REVIEW

Weaning from mechanical ventilation

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Purpose of review
Liberation from mechanical ventilation is a defining moment for intubated patients, and thus a critical clinical decision. Extubating the patient too early exposes the patient to extubation failure and reintubation. Waiting too long increases the complications of prolonged intubation. Tools to help the physician with this critical decision and to test readiness have been available for decades, and are continuously being improved. New methods to improve extubation outcomes are also being developed. This review covers the latest studies in order to help physicians take advantage of the latest developments in a rapidly evolving field.

Recent findings
This review highlights the recent advances in assessing and testing for readiness of weaning and liberation from mechanical ventilation, the cause of weaning failure, the value of weaning protocols, and the role of noninvasive positive pressure ventilation in liberating patients from invasive mechanical ventilation.

Summary
Recent findings are shedding more light on this topic, and transforming 'the artistic' aspect of weaning and liberation from mechanical ventilation into a more 'scientific' approach that will expedite liberation from mechanical ventilation yet without encountering high failure rates, and without exposing patients to unnecessary risks.

Keywords
indexes, liberation, mechanical ventilation, predictors, protocols, weaning

INTRODUCTION

Weaning, the gradual withdrawal of mechanical ventilation and concomitant resumption of spontaneous breathing, is unnecessary in most patients. In 1987, Hall and Wood [1], proposed liberation from mechanical ventilation as the ultimate objective, and subsequently numerous studies investigated methods and tools to identify patient readiness for successful liberation from mechanical ventilation [2–5]. Recently, Peñuelas *et al.* [6■■] analyzed 2714 mechanically ventilated patients for more than 12 h who were weaned and underwent scheduled extubation. They found that 1502 patients (55%) could be classified as simple weaning, 1058 patients (39%) as difficult weaning, and 154 (6%) as prolonged weaning (>7 days) [6■■].

Bickenbach *et al.* [7■] found that prolonged weaning and mechanical ventilation are independent predictors of ICU discharge and 1-year mortality. Thille *et al.* [8■■], found that, when compared with successful extubation, failed extubation was followed by a marked clinical deterioration. These studies re-emphasize the importance of successful liberation from mechanical ventilation, and its effect on acute and long-term prognosis. It is therefore, of utmost importance for clinicians to keep abreast of the latest developments in the field of liberation from mechanical ventilation. This review will go over the latest studies, placing special emphasis on advances in the field of liberation from mechanical ventilation over the last 12 months.

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KEY POINTS

- Weaning from mechanical ventilation should be based on sound clinical judgment.
- Indices for determination of weaning outcome should be multifactorial, and may involve variables reflecting systems other than the respiratory system.
- Use of weaning protocols can expedite the process of liberation from mechanical ventilation.
- Noninvasive ventilation can play a significant role in improving weaning outcome.

ASSESSING READINESS FOR LIBERATION FROM MECHANICAL VENTILATION

Assessing readiness for liberation from mechanical ventilation is the first step in the process of liberation, and begins with the resolution of respiratory failure and/or the events that promoted the need for mechanical ventilation. In 2001, an expert panel [9] published a set of evidence-based weaning guidelines. They noted that minute ventilation (V_E), negative inspiratory force, maximum inspiratory pressure, tidal volume (V_T), breathing frequency (f), breathing frequency to tidal volume ratio (f/V_T) also known as rapid shallow breathing index (RSBI), $P_{0.1}/P_{Imax}$ (ratio of airway occlusion pressure after 0.1 s onset of inspiratory effort to maximal inspiratory pressure) and an integrative index of compliance, rate, oxygenation and pressure (CROP) had some predictive capacity. However, their predictive values have been questioned recently. Monaco *et al.* [10▪], reported that V_T, V_E, f and f/V_T were poor predictors of early successful weaning in 73 cohort patients requiring more than 24 h of mechanical ventilation.

The recognition of the limitation of these simple indices in predicting successful outcome led to the exploration of their use as dynamic and changing variables. New studies are now looking at the complexity, variability, and changes of these simple indices as markers of weaning success. Qualitative and quantitative nonlinear dynamic analysis of the V_T pattern and respiratory rate pattern have emerged as tools for assessing the interbreath variability, and its usefulness in predicting weaning outcome [11,12]. Papaioannou *et al.* investigated heart rate (HR) and respiratory rate complexity in patients with weaning failure or success, using both linear and nonlinear techniques during pressure support ventilation (PSV) of 15–20 cmH$_2$O followed by a 30 min of spontaneous breathing trial (SBT) on a pressure support (PS) of 5 cmH$_2$O. They reported that the successful extubation group had significantly higher respiratory rate sample entropy and higher low frequency, and high frequency components of HR signals than the unsuccessful group. A new prediction model based on cardiorespiratory dynamics using RSBI, respiratory rate entropy, $P_{0.1}$ and cross HR–respiratory rate sample entropy showed increased prognostic impact upon weaning outcome in surgical patients [13▪]. Subsequently, Papaioannou *et al.* [14▪] developed a toolkit of cardiorespiratory dynamics for predicting weaning outcomes. After SBT, increased breathing complexity was seen in successfully liberated patients, and proved to be more reliable than conventional indices in discriminating patients with different weaning outcomes. White *et al.* [15▪] looked at interbreath interval complexity during a SBT, and found that a lower complexity was associated with a higher failure rate. Whenever available at bedside, these metrics may be useful markers of pulmonary health, and assist in clinical decision-making [15▪].

Yang and Tobin [16] first demonstrated that the RSBI measured during the first minute of spontaneous breathing on room air was a good predictor of weaning outcomes at a threshold of 105 breaths/min per l or less. Subsequently, RSBI was shown to have excessive false positive predictions, and its predictive power drops in patients ventilated for more than 8 days, as well as in patients with chronic obstructive pulmonary disease (COPD) and the elderly patients [17–20]. Recently, it was shown that RSBI measured early during SBTs had a low sensitivity, specificity, and diagnostic accuracy in predicting successful T-piece trial outcome [21▪▪]. These findings could be by the fact that RSBI threshold is influenced by the ventilatory support settings [22]. RSBI significantly decreased during a trial of pressure support, continuous positive airway pressure (CPAP) trial on 40% O_2, and CPAP on room air [22–24]. Other variables such as time of day of test and technique of measurement did not affect the threshold. These studies suggest that the threshold of 105 breaths/min per l of the RSBI should be adopted only when performed under similar experimental conditions as Yang and Tobin. Teixeira *et al.* [25] found that the serial f/V_T measurement during a SBT after passing the first measurement of f/V_{1T} of 105 or less did not have a good predictive value to detect extubation failure when a cut-off of 105 or less was used. Recently, Segal *et al.* [26▪] showed that RSBI relative increase of 20% during a 2 h SBT is a better predictor of successful liberation than a single determination of RSBI.

$P_{0.1}$ is effort-independent and correlated well with central respiratory drive. Recently, $P_{0.1}$ was combined with P_{aCO_2} in the assessment for liberation from mechanical ventilation [27▪,28]. The hypercapnic drive response (HCDR), defined as the ratio of $P_{0.1}$ change to P_{aCO_2} change and the hypercapnic ventilator response (HCVR), defined as the ratio of minute volume change to P_{aCO_2}, were evaluated by Raurich *et al.* [27■,28], who reported that the optimal cut-off points to differentiate between prolonged and nonprolonged weaning in 102 ventilated patients were 0.19 cmH_2O/mmHg for HCDR and 0.15 l/min per mmHg for HCVR. The use of $P_{0.1}$ as part of the CO_2 response test improved its predictability, and justifies a new look into its incorporation in clinical practice.

Integrative indices were evaluated for predicting weaning outcome. The CROP index had a sensitivity of 100% and a specificity of 70% [29■] when predicting outcome from mechanical ventilation. Delisle *et al.* [29■] evaluated another integrative index, the CORE index, which includes compliance, oxygenation, respiration, and patient's effort. The CORE index was found to have the highest sensitivity, specificity and positive likelihood ratio with the lowest negative likelihood ratio in predicting the SBT outcome compared with CROP, $P_{0.1}$, and RSBI. The authors recommended a large-scale study to confirm the accuracy of the CORE index.

TESTING READINESS FOR LIBERATION FROM MECHANICAL VENTILATION

A direct method for testing readiness of liberation from mechanical ventilation is a SBT with a T-piece, CPAP, or PSV trial. The exact duration of the trials that best reflect readiness for liberation from mechanical ventilation is not well known. However, convincing evidence [2,3,30,31] supports a trial of 30–120 min.

One advantage of PSV over T-piece or CPAP trials is its capacity to overcome the work of breathing imposed by the ventilator and endotracheal tube, and its possible narrowing by secretions lining the lumen after prolonged intubation [32–34,35■]. The level of PS required remains an important issue, and differs substantially from patient-to-patient. Recently, Molina-Saldarriaga *et al.* [35■] compared the T-piece trial to the CPAP trial in patients with COPD, and showed a tendency toward a higher rate of extubation success in the CPAP group.

New forms of assisted mechanical ventilation modes have been brought to fruition in recent years. Automatic tube compensation (ATC) provides a pressure that is intended to compensate for the endotracheal tube resistance during inspiration according to the actual gas flow [36]. In predicting successful extubation outcome, ATC has been shown to be as effective as PSV [37]. When compared with CPAP with no PSV, ATC showed a trend toward less failure, but no difference in the duration of weaning, days on mechanical ventilation, or rate of successful extubation [38■]. Another promising mode is adaptive support ventilation (ASV). When compared with conventional modes, ASV was associated with a shorter time to extubation in 15% of the patients [39■].

WEANING PROTOCOLS

Weaning/liberation protocols are developed to provide structured guidance for liberation from mechanical ventilation. Typically, they are formed of three components: list of objective criteria to assess readiness to liberate/wean; guidelines to reduce support or 'test readiness'; list of criteria to extubate [40■■].

A recent Cochrane review meta-analysis compared protocolized vs. nonprotocolized weaning and showed that weaning protocols were associated with 25% reduction in total duration of mechanical ventilation [40■■].

To design a weaning protocol, Goodman [41] indicated that a multiprofessional group needs to formulate a protocol, implement it into the ICU, and then maintain an ongoing auditing system.

ETIOLOGY OF LIBERATION FAILURE

When a patient fails a SBT, a prompt systemic search for the factors responsible for the failure should be initiated. New studies are coming out trying to address some of the reversible causes of liberation failure.

Respiratory factors

A major contributor to failing of a SBT is an imbalance between workload on the respiratory system and respiratory muscle capacity [42]. Kim *et al.* [43■■], using M-mode ultrasonography, found diaphragmatic dysfunction in 29% of patients without histories of diaphragmatic disease. These patients had early and delayed weaning failure when compared with patients without diaphragmatic dysfunction. Inspiratory muscle strength training (IMST) is now being investigated to see its effect on inspiratory muscle strength and on weaning outcome. Inspiratory muscle training, done twice a day using a threshold inspiratory muscle device, which provided a threshold inspiratory pressure load between −4 and −20 cmH_2O increased the maximal inspiratory trial, and improved RSBI with reduced weaning time in some patients [44■]. Martin *et al.* [45■] also showed that IMST improved maximal inspiratory pressure and improved weaning outcome. This is a new and innovative approach to tackle this problem with promising early results. One limitation of this study is that it was on postsurgical patients, and the results may not be generalized.

Major organ system failure

Myocardial dysfunction can cause liberation from mechanical ventilation intolerance [46]. Unrecognized congestive heart failure may be a cause of weaning difficulties, especially with the occurrence of an increase in left ventricular filling pressure upon switching from mechanical ventilation to spontaneous breathing [47▪]. Zapata *et al.* [47▪] showed in a small observational prospective study that an elevated B-type natriuretic peptide (BNP) and pro-brain natriuretic peptide (ProBNP) before SBT could predict weaning failure due to heart failure. An increase of BNP and ProBNP during the SBT was an indicator of heart failure as a cause of weaning failure.

Ouanes-Besbes *et al.* [48▪] looked at difficult-to-wean COPD patients ascribed to an increase in left ventricular filling pressure ascertained by an increase in pulmonary arterial occlusion pressure (PAOP) more than 10 mmHg when shifted to spontaneous breathing. They compared levosimendan (a calcium sensitizing drug) and dobutamine effect on these hemodynamic changes and found a decrease in PAOP with both drugs, but more pronounced with levosimendan. Routsi *et al.* [49] studied the use of nitroglycerin in 12 difficult-to-wean COPD patients, and found that nitroglycerin helped in restoring weaning-induced cardiovascular compromises manifested by increases in systemic arterial pressure, rate-pressure product, mean pulmonary arterial pressure, pulmonary artery occlusion pressure, and right ventricular stroke work, and by a decrease in mixed venous oxygen saturation, and thus nitroglycerine resulted in weaning 88% of the patients on the second day after failing their weaning attempt on the previous day. Randomized controlled trials are needed to see if these interventions will become part of weaning care in this patients' category.

Psychological factors

Psychological factors may be an important factor contributing to unsuccessful liberation from mechanical ventilation [50,51,52▪▪]. Communication with the patient and the patient's family helps reduce/eliminate psychological factors. A novel approach to reduce stress is music therapy. Hunter *et al.* [52▪▪] showed that music therapy while undergoing weaning trials had significant positive impact on HR and relative risk, indicating improved levels of stress. Patient and nurse satisfaction was high. However, no significant difference in mean days to wean was found [52▪▪].

NONINVASIVE POSITIVE PRESSURE VENTILATION

Noninvasive positive pressure ventilation (NPPV) provides respiratory support without the need for an invasive airway approach. The use of NPPV can facilitate earlier extubation and lead to a shorter duration of mechanical ventilation, and length of stay [53]. In COPD patients, NPPV facilitated extubation, decreased the period of ventilation support and ICU stay, and increased survival [54]. However, NPPV should be used with caution in non-COPD patients failing extubation. Esteban *et al.* [55] showed that NPPV did not reduce neither mortality nor reintubation rate among non-COPD patients who had respiratory failure after extubation. The mortality rate tended even to be higher when NPPV was used and the patient later intubated, suggesting that delaying necessary reintubation by the use of NPPV may worsen the outcome. Vianello *et al.* [56▪] showed in a prospective analysis of 20 patients with neuromuscular disease, that early NPPV use after extubation with assisted cough significantly decreased the reintubation rates and the use of tracheostomy, but had no effect on mortality. Su *et al.* [57▪▪] looked at the preventive use of NPPV after extubation in a prospective randomized controlled study involving 406 patients. NPPV use did not affect extubation failure or mortality rate. Girault *et al.* [58▪▪] compared weaning with NPPV in chronic hypercapnic respiratory failure to invasive weaning and found that NPPV significantly decreased weaning failure rates to 33% compared with invasive weaning (54%). Also intubation duration was 1.5 days shorter with NPPV. A recent Cochrane meta-analysis assessed the use of NPPV as a weaning strategy [59]. From the 12 trials that involved 530 patients with predominantly COPD, NPPV significantly decreased mortality (respiratory rate 0.55), ventilator-associated pneumonia (respiratory rate 0.29), length of stay in an ICU [weighted mean difference (WMD) 6.27 days] and hospital (WMD 7.19 days), total duration of ventilation (WVD 5.64 days) and duration of endotracheal mechanical ventilation (WMD 7.81 days). Noninvasive weaning had no effect on weaning failures or the duration of ventilation related to weaning.

TRACHEOSTOMY

The effect of early tracheostomy on weaning and liberation from mechanical ventilation was recently evaluated [60▪]. In a retrospective analysis of 296 patients needing tracheostomy due to extubation and/or weaning failure, Bickenbach *et al.* showed that whether tracheostomy was performed in 4 days or less, within 5–9 days, or more than 10 days did not have an effect on the length of weaning after tracheostomy; however, tracheostomy at 4 days or less was superior in reducing the time of mechanical ventilation days and its associated risks.

CONCLUSION

Successful liberation from mechanical ventilation depends on the application of skilled judgment, decision-making, and medical and nursing intervention. To predict who would have a successful extubation, and do it without delay is essential, and making the wrong decision has grave consequences on the patient. Most weaning predictors have limitations, and recent research studies are introducing new predictors and using older ones in an innovative manner. However, some of these predictors remain complicated and cumbersome to be used at the bedside. The use of protocols to expedite weaning is becoming mainstream, and an essential part of weaning. Adjunctive use of NIV, medications, or inspiratory muscle training is also being investigated to improve the chances of success. Finally, liberation from mechanical ventilation is a very active and constantly evolving field of study with new discoveries being made continuously. Therefore, physicians have a vested interest in following it up regularly for better patient management and improved clinical outcomes.

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Conflicts of interest

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