)	8 (2%)	
Before extubation			
Administration of steroids	31 (13%)	64 (16%)	0.2506
Ineffective cough	51/228 (22%)	100/378 (26%)	0.2599
Abundant secretions	91/231 (39%)	144/283 (38%)	0.6574
Oxygenation strategy after extubation #			0.8084
High-flow nasal oxygen	113 (47%)	189 (47%)	
Prophylactic non-invasive ventilation	130 (53%)	209 (53%)	

Data are mean (SD), median (IQR), or n (%).

SBT=spontaneous breathing trial. PSV=pressure-support ventilation. SAPS=Simplified acute physiology score.

High-flow nasal oxygen means that patients were continuously treated by high-flow nasal oxygen alone for 48 hours after extubation whereas prophylactic non-invasive ventilation means that patients were treated by sessions of non-invasive ventilation interspaced with high-flow nasal oxygen for 48 hours following extubation.

Table 2: Comparison of outcomes according to initial spontaneous breathing trial (SBT): pressure-support ventilation (PSV) vs. T-piece.

	PSV (n=243)	T-piece (n=398)	Absolute difference estimate (95% CI)	P value
Primary outcome				
Successful extubation at 72h	162 (67%)	223 (56%)	10.6 (2.8 to 28.1)	0.0076
Extubation after initial SBT	186 (77%)	249 (63%)	13.9 (6.6 to 20.9)	0.0002
Reintubation within 72 hours among patients extubated after initial SBT	24/186 (13%)	26/249 (10%)	2.5 (3.6 to 8.9)	0.4259
Secondary outcomes				
Weaning difficulty #				0.0004
Simple weaning	186 (77%)	249 (63%)	13.9 (6.6 to 20.9)	
Difficult weaning	48 (20%)	137 (34%)	-14.7 (-21.3 to -7.6)	
Prolonged weaning	9 (4%)	12 (3%)	0.7 (-2.1 to 4.1)	
Duration of MV prior to extubation (days)	5 (3-8)	6 (3-11)	-1.3 (-2.5 to -0.2)	0.0014
Post-extubation respiratory failure	53 (22%)	105 (26%)	-4.6 (-11.1 to 2.4)	0.1926
Reintubation at 72 hours	31 (13%)	46 (12%)	1.2 (-3.9 to 6.7)	0.6504
Reintubation at day 7	38 (16%)	57 (14%)	1.3 (-4.2 to 7.3)	0.6491
Reintubation up until ICU discharge	39 (16%)	61 (15%)	0.7 (-4.9 to 6.8)	0.8067
Length of stay in ICU (days)	11 (7-18)	12 (8-20)	-1.6 (-3.8 to 0.5)	0.1082
Length of stay in hospital (days)	23 (14-37)	25 (16-41)	-1.5 (-5.4 to 2.3)	0.1255
Mortality in ICU	15 (6%)	32 (8%)	-1.9 (-5.8 to 2.5)	0.3789
Mortality in hospital	34 (14%)	66 (17%)	-2.6 (-8.1 to 3.4)	0.3804
Mortality at day 90	45 (19%)	83 (21%)	-2.3 (-8.5 to 4.2)	0.4729

Data are median (25th-75th percentiles), mean (SD), n (%) or n/N (%).

SBT=spontaneous breathing trial. PSV=pressure-support ventilation. MV=mechanical ventilation. ICU=intensive care unit.

Weaning difficulty was defined as following: simple weaning included patients extubated after the initial SBT, difficult weaning included patients who failed the initial SBT and were extubated within the 7 following days, and prolonged weaning included patients extubated more than 7 days after the initial SBT.

Table 3: Comparison between patients with successful extubation (defined as extubated after the initial SBT and not reintubated within the following 72 hours) and the others.

	Successful Extubation (n=385)	Not successfully extubated at 72h (n=256)	P value
Characteristics of the patients at admission			
Age, years	70 (10)	69 (10)	0.5239
Male sex	252 (65%)	173 (68%)	0.5775
Body-mass index, kg/m ²	28 (6)	28 (7)	0.8181
SAPS II at admission, points	56 (19)	54 (18)	0.2217
Underlying chronic cardiac disease			
Ischemic heart disease	190 (49%)	116 (45%)	0.3161
Atrial fibrillation	108 (28%)	58 (23%)	0.1267
Left ventricular dysfunction	57 (15%)	46 (18%)	0.2854
Underlying chronic lung disease	51 (13%)	40 (16%)	0.3981
Chronic obstructive pulmonary disease	116 (30%)	97 (38%)	0.0411
Main reason for intubation			
Acute respiratory failure	85 (22%)	65 (25%)	0.0222
Coma	175 (45%)	150 (59%)	
Shock	75 (19%)	37(14%)	
Cardiac arrest	44 (11%)	23 (9%)	
Surgery	45 (12%)	16 (6%)	
Other reason	38 (10%)	25 (10%)	
Other reason	8 (2%)	5 (2%)	
Initial spontaneous breathing trial			
T-piece trial	223 (58%)	175 (68%)	0.0076
PSV trial	162 (42%)	81 (32%)	
Type of SBT performed according to the centers			
In the 11 centers always performing T-piece trials	116 (30%)	113 (44%)	0.0014
In the 6 centers always performing PSV trials	74 (19%)	40 (16%)	
In the 13 centers performing both T-piece or PSV trials	195 (51%)	103 (40%)	
Weaning difficulty #			
Simple weaning	385 (100%)	50 (20%)	<0.0001
Difficult weaning	0 (0%)	185 (72%)	
Prolonged weaning	0 (0%)	21 (8%)	

Before extubation			
Ineffective cough	85/363 (23%)	66/243 (27%)	0.2963
Abundant secretions	133/369 (36%)	102/245 (42%)	0.1629

Data are mean (SD) or n (%). SBT= spontaneous breathing trial. PSV=pressure-support ventilation. SAPS=simplified acute physiology score.

Weaning difficulty was defined as following: simple weaning included patients extubated the initial SBT, difficult weaning included patients who failed the initial SBT and were extubated within the 7 following days, and prolonged weaning included patients extubated more than 7 days after the initial SBT.

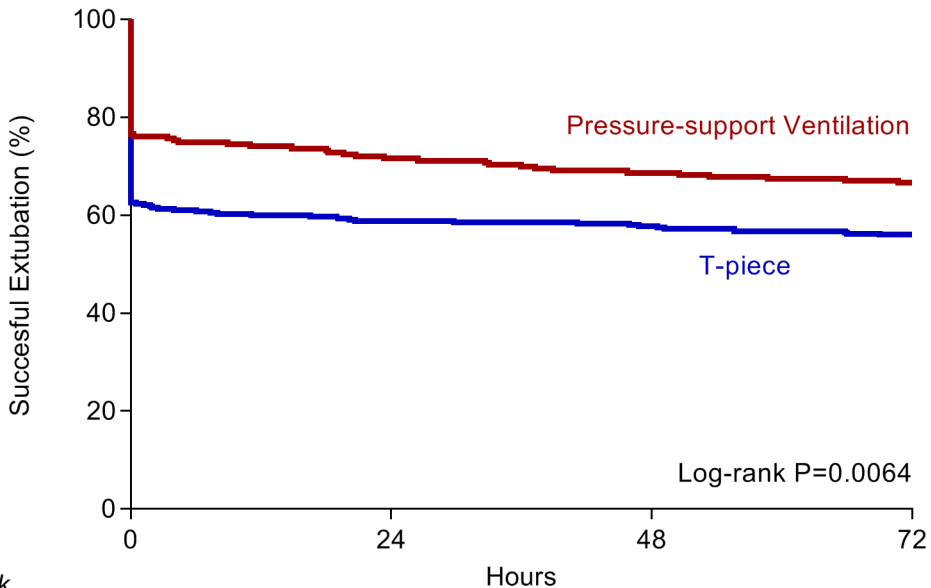
FIGURE LEGEND

Figure 1: Kaplan-Meier curves showing the proportion of patients who were successfully extubated at 72 hours, *i.e.* who were extubated after the initial spontaneous breathing trial and were not reintubated within the following 72 hours, according to initial SBT performed using T-piece or using pressure-support ventilation (PSV).

Figure 2: Bars showing proportion of patients with simple, difficult or prolonged weaning according to the initial spontaneous breathing trial (SBT) performed using T-piece (blue bars) or pressure-support ventilation (PSV) (red bars). The proportion of patients who succeeded in the initial SBT was higher using PSV than using T-piece: 77% (186 out of 243 patients) after a PSV trial vs. 63% (249 out of 398 patients) after a T-piece trial (absolute difference 13.9%, 95% CI 6.6 to 20.9; $p=0.0002$).

Weaning difficulty was defined as follows: simple weaning included patients extubated after the initial SBT, difficult weaning included patients who failed the initial SBT and were extubated within the following 7 days, and prolonged weaning included patients extubated more than 7 days after the initial SBT.

Figure 3: Kaplan-Meier curves showing the proportion of patients who were successfully extubated at 72 hours, *i.e.* who were extubated after the initial spontaneous breathing trial and were not reintubated within the following 72 hours, in the 6 centers always performing initial SBT using pressure-support ventilation (114 patients) and in the 11 centers always performing initial SBT using T-piece (229 patients).



Number at risk

T-piece

398

235

230

223

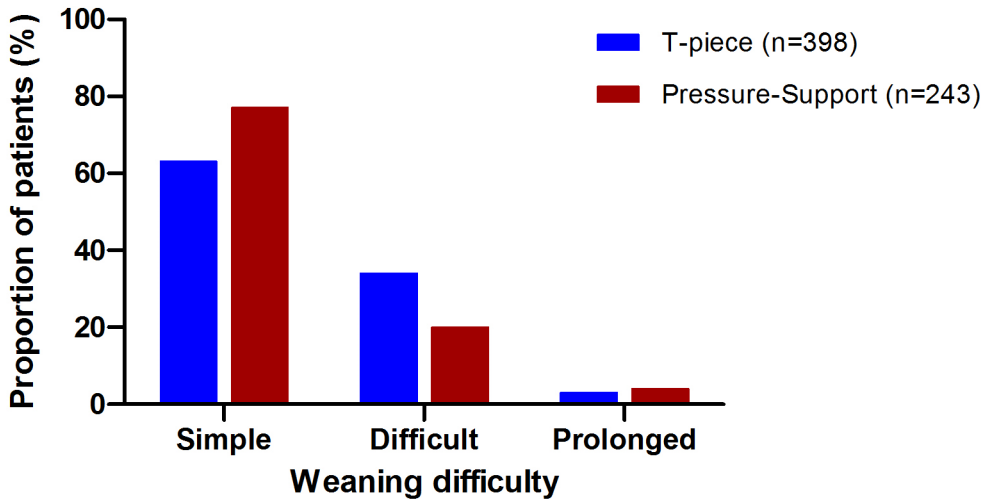
Pressure-support

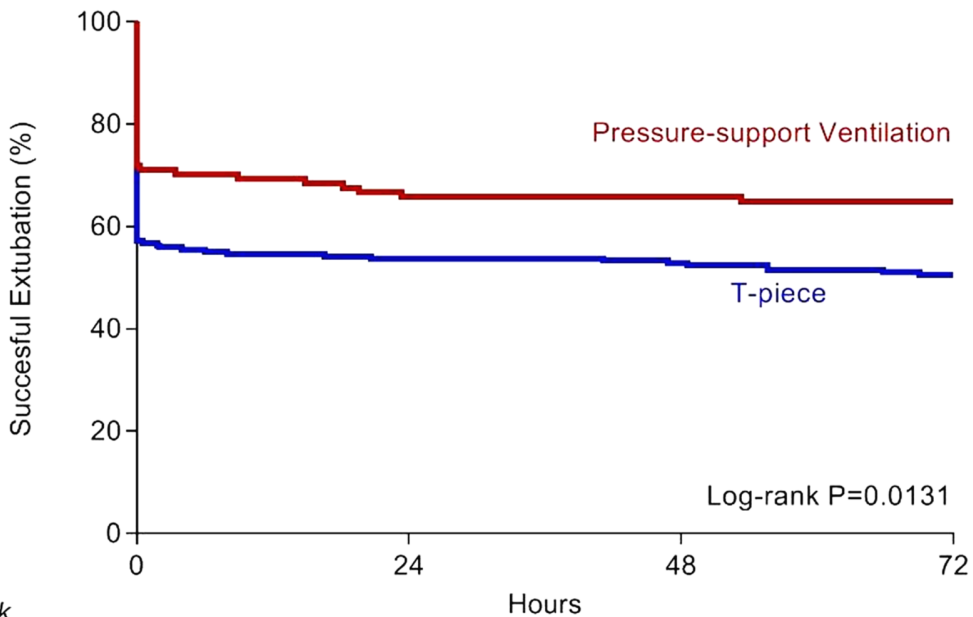
243

175

167

162





Number at risk

T-piece

229

124

120

115

Pressure-support

114

75

75

72