

Impact of a mechanical ventilation weaning protocol on the extubation failure rate in difficult-to-wean patients^{*,**}

Impacto de um protocolo de desmame de ventilação mecânica na taxa de falha de extubação em pacientes de difícil desmame

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Abstract

Objective: To determine whether the predictive accuracy of clinical judgment alone can be improved by supplementing it with an objective weaning protocol as a decision support tool. **Methods:** This was a multicenter prospective cohort study carried out at three medical/surgical ICUs. The study involved all consecutive difficult-to-wean ICU patients (failure in the first spontaneous breathing trial [SBT]), on mechanical ventilation (MV) for more than 48 h, admitted between January of 2002 and December of 2005. The patients in the protocol group (PG) were extubated after a T-piece weaning trial and were compared with patients who were otherwise extubated (non-protocol group, NPG). The primary outcome measure was reintubation within 48 h after extubation. **Results:** We included 731 patients—533 (72.9%) and 198 (27.1%) in the PG and NPG, respectively. The overall reintubation rate was 17.9%. The extubation success rates in the PG and NPG were 86.7% and 69.6%, respectively ($p < 0.001$). There were no significant differences between the groups in terms of age, gender, severity score, or pre-inclusion time on MV. However, COPD was more common in the NPG than in the PG (44.4% vs. 17.6%; $p < 0.001$), whereas sepsis and being a post-operative patient were more common in the PG (23.8% vs. 11.6% and 42.4% vs. 26.4%, respectively; $p < 0.001$ for both). The time on MV after the failure in the first SBT was higher in the PG than in the NPG (9 ± 5 days vs. 7 ± 2 days; $p < 0.001$). **Conclusions:** In this sample of difficult-to-wean patients, the use of a weaning protocol improved the decision-making process, decreasing the possibility of extubation failure.

Keywords: Ventilator weaning; Ventilation; Ventilators, mechanical.

Resumo

Objetivo: Determinar se a acurácia preditiva do julgamento clínico isolado pode ser melhorada com o uso suplementar de um protocolo de desmame objetivo como ferramenta de suporte para a tomada de decisão. **Métodos:** Estudo prospectivo multicêntrico de coorte realizado em três UTIs clínicas/cirúrgicas. Foram incluídos no estudo todos os pacientes de desmame difícil (falha no primeiro teste de ventilação espontânea [TVE]), sob ventilação mecânica (VM) por mais de 48 h, admitidos em uma das UTIs entre janeiro de 2002 e dezembro de 2005. Os pacientes do grupo protocolo (GP) foram extubados após teste de tubo T de acordo com um protocolo de desmame e comparados com o grupo de pacientes extubados sem o uso do protocolo (GNP). O desfecho primário foi a taxa de reintubação em até 48 h após a extubação. **Resultados:** Foram incluídos 731 pacientes — 533 (72,9%) no GP e 198 (27,1%) no GNP. A taxa global de reintubação foi de 17,9%. As taxas de sucesso da extubação no GP e no GNP foram 86,7% e 69,6%, respectivamente ($p < 0,001$). Não houve diferenças significativas entre os grupos quanto a idade, gênero, escore de gravidade e tempo de VM antes da inclusão. Entretanto, DPOC foi mais frequente no GNP que no GP (44,4% vs. 17,6%; $p < 0,001$), ao passo que pacientes sépticos e em pós-operatório foram mais comuns no GP (23,8% vs. 11,6% e 42,4% vs. 26,4%, respectivamente; $p < 0,001$ para ambos). O tempo de VM após a falha no primeiro TVE foi maior no GP que no GNP (9 ± 5 dias vs. 7 ± 2 dias; $p < 0,001$). **Conclusões:** Nesta amostra de pacientes de desmame difícil, o uso de um protocolo de desmame melhorou o processo decisório, reduzindo a possibilidade de falha na extubação.

Descritores: Desmame do respirador; Ventilação; Ventiladores mecânicos.

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Introduction

Although mechanical ventilatory support is a critical life sustaining modality for patients with respiratory failure, a delay in the weaning process increases morbidity, as well as ICU costs.

⁽¹⁾ Aggressiveness in discontinuing mechanical ventilation (MV) should be balanced against the possibility of complications due to premature discontinuation, including difficulties in reestablishing the artificial airway and compromised gas exchange.^(1,2) Extubation failure is associated with adverse outcomes, including higher in-hospital mortality, longer hospital stay, and higher costs, as well as greater need for tracheotomy and transfer to post-acute care.^(2,3) Esteban et al.⁽⁴⁾ estimated that a patient on MV spends as much as 42% of the time on the withdrawal process and that this proportion is likely to be much higher in patients with slowly resolving lung disease. Although an acceptable rate of reintubation has yet to be determined, it has been reported that it should range from 5% to 15%.^(1,5)

The process of discontinuing mechanical ventilatory support begins by recognizing that the patient has begun to recover from the problems that required ventilatory support. Criteria by which clinicians decide whether the patient has sufficiently recovered in order to tolerate the withdrawal of ventilatory support have neither been clearly defined nor prospectively evaluated in a randomized controlled trial. Instead, various combinations of subjective and objective assessment criteria that might be surrogate markers of recovery have been employed.⁽⁶⁻¹²⁾ Many of these physiological predictors have provided major insights into the mechanisms of weaning failure. However, 20-30% of patients have been considered difficult to wean from MV.^(3,13) From a clinical standpoint, trial results have been disappointing. Extubation failure, defined as the need for reintubation within 48 h following extubation, is multifactorial, and a combination of indices might have greater predictive accuracy.

It has been suggested that protocols to manage weaning and the release of patients from mechanical ventilatory support could reduce the time spent on MV.^(14,15) In a recent meta-analysis, it was concluded that there is evidence of a reduction in the duration of MV and weaning, as well as in the length of ICU stay, when weaning protocols are used.⁽¹³⁾ However, even when research clearly supports a change in this

approach, it is very difficult to convince physicians to change their practice and management styles. In addition, the heterogeneous input from weaning research contributes to potential confounding factors, such as sedation protocols and the new weaning classification, i.e., difficult-to-wean patients. This suggests that different weaning approaches can be used in order to manage simple-to-wean patients and those with difficult or prolonged weaning.⁽¹⁶⁾ After the publication of a consensus in 2001, we decided to gather information on the weaning steps in order to validate the findings by applying a protocol for extubation. Therefore, our assumption is that the application of the protocol can reduce extubation failure in difficult-to-wean patients, defined as patients who fail their first weaning trial.^(16,17)

The objective of the present study was to determine whether the predictive accuracy of clinical judgment alone can be improved by supplementing it with an objective decision support tool.

Methods

This was a multicenter prospective double-cohort clinical study approved by the research ethics committees of three institutions.

The study was conducted between January of 2002 and December of 2005 in three medical/surgical ICUs (three tertiary care hospitals in the city of Porto Alegre, Brazil). There were structured daily shifts in the three ICUs, and the investigators were notified whenever a difficult-to-wean patient was identified. Two of the ICUs admit patients from the public health system, and the three are teaching ICUs.

Between January of 2002 and December of 2005, 3,722 patients were admitted to one of the three ICUs. Of those, 2,315 (62%) were on MV for more than 48 h. The study involved 731 difficult-to-wean patients, defined as those who failed the first spontaneous breathing trial (SBT). The patients were older than 18 years of age and were critically ill, having received mechanical ventilatory support for more than 48 h by means of one of the following models of mechanical ventilators: Servo 900C® (Siemens Elema AB, Solna, Sweden); Servo 300® (Siemens Elema AB); Evita 2-Dura® (Dräger Medical AG, Lubeck, Germany); or Evita 4® (Dräger Medical AG). The patients were extubated after a successful SBT. In order to be extubated, all of the patients had to meet

the following criteria: improvement or resolution of the underlying cause of acute respiratory failure; adequate gas exchange, characterized by a $\text{PaO}_2 > 60$ mmHg, an $\text{FiO}_2 \leq 0.4$, and a positive end-expiratory pressure ≤ 5 cmH₂O; and no further need for vasoactive or sedative agents. A patient was presumptively eligible to be included in the study when the ICU staff and the attending physician agreed that the patient was stable and ready to be weaned from MV. The patient was then submitted to an SBT and, in the event of failure, was included in the study.

At that moment, the extubation protocol was presented to the attending physician, being implemented in case the physician agreed to use it. The patients submitted to the protocol formed the protocol group. In case the attending physician declined to use the protocol, extubation was performed on the basis of clinical judgment. The patients who were thus extubated formed the non-protocol group.

For all of the patients, the ventilator settings, respiratory parameters, and arterial blood gas results were recorded prior to the weaning process. Tracheostomized patients and those who never gave written informed consent were excluded from the study. Extubation failure was defined as the need for reintubation within 48 h after extubation. Non-invasive MV was used in both groups, and its use did not characterize extubation failure. In the three institutions, non-invasive MV is a routine procedure used in order to prevent post-extubation failure in patients with COPD or heart failure. The primary outcome measure was reintubation within the first 48 h after extubation.

Our institutional protocol was developed by a multidisciplinary team (including physicians, nurses, and physiotherapists) and required no additional support staff in order to be implemented in the three ICUs. The three ICUs used the same protocol (implemented in 2001 in all of them). After the interruption of mechanical ventilatory support, the patients started an SBT by means of a humidified T-piece and as much oxygen as necessary to achieve an $\text{SpO}_2 \geq 90\%$, as determined by pulse oximetry. In the beginning of the SBT, the frequency-to-tidal volume ratio (f/V_T) and MIP were measured. The f/V_T was measured with a respirometer model 295 (Anesthesia Associates Inc., San Marcos, CA, USA) for 1 min, whereas MIP was measured with a manometer (Famabras, Itaquaquecetuba, Brazil) and was

defined as the most negative value produced by three consecutive inhalation trials against a unidirectional valve.⁽¹⁸⁾ Patients with an $f/V_T < 105$ and an MIP < -30 cmH₂O underwent 30-120 min of SBT, being extubated after showing adequate clinical tolerance to the SBT. Clinical tolerance was defined as follows: an RR < 35 breaths/min; an $\text{SpO}_2 > 90\%$; an HR < 130 bpm with less than 20% change from baseline values; no change in mental status (drowsiness, coma, agitation, or anxiety); no signs of respiratory discomfort; no diaphoresis; and no signs of difficulty in breathing (use of accessory respiratory muscles or paradoxical thoracoabdominal movement). Patients with an $f/V_T \geq 105$, an MIP ≥ -30 cmH₂O, or clinical intolerance to the SBT returned to MV, and the weaning trial was repeated every 24 h.

In the non-protocol group, patients were weaned either with pressure support ventilation without tube compensation or with a T-piece trial, being extubated at the discretion of the attending intensivist. The duration of the T-piece trial ranged from 10 min to 180 min (being determined by the attending physician), and the pressure support level was reduced to 10 cmH₂O or less prior to extubation. Ventilatory parameters such as f/V_T and MIP were not measured in the non-protocol group. The decision to extubate was based on the clinical judgment of the attending physician, and SBT tolerance was defined as the absence of signs of respiratory discomfort, diaphoresis, or increased work of breathing, including the use of accessory respiratory muscles or paradoxical thoracoabdominal movement.

Data were expressed as means and standard deviations or as proportions. Baseline differences between the two groups were analyzed by the Student's t-test or the Mann-Whitney test for continuous variables and the chi-square test for categorical variables, including Fisher's exact test. Pearson's and Spearman's correlation coefficients were used for correlations of parametric and non-parametric variables, respectively. For all statistical analyses, we used the Statistical Package for the Social Sciences, version 13.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

Results

The study sample comprised 731 difficult-to-wean patients. Of those, 533 (72.9%) were included in the protocol group and 198 were

included in the non-protocol group. The baseline characteristics of the patients are shown in Table 1. The groups were similar with respect to age, gender, number of days on MV prior to the weaning trial, Acute Physiology and Chronic Health Evaluation II (APACHE II) score at admission, ventilatory parameters, and blood gas results. Post-operative patients were more frequently included in the protocol group than in the non-protocol group (42.4% vs. 26.4%; $p < 0.001$), as were septic patients (23.8% vs. 11.6%; $p < 0.001$). In contrast, COPD patients were more frequently included in the non-protocol group than in the protocol group (44.4% vs. 17.6%; $p < 0.001$). Coronary artery disease was more common in the protocol group than in the non-protocol group (12.1% vs. 5.0%; $p = 0.004$; Table 1).

Of the 533 patients included in the protocol group, 226 (42.4%) were post-operative patients, 127 (23.8%) had been admitted with sepsis, and 94 (17.6%) had COPD. The mean age was 63 ± 23

years, the mean APACHE II score at admission was 18 ± 10 , and 67.9% were male. Extubation failure occurred in 71 patients (13.3%), of whom 26 (36.6%) had COPD (Table 1).

Of the 198 patients included in the non-protocol group, 52 (26.4%) were post-operative patients, 23 (11.6%) had been admitted with sepsis, and 88 (44.4%) had COPD. The mean age was 60 ± 18 years, the mean APACHE II score was 19 ± 9 , and 51.0% were male (Table 1). In addition, 134 patients were weaned with a T-piece trial, with an extubation failure rate of 30.5%, whereas 64 were weaned with pressure support ventilation, with an extubation failure rate of 29.6%.

The extubation failure rate was significantly higher in the non-protocol group than in the protocol group (30.4% vs. 13.3%; $p < 0.001$; Table 2). The causes of reintubation were post-extubation upper airway obstruction (in 4%), aspiration or excessive secretions (in 11%),

Table 1 – Baseline characteristics of the patients.^a

Characteristic	Protocol group			Non-protocol group		
	All	ES	EF	All	ES	EF
	(n = 533)	(n = 462)	(n = 71)	(n = 198)	(n = 138)	(n = 60)
Age, years ^b	63 ± 23	61 ± 20	63 ± 18	60 ± 18	58 ± 20	61 ± 15
Male gender	362 (67.9)	311 (67.3)	51 (71.8)	101 (51.0)	60 (55.5)	41 (45.5)
APACHE II score ^b	18 ± 10	17 ± 11	18 ± 9	19 ± 9	19 ± 8	18 ± 11
Cause of ARF						
COPD exacerbation	94 (17.6)	68 (14.7)	26 (36.6)	88 (44.4)	59 (42.8)	29 (48.3)
Neurological disorder	86 (16.2)	76 (16.5)	10 (14.1)	35 (17.6)	24 (17.4)	11 (18.3)
Sepsis	127 (23.8)*	112 (24.3)***	15 (21.2)	23 (11.6)	17 (12.3)	6 (10.0)
Post-operative ARF	226 (42.4)*	206 (44.5)****	20 (28.1)	52 (26.4)	38 (27.5)	14 (23.4)
Comorbidities						
Diabetes	60 (11.2)	45 (9.7)****	15 (21.1)	15 (7.5)	10 (7.2)	5 (8.3)
End-stage chronic renal failure	34 (6.3)	21 (4.5)***	13 (18.3)	4 (2.0)	3 (2.1)	1 (1.6)
Hypertension	103 (19.3)	74 (16)***	29 (40.8)	26 (13.1)	18 (13.0)	8 (13.3)
Ischemic heart disease	65 (12.1)**	49 (10.6)****	16 (22.5)	10 (5.0)	7 (5.1)	3 (5.0)
Cirrhosis	6 (1.1)	4 (0.9)	2 (2.8)	2 (1.0)	2 (1.4)	0 (0.0)
Cancer	36 (6.7)	23 (5.0)	13 (18.3)	7 (3.5)	6 (4.3)	3 (5.0)
Ventilatory (PSV) and ABG parameters ^b						
PaO ₂ , mmHg	80 ± 23	79 ± 20	82 ± 26	83 ± 19	82 ± 20	85 ± 16
PaCO ₂ , mmHg	32 ± 5	31 ± 4	33 ± 6	32 ± 6	31 ± 4	33 ± 5
RR, breaths/min	22 ± 6	21 ± 4 ****	24 ± 8	23 ± 3	22 ± 4 ***	25 ± 2
MV prior to weaning trial, days ^b	5.0 ± 1.4	4.4 ± 2.0 ***	6.0 ± 3.3	5.2 ± 2.1	4.9 ± 2.3 ***	6.7 ± 2.9

ES: extubation success; EF: extubation failure; APACHE II: Acute Physiology and Chronic Health Evaluation II; ARF: acute respiratory failure; PSV: pressure support ventilation; ABG: arterial blood gas; MV: mechanical ventilation. ^aValues expressed as n (%), except where otherwise indicated. ^bValues expressed as mean $\pm$ SD. * $p < 0.001$ vs. non-protocol group. ** $p = 0.004$ vs. non-protocol group. *** $p < 0.001$ vs. EF. **** $p < 0.05$ vs. protocol group.

Table 2 – Outcomes.^a

Outcome	PG	NPG	p
	(n = 533)	(n = 198)	
Extubation failure	71 (13.3)	60 (30.4)	< 0.001
Non-invasive mechanical ventilation use	174 (32.6)	89 (44.9)	0.02
Number of days in the ICU ^b	11 ± 4	8 ± 3	< 0.001
Number of days on mechanical ventilation ^{b,c}	9 ± 5	7 ± 2	< 0.001
Mortality in the ICU	24 (4.5)	24 (12.1)	0.001

PG: protocol group; and NPG: non-protocol group. ^aValues expressed as n (%), except where otherwise indicated. ^bValues expressed as mean ± SD. ^cNumber of days on mechanical ventilation computed after failure in the first spontaneous breathing trial and the first extubation.

encephalopathy (in 15%), and respiratory failure (in 70%). The duration of MV prior to the weaning trial (until the first failed SBT) was similar between the protocol and non-protocol groups (5.0 ± 1.4 days vs. 5.2 ± 2.1 days; p > 0.05). However, the total number of days on MV (after the first failed SBT until extubation) was higher in the protocol group than in the non-protocol group (9 ± 5 days vs. 7 ± 2 days; p < 0.001), as was the length of ICU stay (11 ± 4 days vs. 8 ± 3 days; p < 0.001). Mortality was higher in the non-protocol group than in the protocol group (12.1% vs. 4.5%; p = 0.001). Table 2 shows the outcomes of the study.

The extubation failure rate in the 182 COPD patients was 30.2%. Non-invasive MV was more common in the patients in whom extubation failed than in those in whom extubation was successful (87.2% vs. 75.4%; p = 0.02). In an attempt to avoid reintubation, non-invasive MV was used for 6–24 h/day, for a maximum of 72 h.

Discussion

The present study included a non-selected population of patients in three medical/surgical ICUs and reflected our everyday clinical practice. The main finding was that the use of an extubation protocol resulted in a reduction in the extubation failure rates in difficult-to-wean patients.

Extubation failure is known to have a significant independent association with increased in-hospital mortality among general surgical and medical patients.^(11,19–21) In addition, unsuccessful extubation significantly prolongs the duration of MV and the length of ICU and hospital stays, as well as increasing the need for tracheotomy.^(2,20) Protocols are designed to wean patients from MV safely and efficiently, reducing unnecessary or harmful variations in this approach. There is evidence that, under certain circumstances,

weaning protocols can reduce the duration of MV.^(14,15) However, weaning indexes can be poor predictors of extubation outcome in simple-to-wean patients.^(21,22) We believe that a combination of indexes might have greater predictive accuracy for difficult-to-wean patients, and our protocol included a combination of such indexes (f/V_T, MIP, and clinical tolerance to the SBT).

In our study, weaning failure was more common in the non-protocol group, in which mortality was higher. However, because of the stricter extubation criteria, the patients in the protocol group spent more time on MV and had longer ICU stays, which might explain the higher ICU mortality in the non-protocol group. Blackwood et al.⁽²³⁾ showed that weaning based on institutional protocols did not reduce the duration of MV and that weaning was not associated with increased reintubation rates or ICU mortality. Tanios et al.⁽²⁴⁾ demonstrated that including f/V_T in a protocol prolonged weaning time (2.0 vs. 3.0 days; p = 0.04); in addition, that weaning predictor neither conferred survival benefit nor reduced the incidence of extubation failure.⁽²⁵⁾ A multicenter randomized controlled trial with concealed allocation compared the usual care for weaning with computer-driven weaning, and the investigators found a reduction in weaning time (5 days vs. 3 days; p = 0.01) and in the total duration of MV (12.0 days vs. 7.5 days; p = 0.003); however, the reintubation rates did not differ (23% vs. 16%; p = 0.4).⁽²⁶⁾ Kollef et al.⁽²⁷⁾ argued that protocol-guided weaning from MV is safe and leads to extubation more rapidly than does physician-directed weaning. In their study, Cox proportional hazards regression analysis, adjusting for other covariates, showed that the rate of successful weaning was significantly higher in the patients receiving protocol-directed weaning than in those receiving physician-directed weaning

(risk ratio = 1.31; 95% CI: 1.15-1.50; $p = 0.03$), although in-hospital mortality was similar (22.3% vs. 23.6%; $p = 0.77$). Marelich et al.^[28] determined the effect of a single ventilator management protocol used in medical and surgical ICUs on the duration of MV and on the incidence of ventilator-associated pneumonia. The duration of MV decreased from a median of 124 h in the control group to 68 h in the protocol group ($p = 0.0001$) with no adverse effects on patient outcomes. In comparison with the results of that study, our results showed a lower reintubation rate (13.3%) in the multidisciplinary protocol group.

Unsuccessful extubation has been reported to occur in up to 20% of patients.^(1,7,14,21,23) Ely et al.⁽¹⁴⁾ reported that the relative risk of successful extubation in their protocol group was 2.3 (95% CI: 1.55-2.92; $p < 0.001$). Factors that appear to increase the risk are the type of patient (e.g., medical patients), age > 70 years, higher severity of illness at weaning onset, use of continuous intravenous sedation, and longer duration of MV prior to extubation.⁽¹⁴⁾ In the present study, COPD was found to be a major factor influencing the use of the extubation protocol, a finding that is in agreement with those of various studies.^(15,19,21) However, the overall rate of reintubation in the non-protocol group was high (30.4%), which suggests that many of those patients would have been prematurely considered for extubation by many experienced critical care physicians. Nevertheless, ventilatory and arterial blood gas parameters were not different between the two groups.

The strengths of the present study are the large number of patients recruited and its multicenter nature, whereas the major limitation is the study design. This was not a study on weaning; the focus was on extubation in patients in whom the SBT was successful. We did not randomly assign the weaning method. Therefore, the decision to use the protocol or not might have correlated with unmeasured outcomes. The lack of blinding might have introduced an allocation bias, meaning that the attending physicians were more reluctant to allocate COPD patients to the protocol group, although this might have been compensated by the higher number of septic patients in that group. In the non-protocol group, the criteria for tolerance to the T-piece trial and for ventilatory support were determined by the attending physician, whereas, in the protocol

group, the strict criteria adopted minimized the subjectivity of the medical decisions.

A previous trial⁽²⁹⁾ showed that non-invasive MV facilitated early extubation and improved the outcome in selected patients. In our study, non-invasive MV was used in the protocol group (in accordance with the weaning protocol) and in the non-protocol group (depending on the decision of the attending physician). Non-invasive MV was more commonly used in the non-protocol group, especially in the patients with COPD. However, it was not the purpose of the present study to assess the use of non-invasive MV during the weaning process.

The implementation of an extubation protocol reduced the reintubation rate in this specific sample of difficult-to-wean patients, without reducing the duration of MV. Protocols should be developed and implemented by multidisciplinary teams. Protocols should never replace clinical judgment; rather, they should be used in order to complement it. Further studies on the impact of protocol-based weaning are needed to determine the optimal management of specific populations, as well as to validate weaning predictors used in extubation protocols.

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