# Weaning From Mechanical Ventilation

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**Objectives:**

- To review the frequency of weaning failure
- To discuss the logic of weaning, *ie*, questions to ask when approaching the ventilated patient
- To assess available predictors of weaning success and failure
- To describe the techniques of weaning and the evidence supporting their use
- To understand special considerations in weaning, *eg*, auto-positive end-expiratory pressure, imposed work of breathing, cardiac ischemia, the importance of psychological factors, routine interruption of sedation and of a systematic approach to weaning

**Key words:** weaning; mechanical ventilation; work of breathing; auto-positive end-expiratory pressure; pressure support; T-piece

## Introduction

Weaning from mechanical ventilation is the process of freeing the patient from dependence on mechanical ventilatory assistance. The use of the term "weaning" must be distinguished from the term "extubation," which is the removal of the endotracheal tube. As is obvious at the bedside, but sometimes vague in studies that describe the outcomes of ventilated patients, the criteria for weaning differ from those of extubation, as some patients may be able to support normal ventilation but still require an endotracheal tube to provide airway protection.

This chapter will first review the frequency with which weaning fails, and will then discuss the weaning process, beginning with the logic of weaning. A discussion of weaning predictors follows, with emphasis on predictors of weaning success and of weaning failure. Available weaning predictors are assessed critically with specific attention to their diagnostic performance. Techniques of weaning are reviewed, followed by an analysis of available studies regarding the preferred approach to weaning patients from mechanical ventilation. Finally, special considerations in weaning, such as work of breathing measurements, the role of auto-positive end-expiratory pressure (PEEP), psychological factors, and management of sedation are addressed.

In the context that evidence-based guidelines for weaning and discontinuing ventilatory support were issued in late 2001 by a collective task force of the American College of Chest Physicians, the American Association for Respiratory Care, and the American College of Critical Care Medicine.[1] These guidelines are presented (Table 1) and cited where appropriate.

## Logic of Weaning: Questions To Ask

The process of weaning proceeds by addressing two sequential questions: a) Is the patient a candidate to begin weaning? b) If the patient is deemed a candidate to wean, is weaning likely to succeed? This logic is reflected in 1 and 2 of the available evidence-based guidelines on weaning (Table 1). In this context, to initiate weaning, the following conditions must be satisfied:

*Recommendations*

- Improvement in the underlying process causing respiratory failure
- Adequacy of mental status and muscular strength, including
  - Resolution of the effects of sedating and paralyzing medications
  - Wakefulness sufficient to allow cooperation in weaning and to allow subsequent extubation, as well as ability to clear and handle secretions
- Hemodynamic stability, generally considered to be resolution of sepsis or the need for pressor support
- Normality of acid-base and electrolyte status, with special attention given to assuring restoration of baseline acid-base balance (*ie*, allowing hypercapnia if chronically present and avoiding new metabolic alkalosis) and to assuring the normality of electrolytes that affect muscle function (*eg*, phosphate, calcium, and potassium)
- Nutritional repletion
- Adequacy of oxygenation, *eg*, $Pa_{O_2}$ exceeding 60

**Table 1.** *Recommendations from the Task Force for Evidence-Based Guidelines for Weaning and Discontinuing Ventilatory*

***Recommendation 1:*** In patients requiring mechanical ventilation for > 24 hours, a search for all the causes that may be contributing to ventilatory dependence should be undertaken. This is particularly true in the patient who has failed attempts at withdrawing the mechanical ventilatory. Reversing, all possible ventilatory and non-ventilatory issues should be an integral part of the ventilatory discontinuation process.

***Recommendation 2:*** Patients receiving mechanical ventilation for respiratory failure should undergo a formal assessment of discontinuation potential if the following criteria are satisfied:

1. Evidence for some reversal of the underlying cause for respiratory failure.
2. Adequate oxygenation (*eg*, $Pa_{O_2}/F_{IO_2}$ ratio > 150 to 200; requiring positive end-expiratory pressure [PEEP] $\leq$ 5 to 8 cm $H_2O$; $F_{IO_2} \leq 0.4$ to 0.5); and pH (*eg*, $\geq$ 7.25);
3. Hemodynamic stability, as defined by the absence of active myocardial ischemia and the absence of clinically significant hypotension (*ie*, a condition requiring no vasopressor therapy or therapy with only low-dose vasopressors such as dopamine or dobutamine, < 5 μg/kg/min); and
4. The capability to initiate an inspiratory effort.

The decision to use these criteria must be individualized. Some patients not satisfied all of the above criteria (*eg*, patients with chronic hypoxemia values below the thresholds cited) may be ready for attempts at the discontinuation of mechanical ventilation.

***Recommendation 3:*** Formal discontinuation assessments for patients receiving mechanical ventilation for respiratory failure should be performed during spontaneous breathing rather than while the patient is still receiving substantial ventilatory support. An initial brief period of spontaneous breathing can be used to assess the capability of continuing onto a formal spontaneous breathing trial (SBT). The criteria with which to assess patient tolerance during SBTs are the respiratory pattern, the adequacy of gas exchange, hemodynamic stability, and subjective comfort. The tolerance of SBTs lasting 30 to 120 minutes should prompt consideration for permanent ventilator discontinuation.

***Recommendation 4:*** The removal of the artificial airway from a patient who has successfully been discontinued from the ventilatory support should be based on assessments of airway patency and the ability of the patient to protect the airway.

***Recommendation 5:*** Patients receiving mechanical ventilation for respiratory failure who fail an SBT should have the cause for the failed BST determined. Once reversible causes for failure are corrected, and if the patient still meets the criteria listed in Table 3, subsequent SBTs should be performed every 24 hours.

***Recommendation 6:*** Patients receiving mechanical ventilation for respiratory failure who fail an SBT should receive a stable, non-fatiguing, comfortable form of ventilatory support.

***Recommendation 7:*** Anesthesia/sedation strategies and ventilator management aimed at early extubation should be used in post-surgical patients.

***Recommendation 8:*** Weaning/discontinuation protocols that are designed for nonphysician healthcare professionals (HCPs) should be developed and implemented by ICUs. Protocols aimed at optimizing sedation also should be developed and implemented.

***Recommendation 9:*** Tracheotomy should be considered after a initial period of stabilization on the ventilator when it becomes apparent that the patient will require prolonged ventilator assistance. Tracheotomy then should be performed when the patient appears likely to gain one or more of the benefits ascribed to the procedure. Patients who may derive particular benefit from early tracheotomy are the following:

1. Those requiring high levels of sedation to tolerate translaryngeal tubes;
2. Those with marginal respiratory mechanics (often manifested as tachypnea) in whom a tracheostomy tube having lower resistance might reduce the risk of muscle overload;
3. Those who may derive psychological benefit from the ability to eat orally, communicate by articulated speech, and experience enhanced mobility; and
4. Those in whom enhanced mobility may assist physical therapy efforts.

***Recommendation 10:*** Unless there is evidence for clearly irreversible disease (*eg*, high spinal cord injury or advanced amyotrophic lateral sclerosis), a patient requiring prolonged mechanical ventilatory support for respiratory failure should not be considered permanently ventilator-dependent until 3 months of weaning attempts have failed.

***Recommendation 11:*** Critical care practitioners should familiarize themselves with facilities in their communities, or units in hospitals they staff, that specialize in managing patients who require prolonged dependence on mechanical ventilation. Such familiarization should include reviewing published peer-reviewed data from those units, if available. When medically stable for transfer, patients who have failed ventilator discontinuation attempts in the ICU should be transferred to those facilities that have demonstrated success and safety in accomplishing ventilator discontinuation.

***Recommendation 12:*** Weaning strategies in the prolonged mechanical ventilation patient should be slow-paced and should include gradually lengthening self-breathing trials.

mm Hg (8.0 kPa) with $FIO_2$ of <0.5 and PEEP of <5 cm $H_2O$.

When the aforementioned conditions are satisfied, it is reasonable to proceed with weaning. Attention then turns to assessing the likelihood that the weaning effort will succeed. In this regard, many different predictors of weaning have been proposed.[2,3]

## Predictors of Weaning

Weaning prediction is the process of estimating the likelihood that weaning and/or extubation efforts will succeed or fail in a specific patient at a specific time. As with decision-making in clinical medicine in general, weaning success or failure is a dichotomous outcome (*ie*, the patient either does or does not wean) and the process of predicting weaning outcome involves applying a weaning predictor to estimate the probability of weaning or extubation failure or success.[2]

Many different weaning predictors have been proposed (Table 2).[2,3] Available univariate (single variable) predictors include measures of lung mechanics and work of breathing (*eg*, forced vital capacity, maximal inspiratory pressure), measures of gas exchange adequacy (*eg*, ratios of PaO2/FIO2 and PaO2/PAO2), and measures of the adequacy of systemic perfusion (*ie*, gastric intramural pH).

Tables 3 through 5 review the statistical performance of several commonly used univariate weaning predictors (*ie*, the minute ventilation of <10 L/min [Table 3], the forced vital capacity [Table 4], and the maximal inspiratory force of <–30 cm $H_2O$ [Table 5]) and show that the positive predictive values of univariate weaning predictors generally exceed their negative predictive values. Remembering that the positive predictive value estimates the likelihood that the patient will wean if the predictor indicates success and that the negative predictive value estimates the likelihood of weaning failure if the predictor indicates failure, it can be concluded that univariate predictors are more reliable indicators of weaning success than they are of weaning failure. That is, the failure to satisfy the univariate weaning predictor does not confidently predict failure to wean; as shown by Krieger et al,[4] slavish attention to deferring weaning when a univariate weaning predictor is not met could unduly delay weaning (*ie*, in up to 41% of patients using the maximal inspiratory force of <–30 cm $H_2O$ as the criterion).

To improve the capability to predict weaning success and failure, a number of multivariate weaning predictors have been developed and evaluated.[2, 3, 5] As reviewed in Table 6,[2, 6–16] these

**Table 2.** *Proposed Univariate Predictors of Weanability*

Lung Mechanics and Work
- VC > 10 mL/kg
- $V_T$ > 300 mL
- Maximal inspiratory force < - 30 cm $H_2O$
- $P_{0.1}$ < 6 cm $H_2O$
- Dynamic compliance > 25 mL cm $H_2O$
- Respiratory rate < 25 breaths/min
- Minute ventilation < 10 L/min
- MVV > 2 times minute ventilation
- Respiratory frequency/$V_T$ < 105 breaths/min/L
- Oxygen cost of breathing < 15%
- $V_D/V_T$ < 0.60

Gas Exchange and Perfusion
- $P(A\text{-}a)O_2$ < 350 mm hg (46.7 kPa) on $FIO_2$ of 1.0
- $PaO_2/FIO_2$ > 238
- $PaO_2/PAO_2$ > 0.47
- Gastric pH > 7.30 and/or ↓ by < 0.09 during weaning

VC, vital capacity; $V_T$, tidal volume; $P_{0.1}$, airway occlusion pressure; $V_D/V_T$, deadspace volume to tidal volume; MVV, maximum ventilatory ventilation; $P(A\text{-}a)O_2$, alveolar-arterial oxygen tension difference.

**Table 3.** *Minute Ventilation <10 L/min as a Univariate Weaning Predictor*

| Study (date) | N | Sensitivity (%) | Specificity (%) | Prediction Performance: Positive Value | Prediction Performance: Negative Value |
|---|---|---|---|---|---|
| Sahn & Lakshminarayan (1973) [a] | 100 | 92 | 100 | 100 | 71 |
| Tahvanainen et al (1983) | 47 | 45 | 78 | 89 | 25 |
| Krieger et al (1989) [b] | 269 | NS | NS | 93 | 15 |
| Yang & Tobin (1989) | 41 | 24 | 69 | 55 | 37 |

NS, not stated.
[a] Minute ventilation <10 L/min; maximal inspiratory pressure (MIP) <–30 cm $H_2O$; and maximal voluntary ventilation (MVV) >2 times minute ventilation; [b] minute ventilation <10 L/min and MIP <–30 cm $H_2O$.
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multivariate predictors vary in content from simple combinations of univariate predictors (*eg*, maximal minute ventilation > twice minute ventilation, maximal inspiratory force of <–30 cm $H_2O$, and minute ventilation of <10 L/min) to more complex scoring systems that assess dozens of clinical variables and provide an overall score that is used to predict weanability (*eg*, the Adverse Factor and Ventilator Score[7] and the Burns Weaning Assessment Program[13]). In general, these multivariate indices demonstrate higher positive and negative predictive values than the univariate predictors; they are, therefore, more useful and reliable predictors, although their general failure to achieve perfect predictive capability should cause the astute clinician to regard them with circumspection in completely assuring or excluding weanability.

As a specific example of a widely used multivariate weaning predictor, the rapid shallow breathing index (otherwise known as the frequency to tidal volume ratio [$f/V_T$]) calculates the patient's spontaneous breathing frequency divided by the patient's spontaneous tidal volume in liters, both determined with the patient who does not receive mechanical ventilatory assistance (*ie*, breathing through an endotracheal tube connected to a respirometer). As first proposed by Yang and Tobin,[10] an $f/V_T$ value of <105 was found to best discriminate between patients who were successfully weaned (defined as maintaining spontaneous breathing for >24 hrs after extubation) and who were not successfully weaned. This threshold value was developed from a "hypothesis-generating" set of 36 patients and subsequently validated in a "hypothesis-testing" set of 64 patients, in whom an $f/V_T$ of >105 had an overall negative predictive value (the chance that a patient would fail to wean if $f/V_T$ exceeded 105) of 0.95 and a positive predictive value of 0.78. In the subset of 20 patients who received mechanical ventilation for >8 days, the negative and positive predictive values were slightly lower (0.89 and 0.64, respectively), emphasizing the increased difficulty of establishing unweanability in long-term, mechanically ventilated patients. Subsequent studies [1, 15] have largely confirmed the usefulness of the rapid shallow breathing index, while also emphasizing its shortcomings in predicting weaning outcome when nonrespiratory factors are at

**Table 4.** *Vital Capacity (Measured in mL/kg) as a Univariate Weaning Predictor*

| Study (Date) | Criterion | N | Sensitivity (%) | Specificity (%) | Prediction Performance Positive Value | Prediction Performance Negative Value |
|---|---|---|---|---|---|---|
| Milbern et al (1978) [a] | >15 | 33 | 25 | 0 | 58 | 0 |
| Tahvanainen et al (1983) | >10 | 47 | 97 | 13 | 83 | 50 |
| Pardee et al (1984) | >17 | 133 | 90 | 60 | 88 | NS |

NS, not stated.
[a] Vital capacity > 15 mL/kg and maximal inspiratory pressure <-25 cm $H_2O$.
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**Table 5.** *Maximal Inspiratory Pressure ≤–30 cm $H_2O$ as a Univariate Weaning Predictor*

Prediction Performance

| Study (date) | N | Patient Type | Sensitivity (%) | Specificity (%) | Positive Predictive Value | Negative Predictive Value |
|---|---|---|---|---|---|---|
| Sahn & Lakshmin-arayan (1973) [a] | 100 | Mean MV duration 37 hrs | 92 | 100 | 100 | 71 |
| Milburn et al. (1978) [b] | 33 | Mean MV 3.1 hrs | 25 | 0 | 58 | 0 |
| Tahvanainen et al. (1973) | 47 | Mean MV 5 days | 68 | 0 | 74 | 0 |
| DeHaven et al. (1986) | 48 | Mean MV 55 hrs | 49 | 100 | 100 | 12 |
| Krieger et al. (1989) | 269 | Mean age >70 yrs, MV 71 hrs | NS | NS | 92 | 21 |
| Yang & Tobin (1989) | 41 | NS | 76 | 25 | 61 | 40 |

MV, mechanical ventilation; NS, not stated. [a]Maximal inspiratory pressure <–30 cm $H_2O$, minute ventilation <10 L/min, and maximal voluntary ventilation ≥2 minute ventilation; [b]maximal inspiratory pressure <–30 cm $H_2O$ and vital capacity ≥15 mL/kg.
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play (*eg*, congestive heart failure or upper airway obstruction as causes).

At the same time, Vallverdu et al[17] have emphasized that the diagnostic accuracy of different weaning parameters differs according to the underlying cause of respiratory failure. Specifically, in a series of 217 consecutive patients with respiratory failure of various etiologies, the rapid shallow breathing index demonstrated highest diagnostic accuracy in predicting weaning success in patients with chronic obstructive pulmonary disease (COPD) (0.76), but lower accuracy in patients with neurologic disease (0.65) or miscellaneous causes of acute respiratory failure (0.66). In contrast, values of maximal inspiratory pressure and maximal expiratory pressure best distinguished patients who were successfully intubated vs those patients who failed extubation when the cause of respiratory failure was neurologic disease. Overall, the recent evidence-based guidelines report[1] concludes that "judging by areas under the receiving operator curves for all variables, none of these variables demonstrate more than modest accuracy in predicting weaning outcome." The putative reason is that in available studies, clinicians making weaning decisions have already considered the results of weaning predictors when choosing patients for weaning.

## Techniques of Weaning

A variety of techniques for weaning patients from mechanical ventilation has been described,[3,18–21] including T-piece trials of increasing duration that interrupt periods of completely supported breaths, intermittent mandatory ventilation (IMV) weaning in which the IMV rate is decreased progressively, pressure-support weaning in which the level of pressure support is decreased progressively, and combinations of the above (*eg*, pressure-support weaning with an IMV back-up rate). Strategies in use have changed as available ventilatory modes have evolved. For example, a survey of technical directors of respiratory care departments conducted by Venus et al[22] in 1987 indicated that IMV was the primary mode of weaning employed by 72% of the respondents. A survey of practices in 47 Spanish ICUs by Esteban et al.[19] showed that in 195 patients who were being weaned, T-piece trials of increasing duration were used most commonly (24%), followed by synchronized IMV weaning (18%), pressure-support weaning (15%), and combined pressure-support with an IMV back-up rate (9%). Other combinations applied concurrently or in succession were used in 33%. Finally, in a recent randomized trial[22] of daily observation of sponta-

**Table 6.** *Summary of Selected Multivariate Indices for Weaning Prediction*

| Study (Date) (Ref) | N | Index | Patient Type | Positive Predictive | Negative Predictive |
|---|---|---|---|---|---|
| Hilberman et al. (1976) (6) | 124 | Nurse assessments | Open-heart surgery | 82% | 67% |
| Krieger et al. (1984) (4) | 269 | NIF <-30 cm $H_2O$, $V_E$ >10 L/min | >70 yrs old, on MV mean 71 hrs | 93% | 15% |
| Morganroth et al. (1984) (7) | 11 | Adverse factor and vent score | COPD, on MV >30 days | 73% | 97% [a] |
| Higgins et al. (1988) (8) | 29 | Vent dependence score | Post-OHS on MV >48 hrs | NS | NS |
| Yang & Tobin (1989) (9) | 41 | CROP score | NS (abstract) | 87% | 72% |
| Yang & Tobin (1991) (10) | 100 | CROP >13, Freq/$V_T$ <105 | On MV 8.2 $\pm$ 1.1 days | 711% | 70% [b] |
| Jabour et al. (1991) (11) | 38 | Weaning index <4 | MICU on MV <3 days | 96% | 95% |
| Ashutosh et al. (1991) (12) | 24 | Neural network discriminant function | On MV 12.7 days | 100% [b] | 100% [b] |
| Burns et al. (1991) (13) | 37 | BWAP | Stable on MV >1 wk, felt ready to wean | — | 97% |
| Scheinhorn et al. (1995) (14) | 565 | $P(A\text{-}a)O_2$, BUN, gender | On MV >6 wks | 71% | 67% |
| Epstein (1995) (15) | 184 | Freq/$V_T$ >100 | MICU on MV, f/$V_T$ measured within 8 hrs of wean onset | 83% | 40% |
| Gluck et al. (1995) (16) | 55 | Score (5 variables), points >3 | On MV $\geq$3 wks | 83% | 100% |

NIF, negative inspiratory force; MV, mechanical ventilator; $V_E$, minute ventilation; COPD, chronic pulmonary obstructive disease; OHS, open-heart surgery; NS, not stated; BWAP, Burns Weaning Assessment Program; BUN, blood urea nitrogen; MICU, medical intensive care unit; $V_T$, tidal volume.
[a] Hypothesis-generating study, not confirmed in a separate data set; [b] hypothesis-testing data set included.

neous (T-piece) breathing vs "routine" weaning practice, the most common routine weaning mode was pressure-support with IMV (43%), followed by IMV alone (31%), pressure-support alone (15%), continuous positive airway pressure (CPAP) (5%), and other (6%).

Recent attention has focused on comparing available techniques of weaning. Three important studies have provided important insights. Each of the weaning techniques is described below, followed by a summary of the evidence supporting specific techniques of weaning.

*T-Piece Trials*

Also known as Briggs trials, T-piece trials allow the patient to breathe spontaneously through the endotracheal tube (or tracheostomy) connected to a T-piece set-up. CPAP can be applied to the T-piece circuit, although PEEP levels >5 cm $H_2O$ would be unlikely during weaning trials, because adequate oxygenation on acceptably low levels of PEEP is considered a criterion for beginning weaning.

*Intermittent Mandatory Ventilation Weaning*

IMV weaning was first proposed in 1973 as a new and preferred weaning strategy.[23] With IMV weaning, a volume and frequency of breaths are set, and the frequency is decreased gradually until the patient has assumed most of the minute ventilation.

*Pressure Support Ventilation*

Unlike IMV, which is a volume-cycled mode of mechanical ventilation, pressure support ventilation[24] delivers gas at a set pressure level for a duration determined by the patient's inspiratory flow demands (*ie*, flow-cycled). Pressure support weaning involves the gradual diminution of the pressure level, allowing the patient gradually to assume more of the work of breathing (WOB).

## Studies Comparing Weaning Modes

Three controlled trials [18,21,25] have contributed important insights and comparisons of available weaning strategies. Brochard et al.[18] conducted a randomized, controlled trial in which 109 patients who failed initial weaning attempts were randomized to one of three weaning strategies: a) T-piece trials, in which progressively increasing intervals of spontaneous breathing through a T-piece were undertaken until the patient tolerated up to three T-piece trials lasting 120 mins (n = 35 patients); b) synchronized IMV weaning, in which the IMV rate was decreased by 2 to 4 breaths/min twice daily, until the patient tolerated 24 hrs at an IMV rate of <4 (n = 43 patients); or c) pressure-support weaning, in which the level of pressure was decreased by 2 or 4 cm $H_2O$ twice daily until the patient could tolerate breathing at pressure-support of <8 cm $H_2O$ for 24 hrs (n = 31 patients). The study concluded that pressure support was the preferred weaning mode (Figure 1) based on the following: a) Fewer patients failed to wean with pressure-support than with the other modes (23% vs 43% [T-piece] and 42% [IMV], $p < 0.05$); b) time-to-event analysis showed that the probability of requiring continued ventilatory support was lower with pressure support than with the other modes ($p = 0.03$); and c) weaning duration was shorter with pressure support (mean 5.7 ± 3.7 days) than for the other modes pooled (mean 9.3 ± 8.2 days, $p < .05$).

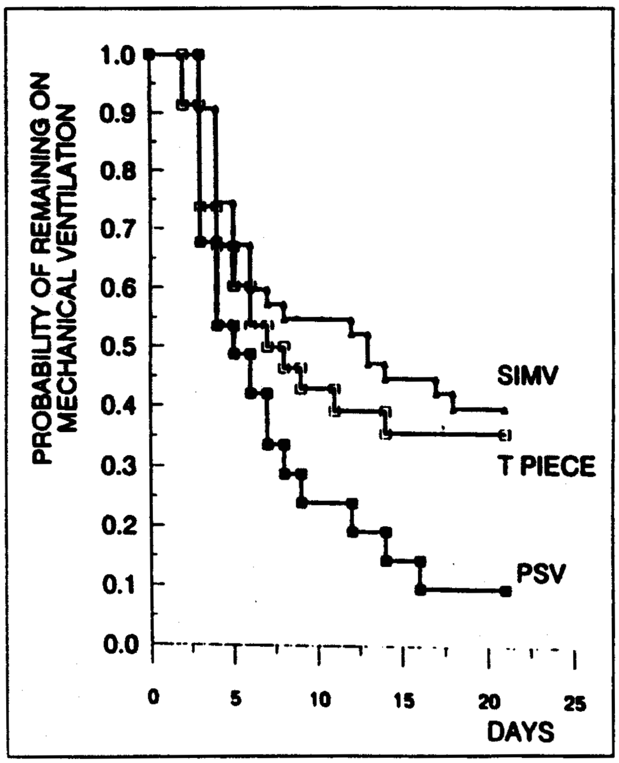


**Figure 1.** Probability of remaining on mechanical ventilation in patients with prolonged difficulties in tolerating spontaneous breathing. This probability was significantly lower for pressure-support ventilation (PSV) than for T-piece of synchronized intermittent ventilation (SIMV) (cumulative probability for 21 days, $p < 0.03$ with the log-rank test). Reproduced with permission from Brochard et al.[18]

In a second randomized trial of weaning modes, Esteban et al.[25] randomized 130 patients who had failed initial weaning attempts to one of four weaning modes: a) IMV weaning, in which the rate was decreased by 2 to 4 breaths/min at least twice daily until the patient tolerated an IMV rate of <5 for 2 hrs (n = 29 patients); b) pressure support weaning, in which the pressure was decreased by 2 to 4 cm $H_2O$ at least twice daily until a pressure support level of 5 cm $H_2O$ was tolerated for 2 hrs (n = 37 patients); c) intermittent trials of spontaneous breathing, in which T-piece trials of increasing length were undertaken at least twice daily until the patient could tolerate 2 hrs of spontaneous breathing (n = 33 patients); and d) once-daily T-piece trials, in which a single T-piece trial was undertaken daily until 2 hrs of spontaneous breathing were tolerated without distress (n = 31 patients). Unlike the study by Brochard et al,[18] this study concluded that a once-daily T-piece trial was the preferred strategy (Figure 2), based on the following findings: a) The rate of successful weaning was higher with this technique than with IMV or pressure support weaning; and b) weaning was more rapid with once daily T-piece trials than with pressure support or IMV modes.

Finally, the most recent controlled trial of different weaning strategies by Ely et al[21] randomized patients to a once-daily respiratory assessment and trial of spontaneous breathing for up to 2 hrs with physician notification of a successful trial (n = 149 patients) versus usual care by the managing physicians (pulmonologist, cardiologist, or intensivist; n = 151 patients). As shown in Figure 3, this study shows that a strategy of conducting daily trials of spontaneous breathing is preferred because this approach was associated with shorter weaning time (median 1 vs 3 days, $p < 0.001$), shorter duration of mechanical ventilation (median 4.5 vs 6 days, $p < 0.003$), fewer total complications (20% vs 41%, $p < 0.001$), a lower rate of reintubation (4% vs 10%, $p = 0.04$), and lower ICU costs (median $15,740 vs $20,890, $p < 0.03$). Overall, these three studies show that contrary to early views and practices,[22] IMV weaning is the least likely to effect successful extubation and requires longer weaning than other

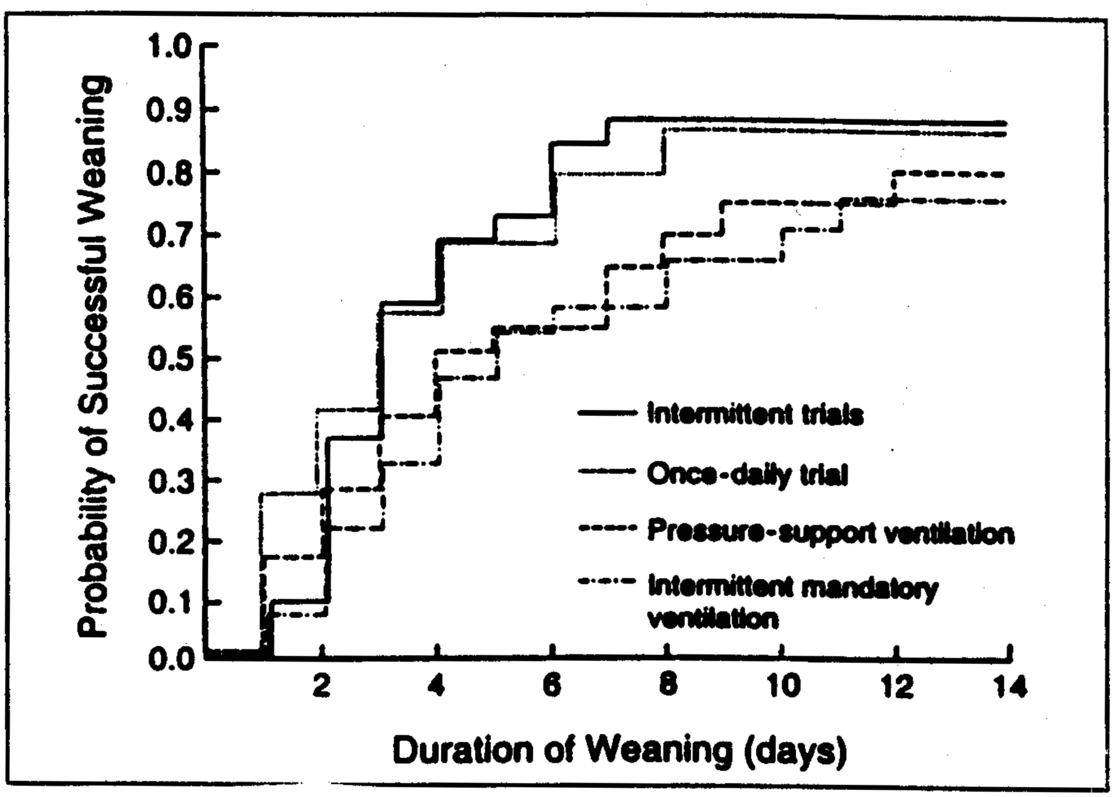


**Figure 2.** Kaplan-Meier curves of the probability of successful weaning with intermittent mandatory ventilation (IMV), pressure support ventilation (PSV), intermittent trials of spontaneous breathing (SB), and a once-daily trial of SB. After adjustment for baseline characteristics in a Cox proportional hazards model, the rate of successful weaning with a once-daily trial of SB was 2.83 times higher than that with IMV ($p < 0.006$) and 2.05 times higher than that with PSV ($p < 0.04$). Reproduced with permission from Esteban et al.[20]

available strategies, and that daily assessment of respiratory status and spontaneous breathing trials was associated with shorter weaning duration than usual practice. Attempts[26] to reconcile the discordant conclusions from the studies of Brochard et al and Esteban et al have attributed the differing results to differing definitions of weaning failure in the two studies (14 days on mechanical ventilation [Esteban et al] vs 21 days), and to different constraining conditions for attempting extubation with the compared weaning modes (*ie*, Brochard et al permitted extubation from 8 cm $H_2O$ of pressure support vs 5 cm $H_2O$ by Esteban et al and Brochard et al required IMV breathing on <4 breaths for 24 hrs before attempting extubation vs an IMV rate of <5 for 2 hrs by Esteban et al).

More recently, Esteban et al[27] examined whether a spontaneous breathing trial should last ≤2 hrs (*ie*, 30 mins) before extubation  In a multicenter trial in which 526 patients were allocated randomly to 30- vs 120-min trials of spontaneous breathing, these investigators found no differences between the two durations in rates of extubation failure or ICU or hospital mortality, but a longer length of hospital stay in the group undergoing a 2-hr trial. These findings, which have been confirmed by Perren et al,[28] endorse use of the shorter, 30-min period of spontaneous breathing before an extubation decision.

Finally, recent attention has turned to the value of noninvasive ventilation in accelerating extubation. Nava et al[29] conducted a randomized, controlled trial in which patients intubated because of acute ventilatory failure complicating COPD were randomized to a traditional pressure-support weaning approach versus a new strategy (in which patients were extubated after 48 hrs and managed thereafter with noninvasive ventilation). Patients managed with noninvasive ventilation experienced several advantages: a) fewer days on mechanical ventilation; b) fewer days in the ICU; c) a higher weaning success rate on day 21; d) a lower rate of nosocomial pneumonia; and e) a higher survival rate at 60 days (92% vs 72%, $p = 0.0009$). These and other, more recent confirmatory results from Girault et al[30] suggest that early extubation with subsequent noninvasive ventilatory support may be a beneficial weaning strategy in patients with respiratory failure due to COPD.

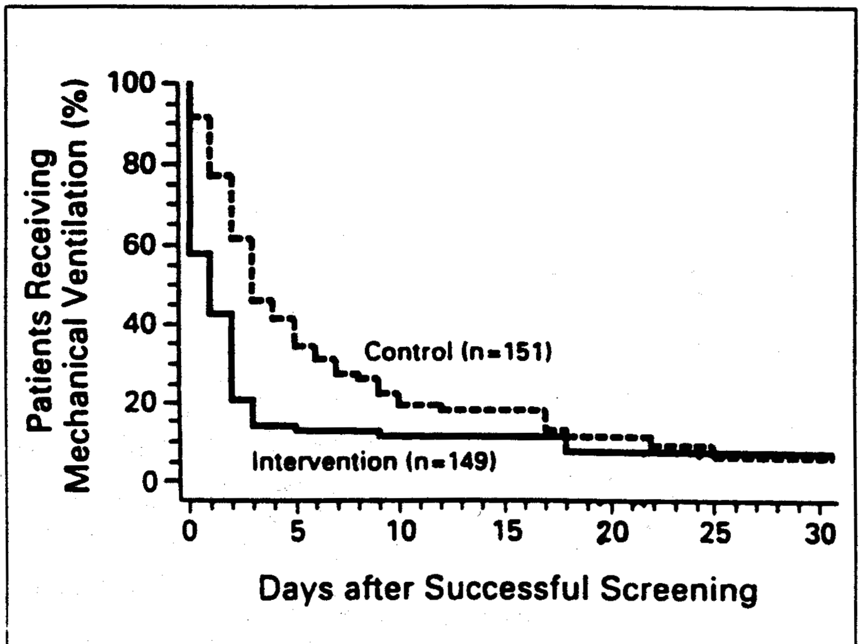


**Figure 3.** Kaplan-Meier analysis of the duration of mechanical ventilation after a successful screening test. After adjustment for the severity of illness at baseline (as measured by the APACHE II score), age, gender, race, location of the ICU, and duration of intubation before enrollment, a Cox proportional hazards analysis showed that mechanical ventilation was discontinued more rapidly in the intervention group than in the control group (relative risk of successful extubation, 2.13; 95% confidence interval, 1.55 to 2.92; $p < 0.001$). Reproduced with permission from Ely et al.[21]

*Special Considerations in Weaning*

To optimize the possibility of weaning, attention to several special considerations can be helpful in some clinical circumstances. These special considerations include: a) the possibility of unsuspectedly high imposed WOB and the contribution of the endotracheal tube, b) auto-PEEP as a source of increased inspiratory work in circumstances where dynamic hyperinflation accompanies airflow limitation, c) occult cardiac ischemia as an impediment to weaning, d) the importance of psychological readiness and motivation to wean, e) the importance of routine daily cessation of sedative medications in patients receiving mechanical ventilation, and f) the importance of implementing protocols by respiratory therapists and/or nurses to accelerate liberation from mechanical ventilation. Each of these special considerations is discussed below.

*Work of Breathing and Role of the Endotracheal Tube*

Measuring the inspiratory WOB by integrating the area under a pressure-volume curve has been advocated because elevated WOB predicts inspiratory muscle fatigue with subsequent weaning failure as an expected consequence. Various threshold values of WOB have been proposed (Table 7),[31-35] but few of these threshold values have been validated prospectively or compared head-to-head with other available weaning parameters. In a small, hypothesis-generating study of 17 patients, Fiastro et al[34] compared WOB with vital capacity, negative inspiratory force, tidal volume, and minute ventilation as weaning predictors and showed that as WOB values decreased <1.60 kg•m/min (16 joules/min), WOB better discriminated between patients with weaning success versus weaning failure than did the other more conventional measures. Until recently, the persisting uncertainty about a useful threshold value for WOB and the lack of methods for easy and widespread clinical measurement precluded adoption of WOB measurement for clinical practice outside of an investigative context. More recently, commercial devices that permit straightforward measurement of WOB have become available and have fostered enthusiasm for using WOB measurements in guiding weaning decisions. For example, Gluck et al[16] compared a weaning protocol using measurements of WOB and f/VT with a clinical approach using conventional weaning criteria (*eg*, minute ventilation, negative inspiratory force, tidal volume, and static compliance) in 23 ventilated patients. This study showed that the protocol incorporating WOB measurements would hasten weaning in at least 41% of instances and that the projected duration of weaning was shortened in these patients by 1.68 days.

Apart from appreciating the potential value of measuring WOB to enhance decision-making about weaning, clinicians should be attentive to sources of imposed WOB that can hamper weaning. That the endotracheal tube can contribute importantly to imposed WOB has been shown by Shapiro et al.[36] In a study of three normal volunteers breathing through endotracheal tubes of various caliber (6- to 10-mm inner diameter), these investigators showed that WOB rose precipitously as the caliber decreased and as minute ventilation rose. For subjects breathing through 6- and 7-mm inner diameter tubes at levels of minute ventilation routinely achieved clinically (15 to 25 L/min), the tension-time index approached values of 0.15 at which respiratory muscle fatigue is expected. Thus, use of larger caliber (*ie*, >7.5-mm inner diameter) endotracheal tubes and avoidance of nasotracheal intubation in patients experiencing weaning difficulty are advised. More recently, WOB measurements have been shown to be useful in helping to identify pa-

**Table 7.** *Proposed Work of Breathing (Transpulmonary) as a Weaning Predictor*

| First Author (Date) (Ref) | No. of Patients | Threshold Value (kg • m/min) | Comment |
|---|---|---|---|
| Peters (1972) (31) | 55 | 1.80 | — |
| Proctor (1973) (32) | 168 | 1.35 | 13.7% false-positive and false-negative rate with value |
| Henning (1977) (33) | 28 | 1.70 | — |
| Fiastro (1988) (34) | 17 | 1.60 | Better discriminator than vital capacity, tidal volume, minute ventilation, negative inspiratory force |
| Brochard (1989) (35) | 8 | 0.8 | — |

tients whose weaning difficulty is attributable to unsuspectedly high imposed WOB.[37] From a group of 116 surgical ICU patients on mechanical ventilation for >48 hrs, Kirton et al[37] identified 28 patients (24%) with oral endotracheal tubes of >8-mm inner diameter who developed marked tachypnea during a CPAP trial despite satisfying simple weaning criteria. WOB measurements in these 28 patients were performed and included a measurement of the work imposed by the endotracheal tube. Using a value of <0.8 joules/L as a WOB threshold, the investigators identified six patients with total WOB below this value, all of whom were successfully extubated. Of the remaining 22 patients whose total WOB measurements exceeded this threshold (mean WOB 1.6 $\pm$ 0.83 joules/L), 21 patients were found to have a major component of their total WOB imposed by the endotracheal tube, leaving their "physiologic" work of breathing below the threshold value. Extubation was successfully undertaken in all 21 (with subsequent reintubation for unrelated and unpredictable reasons in two patients), leading to the conclusion that high imposed WOB can unsuspectedly contribute to weaning failure and that WOB measurements directed at identifying the components of "imposed" and "physiologic" WOB can enhance decision-making in a subset of difficult-to-wean patients.

### *Auto-PEEP as a Source of Imposed Work of Breathing*

Auto-PEEP is defined as PEEP that is present in the alveoli but not measured at the mouthpiece without special maneuvers,[38] *eg*, an end-expiratory hold. Synonyms for auto-PEEP include intrinsic PEEP, occult PEEP, endogenous PEEP, and unidentified PEEP. As shown by Brown and Pierson,[38] auto-PEEP occurs commonly among mechanically ventilated patients (39% of 62 patients assessed) and may produce high alveolar pressures at end-expiration (*ie*, up to 15 cm $H_2O$). Three varieties of auto-PEEP can be considered,[39] each of which may occur under distinct physiologic circumstances even though several types may coexist. The first type is auto-PEEP with dynamic hyperinflation and airflow limitation, which commonly accompanies COPD, both in spontaneously breathing and mechanically ventilated patients. Other types include auto-PEEP with dynamic hyperinflation but no airflow limitation (*eg*, during high minute ventilation or with a small endotracheal tube that hampers lung emptying) and auto-PEEP without dynamic hyperinflation (*eg*, due to expiratory muscle recruitment).

In considering weaning, the first type of auto-PEEP—auto-PEEP with dynamic hyperinflation and air flow limitation—is most significant because such auto-PEEP imposes an inspiratory threshold load that must be overcome by the inspiratory muscles before inspiration can begin.[38, 40, 41] Such auto-PEEP arises when lung emptying is impaired due to expiratory airflow resistance and expiratory flow limitation; end-expiratory lung volume then exceeds resting functional residual capacity; air is trapped at end-expiration and alveolar pressure exceeds downstream pressure (at the mouth) with resulting auto-PEEP. By imposing an inspiratory load, such auto-PEEP can be the source of imposed WOB. As shown by Petrof et al[40] and Smith and Marini,[41] application of external PEEP can decrease the inspiratory WOB by offsetting the inspiratory load imposed by the auto-PEEP. Levels of external PEEP, up to ~85% of the auto-PEEP, can lessen imposed WOB without increasing end-expiratory lung volume or lessening cardiac output. On this basis, clinicians should be attentive to the possibility of auto-PEEP in managing patients on mechanical ventilation. If found in a clinical circumstance favoring dynamic hyperinflation with airflow limitation (*ie*, in patients with COPD), careful application of external PEEP to levels not exceeding the level of auto-PEEP may be helpful to lessen imposed WOB and enhance weaning.

### *Other Special Considerations in Weaning*

Besides giving attention to WOB imposed by the endotracheal tube and by auto-PEEP, clinicians should appreciate other potential impediments to weaning, including unsuspected cardiac ischemia,[42] the patient's anxiety and lack of psychologic readiness to wean,[43] and the lack of a systematic weaning routine in the ICU. Recent studies suggest that weaning can be accelerated by detection and treatment of cardiac ischemia, by providing biofeedback to lessen anxiety and to assure ventilatory targets, and by implementing a team to conduct regular weaning[44] and/or weaning protocols supervised by respiratory therapists and nurses,[45, 46] at least in adults. In contrast to the results from several randomized trials in adults in which protocols implemented by respiratory therapists and/or nurses were associated with accelerated liberation from mechanical ventilation,[45,46] results from a recent trial in mechanically ventilated children (<18 years of age) failed to show that protocols shortened the duration of ventilator dependence.[47] While the precise reason for discordance with the results of the adult trials remains uncertain, it is possible that the already short duration of mechanical ventilation in control pediatric patients (median 2 days) makes it difficult to show significant acceleration of weaning.

Other interventions found to accelerate weaning were use of a collaborative, multidisciplinary weaning approach using a bedside weaning board and flow sheet[48] and respiratory therapists' using a handheld computer on which a weaning protocols is programmed.[49] The former intervention has been associated with a shortened ICU length of stay and a trend toward shortened time on mechanical ventilation in adults. Regarding the second,[49] compared with using a weaning protocol on paper, respiratory therapists' using a handheld computer with a weaning protocol was associated with a shorter time to beginning a weaning trial (mean 49.9 vs 72.5 hours, $p = 0.018$) and had a shorter ICU length of stay (mean 6.2 vs 7.7 days, $p = 0.018$). Finally, a recent randomized controlled trial has shown that daily interruption of sedative medications to reassess neurologic status and weaning readiness in adults is associated with a shortened duration of mechanical ventilation.[50]

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# Notes