Abstract

Weaning from mechanical ventilation is defined as the transition from the ventilatory dependence of the patient to a spontaneous breathing status. Recognizing when a patient is ready to be weaned from mechanical ventilation is greatly influences the outcome, and may prevent compromising a patient. Weaning indices were developed to help the physician predict the outcome of weaning trials, a common concern in the intensive care unit (ICU) setting. Many physiological mechanisms explain the reason why many patients fail weaning trial, mostly related to a noncompliant respiratory function and cardiovascular instability. The primary goal is to reduce failed attempts, and to adopt successful weaning protocols, in order to overcome problems that may arise in the critically ill patients. The ratio of respiratory rate to tidal volume ($f/V_t$), among other indices, and weaning trials like pressure support ventilation (PSV) or spontaneous breathing with the use of T tube are explained.

Key words: Weaning indices, $f/V_t$ ratio, ventilatory support, weaning trials.

Introduction

Mechanical ventilation is arguably one of the most important advances in the history of medicine. The impact of its use on the outcome of many critically ill patients has improved greatly since the development of mechanical ventilation. Unfortunately, the inability to recognize the appropriate time, or the inability to wean a patient off the ventilator has been related to an increase of up to 40% in hospital mortality [1]. Approximately 75% of the patients undergoing mechanical ventilation are withdrawn successfully with no remarkable symptoms of poor tolerance. The remaining 25% may experience a complicated withdrawal that leads to a longer hospital stay. This is particularly concerning as the weaning period may represent up to 40% of the total duration of the ventilatory support, and increases the risk of morbidity and mortality in these patients [2,3]. Additional costs may also be incurred. In response, weaning indices have been developed to aid physicians in identifying the earliest time for discontinuing ventilatory support, as well as to identify patients who are at risk of cardiopulmonary compromise during weaning trials [4].

Clinical and physiological approaches

Early recognition of patients who are ready to be weaned off ventilatory support is an important part of clinical practice. General clinical parameters have been suggested before initiating the weaning process (Table 1). When the patients meet such criteria, they are allowed to breathe spontaneously for a period of time, (i.e., minutes to hours) and then the decision for extubation is made based on their response.
In addition, physiological indicators that may predict weaning outcome such as the frequency to tidal volume ratio, a respiratory rate >35 breath/min, maximal inspiratory pressure <30 cmH₂O, and a vital capacity >10-15 mL/kg body weight have been described by Tobin et al [5]. Nevertheless, due to a lack of sensitivity and specificity, many of those indices are not accurate and should not be used as weaning parameters [2].

**Difficult weaning process and the physiopathological mechanisms**

Abnormal gas exchange, cardiovascular compromise, psychological dependence on the ventilator, and respiratory failure are the main reasons for a failed weaning trial [3]. Left ventricular failure may result due to physiological changes that arise during the weaning trials; such as the switch from a positive to negative intrathoracic pressure environment, increase in the catecholamine levels, and the increase in respiratory effort.

Decreases in pleural pressure, which occur during spontaneous breathing trials, increases both left ventricular afterload and left ventricular end diastolic pressure. Such mechanisms may precipitate a myocardial ischemic event due to an increased myocardial consumption. Following the ischemic event, left ventricular dysfunction with pulmonary edema and arterial hypoxemia arise [4].

A vicious cycle created by catecholamine release and the increase in respiratory effort may contribute to an increase in the myocardial oxygen consumption, which leads to deterioration of myocardial ischemia contributed by arterial hypoxemia and pulmonary edema. Respiratory pump failure may be contributed to by decreased output in the respiratory centers due to anesthetics, sedatives and narcotic agents.

Neural complications such as phrenic dysfunction or other peripheral disorders may be contributed to mechanical defects of the chest wall and increase in the ventilatory demands [4]. Central nervous system disorders, such as bleeding, stroke, post surgical outcome, infections, etc, and brain steam diseases

<table>
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<tr>
<th>Table 1. GENERAL CLINICAL PARAMETERS TO BE MET BEFORE INITIATING WEANING</th>
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<tbody>
<tr>
<td>Resolution or significant improvement of the cause for which mechanical ventilation was instituted</td>
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<tr>
<td>Adequate gas exchange, SaO₂ ≥90% with FiO₂ &lt;0.4 or PaO₂/FiO₂ &gt;200 with PEEP &lt;5 cmH₂O</td>
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<tr>
<td>Absence of fever</td>
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<td>Adequate hemoglobin levels</td>
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<td>Appropriate neurological and muscular status</td>
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<td>Stable cardiovascular function</td>
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<td>Correction of metabolic and/or electrolyte disorders, if the case</td>
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<td>Adequacy of sleep</td>
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Adapted from Mancebo J. Eur Respir J. 1996;9:1923 31 [2]

SaO₂: arterial oxygen saturation; FiO₂: inspiratory oxygen fraction; PaO₂: arterial oxygen tension; PEEP: positive end expiratory pressure.
be accompanied by an altered level of consciousness and depressed respiratory drive, making weaning from mechanical ventilation difficult to achieve.

Sequelae related to respiratory muscle non-compliance such as dynamic pulmonary hyperinflation should be assessed. Malnutrition as well as increased muscular catabolism and prolonged bed rest, can lead to muscle dysfunction. Patients with poor muscle mass, chronic heart or renal failure and severe emphysema may also present with severe muscle dysfunction.

**Weaning indices**

**The ratio of respiratory frequency to tidal volume (f/Vt)**

The ratio of respiratory frequency to tidal volume (f/Vt) index was first identified by Tobin *et al* in a prospective study found that a f/Vt ratio >105 bpm/L was the most accurate predictor of weaning failure [5]. It was calculated by counting the frequency of full breaths and dividing the result by the average inspiratory tidal volume over a 30 second period. Also referred as the rapid shallow breathing index (RSBI) is often utilized in patients that are yet able to be extubated. The reason patients develop rapid shallow breathing patterns remains unclear, although one hypothesis is that it results from a combination of muscle weakness and impaired pulmonary mechanics [5,6]. However, respiratory muscle failure is unlikely to be the cause of weaning failure as patients adopt this pattern prior to developing muscle fatigue, when they are withdrawn from ventilatory support. Tobin and Yang determined that a ratio >105 bpm/L was likely to indicate a weaning process failure. Despite the wide use of this index, many authors have questioned its efficacy.

Krieger *et al*, [7] in a retrospective analysis, found a predictive value of 88%, but a negative predictive value of 11%, resulting in a diagnostic accuracy of only 75%. However, study was performed in an elderly population (threshold value of ≤130 bpm/L is more appropriate for this population than previously published values of ≤105 bpm/L); therefore parameters determined from this demographic group may not apply to other populations. Epstein found that the RSBI lost his discriminatory power in patients ventilated for more than eight days in an ICU [6]. The RSBI scores were higher in those patients with a smaller endotracheal tubes, as well as women, so the threshold was adjusted according with the patient’s condition.

Rivera *et al* [7], in a strict surgical ICU (where sepsis and volume overload are the major reason for intubation), found that a lower f/Vt (i.e., 65 bpm/L) discriminated between patients undergoing successful weaning and those who failed. These findings were supported by other studies on the efficacy of this index.

Vassilakopoulos *et al* [8], found that each time patients failed to wean from mechanical ventilation, the load of the expiratory muscles increased as compared to those who were successful in weaning from mechanical ventilation. The f/VT ratio was a major determinant of the weaning outcome, which was different for the same patients during weaning failure and success as evidenced by the higher values of P/P_{max}, R_{max}, R_{min}, and PEEPi.

**Tension time index**

Vassilakopoulos *et al* [8], performed a prospective study on patients who initially failed a weaning process and succeeded on a later occasion. Their goal was to clarify the pathophysiological state that determined the inability to successfully wean from mechanical ventilation. The tension-time index (TTI) concept that was originally studied on heart and limb muscles was applied to the diaphragm by Bellemare and Grassino [9] to determine its endurance characteristics. They found that when TTI was >0.15, the breathing task could not be sustained resulting in diaphragmatic fatigue and subsequent weaning failure. Hence, the decrease in the load that was imposed on the respiratory muscles, with an increasing in neuromuscular capacity resulted in diminished energy demands (i.e., TTI) and resulted in a more efficient breathing pattern (i.e., f/VT), which were the main changes between those patients who succeed and those who failed.
Respiratory drive (P0.1)

Despite controversial predicting values, studies have shown a promising correlation for those patients who undergo a weaning trial and beneficial outcome. Respiratory drive measures the airway pressure that is generated within the first 100 msec (0.1 sec) of inspiratory effort when there is airway occlusion. Inspiratory neuromuscular drive is reflected in this parameter, and has been useful for patients with chronic obstructive pulmonary disease to determine if a patient may wean successfully from ventilatory support. The optimum values range between 2-4 cmH2O, and successful weaning is not likely when the value is >6 cmH2O. Montgomery et al [10] found that during hypercarbic, but not normocarbic, breathing the P0.1 was a useful weaning indicator.

Inspiratory pressure/maximal inspiratory pressure ratio

Considering that respiratory muscle fatigue is a primary reason that a patient may fail a weaning process has been noted among patients who successfully wean from mechanical ventilation, that the ratio between inspiratory pressure (P1) and the maximal inspiratory pressure (Pmax) is lower than those who fail the weaning process [11]. Yang et al, in a prospective study of 31 intubated patients ready to undergo weaning trial, measured the respiratory frequency and minute ventilation of patients taken of ventilatory support and breathing room air spontaneously for 1 minute. The patients were then placed back on ventilatory support for at least 5 minutes or until the patient’s SaO2 and heart rate were back to baseline values. Inspiratory pressure and Pmax measurements were performed when the patient was clinically stable. A P1/Pmax ratio ≤0.3 was a positive predictor for successful weaning, while higher values correlated with a greater number of weaning failures. Moreover, when the index is used in conjunction with the f/Vt ratio, its sensitivity is 81%, specificity is 93%, and predictive value is 93%. Based on these findings, inspiratory pressure/maximal inspiratory pressure ratio may be an additional useful index in predicting weaning outcome.

Other indices used

Many other indices have been developed, but their use is still controversial [12-15]. Pressure time product (PTP) is an indicator of the breathing effort, and varies with total lung resistance. The PTP has been suggested to be an actual estimate of respiratory muscle oxygen consumption by some authors [12]. Normal values range from 60-80 cmH2O/min when the patient is intubated. While when patient is extubated normal PTP values range between 200-300 cmH2O/min. The reason for the difference depends upon the degree of ventilator induced support, as increasing the work of mechanical ventilation, diminishes the effort required for breathing.

Respiratory time fraction (Ti/Ttot), is a method that indicates the endurance and it may be defined as the ratio between the inspiratory time to the total time of the respiratory cycle on the patient. Normal values range between 0.3-0.4, while a higher number will indicate fatigued patients, which may be traduced in respiratory muscle failure to sustain the breathing effort. This may be used to understand the energy consumption that is required by the patient to sustain a breath, in order to assess a successful weaning trial.

Methods of weaning from mechanical ventilation

Many different techniques have been used to wean patients off the ventilatory support. The most commonly used are pressure support ventilation (PSV), synchronized intermittent mechanical ventilation (SIMV), spontaneous breathing trials using T tubes, and continuous positive airway pressure (CPAP).

Pressure support ventilation

This mode of mechanical ventilation allows the patient to virtually have control over the respiratory rate and timing, as well as inspiratory flow and tidal volume. Whenever the inspiratory flow reaches a certain threshold level, the cycling from inspiration to expiration occurs. One of the main advantages of
this mode of mechanical ventilation, is that improves patient’s spontaneous breathing and reduces oxygen consumption due to external work during a weaning trial. One of the strategies employed when a patient is weaning is the addition of external PEEP, which will be beneficial with regard to energy consumption in patients who have dynamic pulmonary hyperinflation with dynamic airway collapse [13]. Brochard et al demonstrated successful weaning trials in patients using this mode versus SIMV and T piece trials, by reducing the total time of weaning time [13]. Conversely, other studies have evidenced poor outcome in patients using this method when compared with SIMV and T piece trials. Conclusive evidence of the efficacy of this approach has yet to be established.

Esteban et al successfully demonstrated after 2 weeks of weaning trials the advantages of the T-piece as compared to other methods such as pressure-support ventilation (PSV) or synchronized intermittent mechanical ventilation (SIMV). Success was higher with a once daily trial of T piece than with SIMV or PSV, and weaning duration was significantly shorter with once daily trial of spontaneous breathing with T piece (3 days) than with SIMV (5 days) (rate ratio, 2.83; 95% confidence interval [CI], 1.36 to 5.89; p <0.006) or PSV (4 days) (rate ratio, 2.05; 95% CI, 1.04 to 4.04; p <0.04) [14]. Despite such results, it should be noted that success of such ventilatory techniques used often depends on the skills of the clinicians, as well as the technique itself.

**Synchronized intermittent mechanical ventilation**

Synchronized intermittent mechanical ventilation (SIMV) is a ventilator mode allows the patient to spontaneously breathe between ventilator induced breaths. Theoretically, it has the advantage of allowing a smooth transition from total dependence of ventilator to full spontaneous breathing; however, one of the problems related to SIMV is that there is additional work associated with breathing due to the demand of valve systems and the resistance of the external ventilator circuits and humidifiers. In addition there is an inability for patients to exhibit breath to breath adaptations to the mechanical device. Synchronized intermittent mechanical ventilation has the potential to increase the weaning time if the mandatory rate is not carefully reduced [2]. Two published studies [13,14] compared the efficacy different weaning techniques; and the results revealed that SIMV performed worse than either PSV or a T piece with regard to weaning timing and probability of successful weaning after 14 or 21 days.

**Spontaneous breathing trials with a T tube**

The most valuable advantage of spontaneous breathing trials with a T-tube is that allows periods of respiration that are alternated with periods of rest, or reduced muscular activity. The T-tube system offers poor resistance to gas flow and there is no additional imposed work associated with breathing, as there are no ventilator circuits or valves involved. It is a valuable test to evaluate the ability of the patient to sustain autonomic spontaneous breathing [15]. Despite the great advantages of this method, the absence of a connection to ventilatory support may interfere with the evaluation of the patient as it is unmonitored and there is no apnea backup available.

Unfortunately, the optimal duration of the spontaneous breathing trials remains uncertain. Once daily 2 hour trials are commonly used. Typically, patients who tolerate a 2 hour trial without any sign of intolerance or distress are extubated. In a 2 hour T tube trial for 192 patients (78% of the total group), who successfully completed the trial, were immediately extubated; 36 of those (18.7%) required intubation within 48 hours [14]. The remaining 54 patients had signs of poor tolerance during the trial of spontaneous breathing, which lasted a median of 30 minutes (25th–75th percentiles: 15 to 60) and were reconnected to the ventilator.

In a study by Esteban and colleagues on the intermittent mode of T-tube trial, patients were disconnected from ventilatory support [14] and were allowed to breathe spontaneously through either a T tube circuit or a continuous flow circuit, which was designed to provide a continuous positive airway pressure (CPAP)
of ≤5 cmH₂O. The duration of the trial was then increased gradually, and the intermittent mode was attempted twice a day. Between the trials assist control ventilation was given for at least 1 hour. Patients able to successfully breathe on their own for ≥2 hours, without any signs of poor intolerance or distress, were extubated immediately [14].

**Conclusions**

Mechanical ventilation, despite its wide use in medical practice, may lead to numerous complications, particularly in those with longer ventilatory dependence. Early identification of patients on mechanical ventilation that can be discontinued is crucial in improving patient outcome and recovery. In addition, the clinician must be careful to avoid premature trials and to minimize the complications related to those with failed trials. The use of weaning indices is crucial to achieve better patient outcomes as well as more successful weaning trials. Supported by its clinical use, the f/Vt ratio is likely the best predictor of weaning outcome; moreover, it plays a major role in the pathophysiology of these patients. Likewise, it can be easily measured at the bedside and can be instituted independent of patient effort/cooperation.

**References**