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Protocol-directed weaning from mechanical ventilation: clinical outcome in patients randomized for a 30-min or 120-min trial with pressure support ventilation

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Abstract *Objective:* To investigate the possibility of successful extubation performing a spontaneous breathing trial (SBT) in pressure support ventilation (PSV) with target durations of 30 and 120 min.
Design and setting: Prospective and randomized study in two medical-surgical adult intensive care units.
Patients and participants: 98 adult patients supported by mechanical ventilation for at least 48 h and considered ready for a weaning trial.
Interventions: An SBT conducted in PSV with 7 cmH_2O and patients randomly assigned to two groups with target durations of 30- and 120-min.
Measurements and results: In the 30-min group 43 patients (93%) tolerated the SBT and were extubated while 4 (9%) needed reintubation within 48 h; in the 120-min group 46 patients (88%) successfully completed the trial and were extubated while 2 (4%) were reintubated. ICU mortality in the groups with short and long periods was 6% and 4%, and in-hospital mortality 20% and 17%, respectively. Those successful in the 30- and 120-min groups had similar length of ICU stay (6 and 7 days, respectively) and in-hospital length of stay (20 and 25 days, respectively). Compared to the successfully extubated, the reintubated patients had significantly higher length of ICU stay and mortality (17 vs. 6 days and 33 vs. 3.6%, respectively).
Conclusions: An SBT with PSV of 7 cmH_2O lasting 30 min is equally effective in recognizing the successfully extubated patients as a 120-min trial.

Keywords Weaning · Clinical outcome · Pressure support ventilation · Duration of weaning trial · Extubation · Adults

Introduction

Disconnecting patients from mechanical ventilation in the ICU is a intriguing and difficult task. Controversy still exists over how to proceed during the spontaneous breathing trial (SBT), and which criteria should be fulfilled to start it. Single weaning parameters used to predict extubation success [1, 2, 3] seem to have a rather low accuracy [2, 4], and some of them may even have a low negative predictive value [4]. Moreover, authors still disagree about the validity of standard respiratory functional variables determined prior to weaning and supposed to represent prediction criteria for a successful extubation [5, 6, 7, 8]. Therefore recent prospective and randomized protocol-directed weaning studies have assessed weaning readiness by means of a structured evaluation [5, 9, 10, 11, 12, 13]. Prior to the weaning trial the patients had to pass a collection of standardized readiness criteria that focused on: (a) reversal of the causative process for ventilatory support, (b) respiratory and ventilatory patterns, (c) ability to protect the airway, and (d) stability of hemodynamic and metabolic parameters. Although these criteria may be helpful in predicting successful extubation, they are not perfect, and the patient's tolerance of an SBT remains the most reliable criterion.

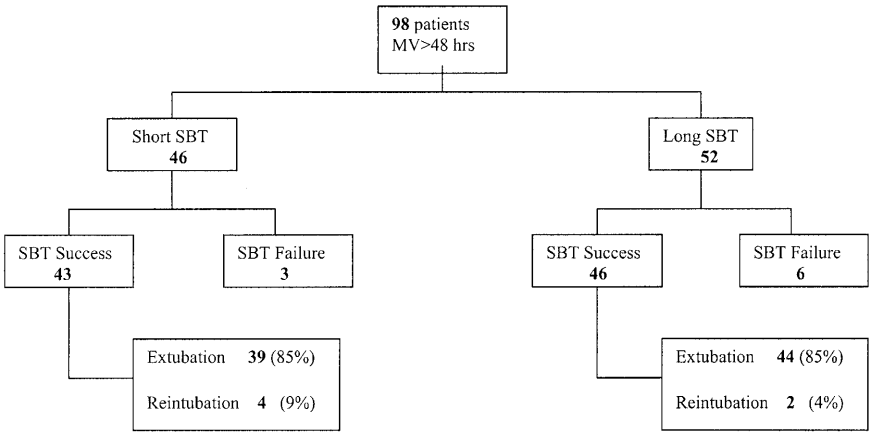

Fig. 1 Distribution of the studied patients after randomization. *SBT* Spontaneous breathing trial

With regard to the weaning strategy two important studies yielded the following common conclusions: firstly, the weaning strategy influences the duration of mechanical ventilation, and, secondly, synchronized intermittent mandatory ventilation is the least efficient method of weaning [9, 10]. Weaning is therefore generally better performed with PSV or the T-tube strategy [9, 10], whereas once-daily and multiple-daily T-tube trials have been demonstrated to be equally effective [10].

In all but one study – the Spanish Lung Failure Collaborative Group study [13] – the SBT duration has received very little attention. In the past it has been arbitrarily set at 2 h [9, 10, 11]. However, the weaning trial is an especially demanding period for the nursing staff, since the patients must be observed very closely. It seems therefore reasonable to shorten the SBT duration. The above trial showed in fact that a 30-min final SBT with a T-piece is as effective in predicting a successful extubation as the usual 2 h trial.

It is not known whether the same results could be obtained with another weaning trial strategy, i.e., PSV. We therefore conducted a prospective protocol-directed weaning study in two miscellaneous groups of mechanically ventilated patients, using PSV as the weaning technique. After obtaining simple readiness criteria for starting the process of liberation, we randomized the patients with target durations of 30 and 120 min. We hypothesized that extubation would be equally successful with the two durations using the selected protocol-directed weaning technique.

Patients and methods

Study location, patients, and criteria for final weaning

The study was conducted between April and December 1999 in the multidisciplinary ICUs (15 beds) of two regional hospitals in southern Switzerland. The investigation was approved by the Cantonal Ethics Committee, and informed written consent was obtained from the next of kin of every patient.

A total of 153 patients were mechanically ventilated for more than 48 h during the study period. Of these, 55 could not be considered due to one of the following exclusion criteria: tracheostomy, terminal weaning, age younger than 16 years, and the requirement of mechanical ventilation to allow organ retrieval due to brain death.

If the internal diameter of the endotracheal tube was less than 8 mm, it was changed for a larger size according to sex and anatomy of the patient. Patients were ventilated in pressure support during the entire weaning period. The levels of inspiratory pressure support (IPS) and positive end-expiratory pressure (PEEP) were progressively reduced depending on the patient's clinical assessment and blood gas monitoring values. A patient was enrolled in the study only when he fulfilled all of the following readiness criteria for the SBT: improvement or resolution of the underlying cause of acute respiratory failure, awake and collaborative (Ramsay sedation score of 2), adequate gas exchange as indicated by a PaO_2/FIO_2 ratio of at least 200 mmHg with a maximal FIO_2 of 0.40, maximal PEEP of 5 cmH_2O, maximal IPS of 12 cmH_2O, maximal ratio of respiratory frequency to tidal volume of 105 breaths min^{-1} l^{-1}, stable hemodynamics without further need of vasoactive agents, core temperature between 36° and 38°C, hemoglobin level higher than 10 g/dl, and no relevant electrolyte disorder. As soon as the patient was ready for the SBT, he or she was randomly assigned to the short (30-min) or the long (120-min) study arm. Randomization was carried out in a blinded fashion using opaque and sealed envelopes.

Protocol

All patients in the study were continuously assessed in view of the readiness criteria. The screening had to be performed in the morning or early afternoon to permit a possible extubation at 5:00 pm at the latest. Sedation was carefully titrated and eventually adjusted during the night to have the patients awake and collaborative on the following morning.

As soon as a patient was considered ready for starting the final SBT, IPS was reduced to 7 cmH_2O while the other ventilator settings (FIO_2, PEEP, trigger sensitivity) were left unchanged. During the SBT the patients were closely observed. Monitoring of respiratory rate (RR), heart rate (HR), systolic arterial blood pressure (SAP), and transcutaneous oxygen saturation (SpO_2) was continuously carried out and recorded every 10 min. Arterial blood gas (ABG) analyses were performed immediately after the beginning and at the end of the SBT.

The trial was terminated if the patient met one or more of the following failure criteria: RR 35 breaths/min or higher, HR 140 beats/min or higher, SAP 180 mmHg or higher, or 90 mmHg or lower, SpO_2 less than 90%, agitation, anxiety, or diaphoresis. Patients who failed the final weaning trial were excluded from the study (SBT failure; Fig. 1). They resumed spontaneous ventilation

Table 1 Characteristics of the patients in the two study groups (*SAPS II* Simplified Acute Physiology Score, *MV* mechanical ventilation, *COPD* chronic obstructive pulmonary disease, *ALI* acute lung injury, *ARDS* acute respiratory distress syndrome)

	30 min (*n*=46)	120 min (*n*=52)	*p*
Age (years)	68±20	65±14	0.1
Gender: M/F	28/18	31/21	0.5/0.2
SAPS II	45±20	43±14	0.6
Duration of MV before randomization (h)	68±81	96±94	0.08
Indication for MV			
Coma	8 (17%)	7 (13%)	
COPD	7 (15%)	8 (15%)	
Postoperative state	6 (13%)	10 (19%)	
Multiple trauma	5 (11%)	6 (12%)	
Sepsis	5 (11%)	6 (12%)	
ALI/ARDS	4 (9%)	5 (9%)	
Heart Failure	3 (7%)	3 (6%)	
Pneumonia, community acquired	2 (4%)	3 (6%)	
Pneumonia, hospital acquired	2 (4%)	2 (4%)	
Neuromuscular disease	1 (2%)	2 (4%)	
Others	3 (7%)	0	

Table 2 Respiratory and ventilatory functional parameters prior to spontaneous breathing trial. (*PEEP* positive end-expiratory pressure, *IPS* inspiratory pressure support, f/V_T ratio of respiratory frequency to tidal volume)

Parameter	30 min (*n*=46)	120 min (*n*=52)	*p*
PaO_2/FIO_2 ratio	295±61 (200–518)	289±79 (200–546)	0.30
f/V_T (breaths min^{-1} l^{-1})	34±20 (6–90)	35±22 (11–107)	0.82
PEEP (cmH_2O)	4.5±1.4 (2–5)	4.5±1.4 (2–5)	0.90
IPS (cmH_2O)	9.7±12.2 (6–12)	9.8±12.9 (6–12)	0.78
FIO_2	0.29±03 (0.25–0.40)	0.28±.03 (0.21–0.40)	0.93

with the same settings as prior to SBT and any further weaning attempt was at the discretion of the attending physician. Those who successfully completed the 30-min or the 120-min period were immediately extubated. Supplemental oxygen was then administered by nasal prongs or a face mask to obtain a SpO_2 of at least 90%. Extubation failure was defined as reintubation within 48 h. The follow-up was continued until discharge from the hospital or death. The reasons for reintubation and any other relevant complication were prospectively recorded, and the causes of relapse were listed as recommended by Esteban et al. [13].

Statistical analysis

Values are given as mean±SD. Categorical variables were analyzed by χ^2 or Fisher's exact test. Differences on continuous variables were compared by Student's *t* test or the Mann-Whitney *U* test depending on variable's distribution. Analysis of variance or Kruskall-Wallis tests were used for comparisons between the trial failure groups, the successful extubation groups, and the reintubation groups.

Results

The study thus included 98 patients. These were randomized to the short period (*n*=46) or the long period (*n*=52) of SBT. Patient demographics and baseline data in the two treatment arms were similar with regard to age, gender, Simplified Acute Physiology Score II (SAPS II), reasons for mechanical ventilation, and period of ventilatory support before starting the SBT (Table 1). Mean PaO_2/FIO_2 ratio, respiratory frequency to tidal volume ratio, PEEP level, and IPS values did not differ significantly in the groups before starting the final trial (Table 2).

In the 30-min group 43 patients (93%) showed no signs of poor tolerance during or at the end of the SBT and were therefore successfully extubated. Four of them (9%) had to be reintubated within 48 h due to upper-airway obstruction (*n*=2), impaired clearance of secretions (*n*=1), or worsening hypoxemia (*n*=1). Three patients (7%) did not tolerate SBT, according to our criteria, and resumed the previous ventilatory support after a mean duration of 17±6.1 min (Fig. 1). In the 120-min group 46 patients (88%) successfully completed the trial and were immediately extubated. Reintubation within 48 h occurred in 2 (4%) of them due to upper-airway obstruction (*n*=1) or impaired clearance of secretions (*n*=1). Six patients (12%) failed to complete the SBT, which lasted a mean of 32±10.9 min and therefore remained intubated (Fig. 1). In the short and long SBT arms there was the same percentage (85%) of patients who remained extubated for 48 h or longer. The rate of reintubation was similar in the two groups (9% in the 30-min vs. 4% in the 120-min period arm, n.s.), as was the SBT failure rate (7% in the short vs. 12% in the long arm, n.s.; Fig. 1).

The reasons for failing the 30-min SBT were SpO_2 less than 90% (*n*=1), RR 35 breaths/min or higher (*n*=1),

Table 3 Mortality and length of stay (*LOS*) in the study groups

	30 min (*n*=46)	120 min (*n*=52)	*p*
ICU mortality	3 (6.5%)	2 (3.8%)	0.66
In hospital mortality	9 (19.5%)	9 (17.5%)	0.97
LOS in ICU (days)	6±7	7±7	0.20
LOS in hospital (days)	20±14	25±14	0.45

and agitation (*n*=1). The 120-min SBT was prematurely terminated because of SpO_2 less than 90% (*n*=2), agitation (*n*=2), RR 35 breaths/min or higher (*n*=1), and diaphoresis (*n*=1). There were no statistically significant differences at the end of the trail between patients considered SBT failures and those considered SBT successes in regard to SaO_2 (94±1.7% vs. 95±2.5%) and RR (21.3±8.3 vs. 17.3±5.5 breaths/min).

Mortality and length of stay (LOS) in ICU and hospital did not differ significantly between the two groups (Table 3). However, the mortality rate was higher among patients requiring reintubation than in those who were successfully extubated (33% vs. 3.6%; p=0.03). The ICU LOS in reintubated patients was markedly longer than in the successfully extubated (17±5 vs. 6±5 days; $p<0.001$). We observed no direct or immediate complications due to reintubation, and there were no unplanned extubations during the study.

Discussion

This study confirms that a protocol-directed SBT with PSV allows shortening of the trial duration from 120 to 30 min without observing any differences in rates of successful extubations, reintubations, or mortality. Our findings are in agreement with those of Esteban and colleagues [13], who compared the clinical outcome in spontaneously breathing patients weaned with the T-tube technique and the same two target durations. They reported that in the short and long trial groups, respectively, 87.8% and 84.8% of patients completed the trial without distress and were extubated, whereas 13.5% and 13.4% required reintubation within 48 h. Furthermore, the ICU mortality rates did not differ significantly between the 30- and 120-min trial groups (13% and 9%) nor did the in-hospital mortality rates (19% and 18%). The proportion of successful extubations was similar in our study groups as in the far larger investigation of the Spanish Lung Failure Collaborative Group [13]. However, the rates of reintubation and ICU mortality were slightly lower in the present investigation.

To explain these differences we may consider the reasons for and duration of mechanical ventilation, mean SAPS II value, and ICU LOS. The case mix of our study population was similar to that in the study by Esteban et al. [13] but ventilatory support before SBT was longer in the Spanish trial (5.5 vs. 3.5 days). In spite of a higher SAPS II in our study (44 vs. 37) we observed a shorter ICU LOS (6.5 vs. 11 days). Special points in our study protocol was the continuous screening for the readiness criteria and the careful titration of the sedation to minimize the global intubation period. We believe that shortening the ventilatory support prior to the final SBT reduced subsequent morbidity, therefore decreasing ICU mortality and LOS and probably reintubation rate.

In contrast, Esteban et al. [13], who performed the weaning trial with the T-piece and designed partially different readiness criteria, our patients were not disconnected from the ventilator and were finally weaned by the PSV technique (7 cmH_2O). PSV is our preferred weaning method, and it was selected for this study because of its easy handling and feasibility. The use of an IPS at the end of the weaning period is probably needed mainly to compensate for the resistance and the dead space of the ventilator circuit and not of the endotracheal tube. Straus et al. [14] have shown that the work of breathing shortly after a 2-h T-piece trial is identical before and after extubation. Therefore the anatomical characteristics of the upper airway after extubation are considered to be similar to those while the endotracheal tube is in place. Moreover, pressure support improves oxygen consumption by the respiratory muscles during weaning [15]. Several studies have shown that this technique may compensate for the additional muscle work although the compensatory IPS levels may range from 3 to 14 cmH_2O [10, 15, 16]. According to our results, an IPS value of 7 cmH_2O is suitable for achieving extubation in the great majority of patients. T-tube and pressure support techniques, however, are both considered proper methods for a successful final weaning, and no study so far has demonstrated the superiority of one method over the other.

Patients who required reintubation had an approximately nine times higher mortality rate than those who were successfully extubated. These data are similar to those reported in the recent literature [13, 17]. As pointed out by other authors [13, 17, 18], we believe that the poorer prognosis of this subgroup is an expression of the underlying disease (e.g., more severely ill patients) and not of the failed extubation per se. In contrast to Esteban et al. [13] and probably due to the small number of patients who failed the SBT, we found no significant difference in the mean values of the objective parameters at the end of the SBT between the success and failure subgroups.

Recent investigations have shown that nurses using protocol guidance wean patients from mechanical ventilation safely and more quickly than a medical team following the traditional practice of physician-directed weaning [11, 12]. In Switzerland ICUs are relatively closed units, and specialized nurses have some autonomy in the strategy and handling of ventilatory support and weaning. Our nursing staff was involved in the study and

autonomously guided the entire weaning period, including the SBT, according to the weaning protocol. Since the nursing section was not expected to take part in the study, we do not have objective data on the efficacy or role of nurses or respiratory therapists in protocol-directed weaning. Further studies are required to investigate this interesting topic.

For safety reasons our investigation was programmed such that all relevant screening, decisions, and weaning trials had to be performed in the morning or early afternoon, with extubation at 5:00 pm at the latest. After this point patients were not extubated, and the SBT was postponed to the next morning. This is a typical situation in most ICUs, where extubation is felt to be a daytime responsibility. This means that patients remain intubated longer than necessary, with growing risks of ventilator-associated problems (prolonged sedation, unplanned extubation, pneumonia) as well as increased need of personal resources and devices. We question this behavior, but we did not address this point in our study. For this reason we can only speculate that the good results obtained might be extrapolated for patients ready to be extubated during the evening or the night. Further trials on this question as well as investigating the potential advantages in outcome of a standardized time-assessed SBT compared with a prompt extubation are warranted.

The main limitation of this study is the relatively small number of patients enrolled in the protocol, which reduces the power of the analysis. Nevertheless some factors support the credibility of results obtained in the 30-min trial group. First, the reintubation rate of 9% is similar to or even slightly lower than the rates constantly declared in the literature [5, 9, 10, 12, 13]. Second, as demonstrated by Esteban et al. [13], the duration of the T-tube trial can be safely shortened from 120-min to 30-min. Finally, two studies have found the two weaning methods (T-tube and PSV) to be of equal value [5, 19].

In conclusion, for this subset of patients our findings add the following information to the ongoing discussion about weaning strategies: with the outlined readiness criteria a 30-min weaning trial with PSV of 7 cmH_2O is equally as effective as a four times longer 120-min trial for identifying patients who can be safely extubated. Considering that the short trial is as effective as the long one, the traditional 2-h SBT does not seem to be further justified.

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