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Weaning from Mechanical Ventilation

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Mechanical ventilation (MV) is a life-supporting modality that is used in a significant proportion of patients in ICUs. Most such patients are extubated quite readily. As many as 20% of mechanically ventilated patients, however, will fail their first attempt at weaning, and more than 40% of the total duration of MV is spent in the weaning process [1,2]. Prolonged MV is associated with a host of complications (eg, infection, gastrointestinal [GI] bleeding, and deep venous thrombosis). On the other hand, premature extubation followed by reintubation is associated with increased morbidity and mortality [3]. Choosing the right time for a successful discontinuation of MV, in the light of available physiologic and laboratory factors, remains a challenge. This article reviews the causes of weaning failure and an approach to liberating patients from MV.

Pathophysiology of respiratory failure during weaning and extubation failure

Weaning from MV depends on the strength of respiratory muscles, the load applied to those muscles, and the respiratory drive to breathe. Respiratory failure may occur because of any of these. For example, muscular dystrophy (weakness of respiratory muscles), acute bronchospasm (increased respiratory load), or narcotic overdose (reduced central drive) all may lead to respiratory failure. In general, the etiology of unsuccessful weaning is the imbalance between the respiratory muscle pump and the respiratory muscle load. This could happen secondary to inadequate resolution of the initial problem that rendered the patient on MV, a rise of a new problem, a ventilator-associated complication, or a combination of these factors. It

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is imperative to correct the key elements listed in Box 1 to optimize the chance of successful weaning.

The relationship between respiratory load and muscle strength may be viewed as a balance. If the load is too heavy, or muscle strength is too weak, muscular contraction cannot be maintained, and muscles acutely fail. This is termed fatigue. The predominate feature of the pathophysiology of weaning failure is high levels of load relative to the strength of the respiratory muscles. As compared with those who succeed with a weaning trial, for those who fail, load increases. Almost always, the drive to breathe is high in such cases.

Many investigators have combined the failure to liberate from MV and extubation failure into one entity. In contrast, recent work indicates that these are distinct processes with discrete pathophysiological causes and outcomes [3].

An extubation failure may occur secondary to upper airway obstruction or respiratory secretions that could not be managed by the patient. These factors do not manifest themselves until the removal of the translaryngeal tube. Significant trauma to the airway from translaryngeal intubation is more common in females and increases with increased duration of intubation.

Another potential reason for extubation failure is the loss of positive pressure in the thorax after extubation in pressure support ventilation (PSV)-weaned patients. The transition from intrathoracic positive-pressure ventilation to negative-pressure ventilation occurs after the removal of the endotracheal tube. This may cause left heart failure, because the positive-pressure ventilation acts to reduce afterload on the left ventricle. This phenomenon is not seen by using a T-piece trial for weaning.

It is important to remember that the extubation failure that requires reintubation is associated with an increase in the duration of MV, ICU and hospital length of stay [4]. There is also a significant increase in hospital

Box 1. Key elements to optimize weaning

Determine cause of ventilatory dependency
Rectify correctible problems
- Pulmonary gas exchange
- Fluid balance
- Mental status
- Acid-base status
- Electrolyte disturbance

Consider psychological factors
Optimize posture
Provide ambulation

mortality, especially in the case of delayed reintubation. This is why there has been so much effort directed at improving the prediction of extubation outcome to prevention extubation failure.

Timing for the initiation of weaning

Recognizing and treating the processes that caused the patient to go on the ventilator is the first goal in liberating him or her from MV. The complete resolution of the inciting event that led to respiratory failure does not need to be accomplished to start the process of weaning. Partial resolution of the cause of respiratory failure may be enough to be able to discontinue MV.

There are many reasons to attempt to get patients off MV as soon as possible. Common side effects of MV are hemodynamic disturbances, need for sedation, tracheal damage, ventilator-associated pneumonia (VAP), increased incidence of GI stress ulcers/bleeding, skin breakdown and decubiti, muscle wasting and weakness, and barotrauma. It is imperative to attempt to decrease the occurrence of these iatrogenic problems (eg, reducing plateau airway pressure, reducing tidal volumes, and semirecumbent position 30 to 45 degrees upright) and reduce the time of exposure by reducing the length of MV. Not only have studies shown that about 40% of the time during MV is devoted to weaning, but they also have shown that the most common approach to weaning is a progressive reduction of ventilatory support [5,6]. Others have noted that most patients do not need progressive withdrawal of MV [7]. Evidenced-based practice now supports early attempts at weaning in a protocol-driven fashion [2,8–10]. Successful extubation in the shortest possible time is associated with improved patient outcomes and minimized cost associated with MV.

About 70% to 80% of patients who require MV for respiratory failure will be extubated after a trial of spontaneous breathing trial once the precipitating process has been corrected. About 20% to 30% of patients who require intubation, however, do not tolerate initial attempts to breathe without the help of the ventilator [11,12]. This is especially true in the patients who required MV for more than 24 hours. As stated, failure to wean is caused by the imbalance between the capacity of the respiratory system and the load placed on the system.

The following problems found in mechanically ventilated patients will affect either the capacity of or the demand on the respiratory system. These include: hemodynamic instability, acid–base disorders, electrolyte disturbances, volume overload, altered mental status, and decreased respiratory muscle function. To improve chances of weaning, all should be addressed and corrected. Box 1 lists the key elements to optimize outcomes in patients weaning from MV. In regards to hemodynamic stability, the patient should have no evidence of myocardial ischemia, new arrhythmia causing significant decrease in cardiac function, or have need for vasopressors. As far as the acid–base status is concerned, a normal serum pH (7.35 to 7.45) is desired but not essential. Treating acidosis is important, because acidosis increases the minute ventilation required to normalize pH. Of special note, in chronic hypercapnic patients, correcting PCO2 by the ventilator during MV will promote bicarbonaturia through renal compensation to normalize the pH. This likely will produce acute respiratory acidosis at the time of spontaneous breathing trials and lead to failure.

Electrolyte disturbances during weaning have been studied extensively. It has been shown that hypophosphatemia, hypocalcemia, hypomagnesemia, and hypokalemia reduce muscle contractility and affect weaning [13]. These disturbances must be corrected before weaning attempts.

Volume overload frequently occurs during treatment of the systemic inflammatory response syndrome precipitated by severe infection, pancreatitis, major surgery, or other issues. This extra volume will lead to decreased functional residual capacity of the lungs and alveolar collapse. This is associated with ventilation/perfusion mismatch, which requires an increase in the positive end-expiratory pressure (PEEP) to keep the alveoli opened and maintain good oxygenation. The mobilization of such fluid usually happens upon resolving the systemic inflation, and may be augmented at that time by diuretics.

Neurological deficit secondary to brain injury may impose quite a challenge as to the optimal time for weaning and/or extubation. Many clinicians believe that extubation of brain-injured patients who lack a gag reflex, are comatose, or have significant respiratory secretions should be delayed. In a recent study by Coplin and colleagues [14], it was shown that the delay in extubation of brain-injured patients capable of spontaneous breathing secondary to the reasons mentioned carried an increased risk of pneumonia and longer hospital and ICU stays.

In general, altered mental status in the ICU is multifactorial. Causes include pain, anxiety, delirium, and toxic/metabolic processes. All of these should be addressed and/or treated, before the initiation of weaning. It has been shown that oversedation with long-acting sedatives prolongs the days of MV, ICU stay, and subsequently hospital stays [9]. Many institutions have implemented protocols and guidelines to help in the administration of sedatives in the mechanically ventilated patient. Some of these guidelines use a scoring system, daily interruption of sedation, and automatic reduction of dosing [15].

Fatigue of patients undergoing weaning from MV is a major factor in failure to wean. Several studies showed by electromyogram (EMG) diagnosis that diaphragmatic fatigue occurs in the first day in all patients on MV, and those who recovered were extubated successfully [16,17]. The patients who continued to exhibit fatigue needed reintubation. It is not known how much diaphragmatic strength is needed to sustain spontaneous breathing, or how long the resting period should be to recover from diaphragmatic fatigue. It is possible that 1 day of rest, fully supported by MV, may be enough for diaphragmatic recovery [18].

Adequacy of sleep and sleep deprivation should be considered when agitation and lethargy are hindering the weaning. It is unrealistic, however, to delay weaning until the patient has achieved a normal sleeping pattern. In addition, one should not ignore the psychological factors in achieving successful weaning. If the patient is alert he/she should be informed about the weaning trial with explanation and assurance that may decrease the level of stress. Daily orientation to the day, time, and surroundings, and environmental stimulation by using televisions, books, and radio are widely used now in many ICUs in the country.

Malnutrition causes reduction of muscle mass, endurance, and muscle strength. It also causes decreased immunity, predisposing the patient to further infections. Nutrition repletion in critically ill patients showed improved respiratory forces and facilitated weaning [3,13].

Weaning criteria and physiologic indices: key elements for successful weaning

The difficulty in integrating all the physiological parameters involved in weaning from MV has fueled a range of research to find the weaning parameters to determine readiness to wean. Conventional criteria for readiness to wean are relatively easy to use, but their sensitivity and specificity are relatively poor. These criteria include tidal volume (VT), minute ventilation (MV), vital capacity (VC), maximum voluntary ventilation (MVV), respiratory frequency, maximal inspiratory pressure as well as integrative indexes.

VC is the greatest volume of gas that a patient is able to exhale in taking a maximum inspiration from residual volume. VT is that volume of gas moved during a normal respiratory cycle. The threshold values for these two parameters predictive of weaning remain controversial but are in the order of 5 to 8 mL/kg for VT and 10 to 15 mL/kg for VC. Measurement of VC is relatively difficult, because it depends on considerable cooperation of the patient. Given the large variability in VC, it is not surprising that some studies have shown that VC often failed to predict weaning outcome with a high degree of accuracy [19,20]. Using a VT cutoff of 4 mL/kg, the positive predictive value was 0.67, and negative predictive value was 0.85 [8].

Maximum voluntary ventilation (MVV) is the volume of air that can be exhaled with maximum effort over 1 minute. Normal values for MVV range from 50 to 200 L/min. In a resting, healthy adult, MV is about 6 L/min. The relationship between resting MV and MVV indicates the proportion of the patient's ventilatory capacity required to maintain a certain level of $PaCO_2$ and also indicates the reserve available for further respiratory demands. The combination of a MV of less than 10 L/min and the ability to double this value during an MVV maneuver was associated with the ability to wean successfully [21]. Both of these tests, however, are associated with significant false-positive and -negative rates. Furthermore, the MVV can be difficult to obtain in critically ill patients, as they may be unable to cooperate.

Measuring muscle strength is one simple assessment of respiratory muscle function. Respiratory muscle function can be measured at the patient's bedside by recording the maximal inspiratory pressure (MIP) by means of an aneroid manometer. Maximum static inspiratory pressures for healthy young men and women are approximately -120 cm H_2O and -90 cm H_2O, respectively. Maximal inspiratory efforts may be performed easily in uncooperative intubated patients by using a one-way valve connected to the manometer, which allows the patient to exhale freely but forces the patient to inhale against the manometer. An MIP less than -30 cm H_2O is associated with successful extubation, but an MIP greater than -20 cm H_2O is associated with the inability to maintain spontaneous breathing. Studies have shown these values to have a better negative than positive predictive value [22,23].

Several more recent predictive criteria of weaning outcome have been described (Box 2). These include measurement of transdiaphragmatic pressure, airway occlusion pressure, gastric intraluminal pH (pHi), and several integrative indices. These techniques, however, all share in common the

Box 2. List of commonly used weaning parameters

Simple ventilatory parameters [3,22]
- Vital Capacity (VC)
- Minute ventilation

Oxygenation parameter
- PaO2/F_{IO_2}

Respiratory muscle strength parameters [22]
- Maximum inspiratory pressure (MIP)
- Maximum expiratory pressure (MEP)

Central respiratory drive parameter [24]
- Airway pressure developed 100 ms after the beginning of inspiration against an occluded airway (P0.1)

Respiratory muscle reserve parameters [20]
- Maximal voluntary ventilation/minute ventilation (MVV/MV)
- Mean transdiaphragmatic pressure per breath/maximal transdiaphragmatic pressure (Pdi/Pdimax)

Pattern of spontaneous breathing parameter [22]
- Respiratory rate/tidal volume (f/Vt) rapid shallow breathing

Integrated multiple variables index [22]
- P0.1 X f/Vt
- Compliance, rate, oxygenation, and pressure

requirement for specialized equipment, difficulty of measurement, or complicated equations, which make bedside utility poor [3].

One exception is the rapid shallow breathing index described by Yang and Tobin [22]. They found that MV is well-maintained in patients who fail a weaning trial, but its components VT and respiratory frequency are combined in a manner that results in inefficient gas exchange. In general, patients who fail weaning trials drop their tidal volumes and increase their respiratory rates. Tobin and Yang have shown that the rapid shallow breathing index as reflected by frequency (breaths/minute)/VT (liters) is an accurate predictor of weaning outcome. Using a threshold of less than 105, the frequency (f)/VT ratio had a positive predictive value of 0.78 and a negative predictive value of 0.95.

The advantages of the f/VT ratio as a weaning predictor are that it is easy to measure and not dependent on patient cooperation and effort. The f/VT ratio was evaluated while patients were breathing spontaneously through an endotracheal tube. A bedside spirometer was used to measure VT. The predictive value of this index may be lower if measured while patients are on the ventilator with either continuous positive airway pressure (CPAP) or pressure support.

It is important to understand that no index has proven to be ideal and highly predictive of weaning. In patients mechanically ventilated for less than 72 hours, it is likely that conventional weaning parameters and bedside assessment by an expert physician have predictive value that would equal the measurement of the work of breathing. In complex long-term ventilated patients, however, work of breathing may be more predictive of successful weaning outcome (ie, successful spontaneous breathing for at least 24 hours post extubation).

Weaning modes of mechanical ventilations there a preferred technique?

Weaning from MV has been described as either a gradual decrease of ventilator support to allow liberation from the ventilator or determining when the patients will have the ability to be separated from the ventilator safely. Multiple different techniques have been proposed to facilitate the transition to spontaneous ventilation. The studies that have addressed this issue, however, have conflicting results. These studies focused on the impact of the weaning mode on the work of breathing, rather than the relevant outcome of a timely and successful weaning.

There is a significant heterogeneity in the population on MV. The weaning of a short-term ventilated patient who is in the ICU for a drug overdose differs markedly from weaning a long-term ventilated patient with COPD, pneumonia, or ARDS. Many of these studies focused on short-term ventilated patients less than 72 hours. Nevertheless, the commonly used techniques of weaning are T-piece, synchronized intermittent mandatory ventilation (SIMV), or PSV. The important question is: In difficult-to-wean patients, which of these three techniques will lead to the highest proportion of successfully weaned patients and the shortest weaning time?

Unfortunately, the optimal mode of MV used during weaning remains controversial. It generally is accepted that SIMV weaning prolongs the duration of MV. Daily T-piece trials consistently have been superior to the SIMV mode in weaning, and at least equivalent to PSV weaning. More than once daily T-piece trials have not been shown to be superior to daily trials [25].

PSV provides a progressive unloading of inspiratory muscles compared with SIMV. The results of trials with PSV, however, have been variable. What appears to be consistent is that a protocol-directed weaning strategy leads not only to a significant reduction in the duration of MV, but also to a significant decrease in the number of complications and costs [2,8–10]. Several of the PSV weaning trials have been protocol-driven, and questions remain as to whether SIMV could do better in weaning if used in a different way (eg, volume-controlled mandatory breaths interspersed with spontaneous pressure-supported breaths reduced in a protocol driven fashion).

Noninvasive positive pressure ventilation (NPPV) also has been used as a method to support ventilation following early extubation [3,26]. A clinical study showed that this technique ,compared with standard oxygen therapy, averted respiratory failure after extubation and decreased ICU mortality among patients at increased risk. The benefits in mortality, however, were seen only in the hypercapnic patients. The length of ICU and hospital stays, and mortality at 3 months were similar in the two approaches [26].

With recent advances in technology, new features on ventilators like automatic tube compensation (ATC) have been developed. Several new trials have been performed to evaluate the prediction of weaning outcome using this new feature [27,28]. ATC compensates for the pressure drop across the endotracheal or tracheostomy tube by delivering exactly the amount of pressure necessary to overcome the resistive load imposed by the tube for the flow measured at the time (variable pressure support). ATC has been shown to decrease the work of breathing necessary to overcome endotracheal tube resistance more effectively than PSV or CPAP. It is possible, however, that ATC could allow more marginal patients to tolerate a breathing trial, who then would develop ventilatory failure after extubation. No comprehensive trial has been done to compare ATC with T-piece in terms of successful weaning outcome.

Lastly, another new technique holds some promise in the field of weaning from mechanical ventilation. Proportional-assist ventilation (PAV) is a form of synchronized partial ventilatory support in which the ventilator generates pressure in proportion to the patient's instantaneous effort. This proportionality applies from breath-to-breath as well as continuously throughout each inspiration. In fact, patient effort is amplified as if the patient has acquired additional inspiratory muscles that remain under the control of the patient's own respiratory control system. Unlike other modes of partial support, there is no target flow, tidal volume, ventilation, or airway pressure. The objective of PAV is to allow the patient to comfortably attain whatever ventilation and breathing pattern his or her control system sees fit. The responsibility for determining the level and pattern of breathing is shifted from the caregiver to the patient.

To accomplish the objectives of PAV, the machine provides pressure assistance in proportion to an ongoing inspiratory flow (flow assist [FA]) and volume (volume assist [VA]). For FA and VA to result in airway pressure being proportional to instantaneous effort, both FA and VA need to be used simultaneously. FA (expressed in cm $H_2O/L/s$) must be less than the patient's resistance (Rrs). VA (expressed in cm H_2O/L) must be less than patient's elastance (Ers), and finally the fractions (ie, FA/Rrs and VA/Ers) ideally should be similar [1].

Protocolized weaning from mechanical ventilation—the role of nonphysician health care professionals

Several studies have evaluated weaning parameters to identify patients who are ready for extubation and how to apply those parameters in a guideline or protocol for the weaning to be successful in the shortest possible time [2,8–10]. Fig. 1 is an example of such a guideline. The initial step in any protocol-driven ventilator weaning is daily screening for readiness to wean using several weaning parameters. To do so, every appropriate patient in the ICU also should undergo a daily interruption of sedation to be in optimal neurological condition for the screening [9,15].

Most of these guidelines start by identifying potential candidates for the daily screening. Candidates for such a protocol are patients who have adequate oxygenation (PaO2 >60 mm Hg with $F\text{IO}_2 \leq 0.5$ and PEEP ≤ 8 cm H_2O). The screening for readiness may include calculation of the rapid shallow breathing index (RSBI), which is the frequency to tidal volume ratio (f/Vt) measured after 1 minute of spontaneous breathing. In general, patients who fail weaning trials drop their VTs and increase their respiratory rate. Yang and Tobin [21] have shown that the RSBI is an accurate predictor of weaning outcome. Using a threshold of less than 105, the f/VT ratio had a positive predictive value of 0.78 and a negative predictive value of 0.95. After manifesting adequate coughing during suctioning to ensure intact airway reflexes, those patients passing the rapid shallow breathing trial will be subject to spontaneous breathing trials using PS, CPAP, or T-piece for up to 120 minutes.

The spontaneous breathing trial (SBT) is terminated if the patient successfully tolerates SBT from 30 minutes to 2 hours or starts showing signs and symptoms of failing (respiratory rate >35 for >5 minutes, SaO2 $<90\%$ for >30 seconds, 20% increase or decrease in heart rate for

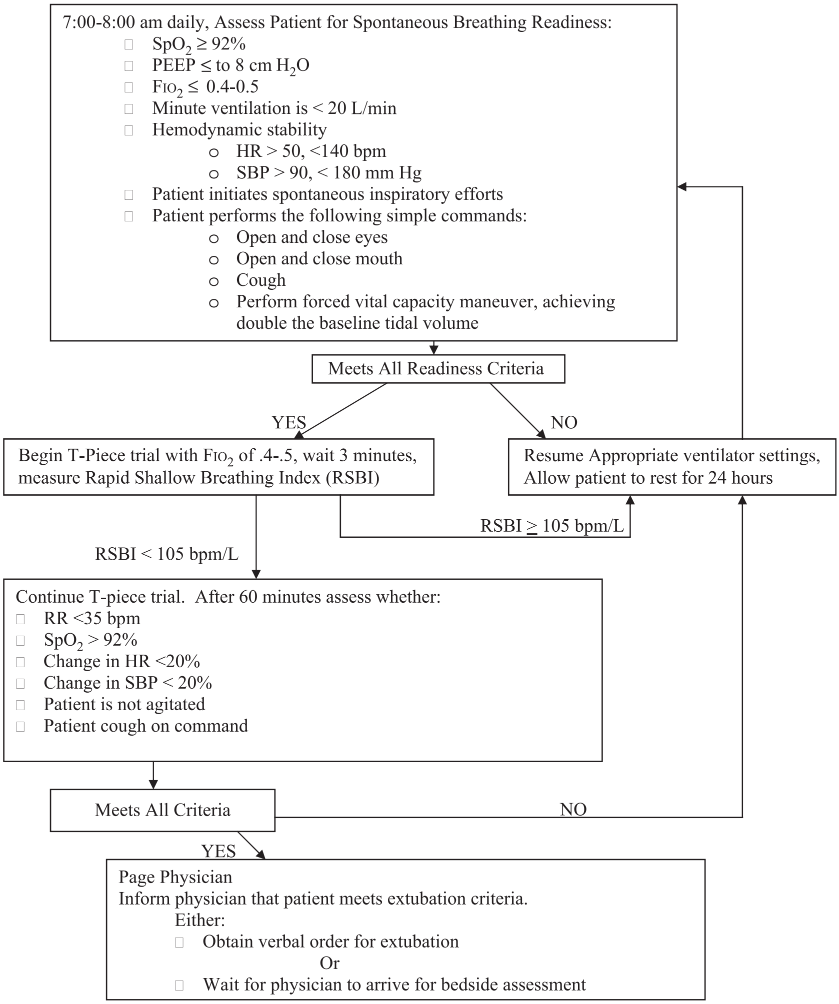

Fig. 1. Example of mechanical ventilation weaning protocol flow diagram.

> 5 minutes, systolic blood pressure SBP > 180 or SBP < 90 for 1 minute with repeated measurements, agitation, anxiety, or diaphoresis as a change from the baseline).

In general, these protocols are driven by the unit respiratory care practitioners and/or nurses. Several recent studies have shown that protocol-driven weaning by nurses or respiratory therapists is superior to independent physician-directed weaning regardless of what weaning mode is employed [8,10]. This is likely because providers are distracted easily by more acute patients, and stable weaning patients may not undergo their daily trial of spontaneous breathing unless it is under protocol direction.

The next improvement of protocolized weaning may be computer-driven. Closed-loop knowledge-based algorithms have been introduced into ventilators to act as a computer-driven weaning protocol. The computerized protocol used in a recent trial included an automatic gradual reduction in pressure support, automatic performance of SBTs, and the generation of an incentive message when an SBT was passed successfully [2]. This computer-driven system reduced MV duration from 12 to 7.5 days ($P = .003$) and ICU length of stay 15.5 to 12 days ($P = .02$) and caused no adverse effects when compared with physician-controlled weaning. This approach will need to be compared with protocolized weaning rather than standard of care before universal adoption of computer-driven weaning.

Summary

MV is a life-sustaining therapy fraught with side effects. The successful removal of MV at any time is associated with a higher survival rate. Therefore, removing the patient from the ventilator as soon as possible is in the patient's best interest. The best approach to weaning patients from MV involves a team approach of all caregivers (physician, nurses, respiratory therapist, physical therapist, and nutritionists). The team uses a weaning protocol that gives the nurses and/or the respiratory therapist the authority to start a daily screening of ventilated patients. If patients meet certain criteria, a trial of spontaneous breathing (positive pressure flow mode or T-piece) is undertaken. If patients pass the trial, they are extubated. Patients who do not pass the SBT will be reassessed to identify and treat any reversible factors and undergo daily SBTs if they continue to meet the criteria.

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