# 63 Weaning from Mechanical Ventilation

Hernán Aguirre-Bermeo, Ferran Roche-Campo, and Jordi Mancebo

## THE CONCEPT OF LIBERATION AND EXTUBATION

Weaning from mechanical ventilation represents the period of transition from total ventilatory support to spontaneous breathing. About 70% of intubated mechanically ventilated patients are extubated on the first spontaneous breathing trial (SBT) attempt, whether by disconnection from the ventilator or after breathing at low levels of pressure support for short periods of time, such as 30 to 120 minutes.[1,2] The remaining patients (about 30%) require progressive withdrawal from artificial ventilatory support.

Early liberation from mechanical ventilation and removal of the endotracheal tube is clinically important. Unnecessary prolongation of mechanical ventilation increases the risks of complications, including infections (particularly of bronchopulmonary origin), barotrauma, cardiovascular compromise, tracheal injuries, and muscle deconditioning. Clinicians should hasten the process that ultimately leads to removal of the endotracheal tube to maximize patient outcome.[3]

Liberation and extubation are different issues.[4] Liberation refers to weaning from mechanical ventilation and means that a patient no longer requires ventilatory support. When this step is achieved, the clinician has to consider a different question, i.e.: "Is the patient able to breathe spontaneously without the endotracheal tube?" Removal of the endotracheal tube is referred to as extubation. Regarding magnitude, the extubation failure rate (i.e., the need to replace the endotracheal tube and reinstitute mechanical ventilation) is variable and ranges from 5% to 20% of extubated patients.[1,5-7]

## MECHANISMS EXPLAINING LIBERATION FAILURE

### Respiratory Pump Failure

The most common reason for weaning failure is respiratory pump insufficiency and is caused by an imbalance between the patient's capabilities and respiratory demands.[8-11] Jubran and Tobin[12] investigated the progression of respiratory mechanics during SBT in patients with chronic obstructive pulmonary disease (COPD). At the very beginning of the trials, patients who subsequently failed had a slightly higher airway resistance, respiratory system elastance, and intrinsic positive end-expiratory pressure (PEEP) compared to those who succeeded. However, during the trials, respiratory mechanics progressively worsened in patients who failed to be liberated from the ventilator. Subjects who failed developed rapid, shallow breathing and most developed an increase in $PaCO_2$. Together, these abnormalities resulted in increased inspiratory muscle effort, which in some patients was likely close to the threshold of muscle fatigue.

Laghi et al.[13] studied 19 intubated patients during weaning from mechanical ventilation, of which 11 patients failed and 8 succeeded. Several physiologic indices were measured before and 30 minutes after SBT. The transdiaphragmatic twitch pressure, elicited by magnetic bilateral phrenic stimulation, did not differ before the SBT between the patients that failed or succeeded at ventilator liberation, and this variable did not decrease after the trial in either group. Patients failing the SBT were reconnected to the ventilator due to clinical signs of intolerance. It was concluded that weaning failure was not accompanied by low-frequency diaphragmatic fatigue, although weaning failure patients exhibited severe diaphragmatic weakness since twitch pressures were always low.

#### Common Disorders That Alter the Balance of Capacity and Load in Critical Illness

**Reduced Neuromuscular Capacity.** Previous studies have shown that diaphragmatic injury and atrophy are associated with the use of passive assisted control ventilation[14,15] and are significantly correlated with longer periods of ventilator support.[16] Critical illness polyneuropathy and myopathy, which are frequent complications of sepsis and multiple organ system failures, may also impede weaning.[17] In addition, respiratory muscle weakness is associated with delayed extubation.[18] Finally, malnutrition and deconditioning due to prolonged bed rest during critical illness can induce severe muscle dysfunction.[19]

**Increased Muscle Loads.** The increased work of breathing results from increased mechanical loads (elastic and/or resistive). Increased elastic workloads occur when lung and chest wall compliance are reduced (e.g., pulmonary edema, extreme hyperinflation during an acute asthmatic attack, pulmonary fibrosis, abdominal distension, obesity, trauma, or thoracic deformities).[13] The presence of intrinsic PEEP is another example of increased elastic workload and is a relatively common phenomenon, especially in patients with COPD.[20,21] Resistive work for breathing during critical illness may increase as a result of bronchospasm, excessive secretions, endotracheal tube resistance (which augments with kinking and deposition of secretions), and ventilator valves/circuits and humidifiers, especially when conditioning of inspired gases is provided with heat and moisture exchangers. The latter also increases the instrumental dead space.

#### Cardiovascular Dysfunction

The presence of cardiovascular dysfunction can contribute to weaning failure by augmenting the loads on the respiratory system and by reducing neuromuscular capacity.[22,23] Cardiovascular dysfunction can result from physiologic changes that occur during the resumption of unassisted spontaneous breathing.[24] When spontaneous breathing resumes, the intrathoracic pressure during inspiration is negative. This becomes a situation that results in increased left ventricular preload and afterload. Increased heart loads augment myocardial oxygen demand and may precipitate myocardial ischemia in patients with coronary artery disease.[25]

Jubran et al.[26] examined hemodynamics and mixed venous saturations in patients during weaning trials. Successfully weaned patients demonstrated increases in cardiac index and oxygen transport compared to values during mechanical ventilation. Patients who failed weaning did not increase oxygen delivery to the tissues due in part to the elevated right and left ventricular afterloads. Consequently, these abnormalities can jeopardize respiratory muscle function.

In intensive care unit (ICU) patients, congestive heart failure may occur as a consequence of an increase in venous return, volume overload, or catecholamine release induced by physiologic stress, such as weaning.[24,27,28] Impairment of cardiovascular function can be magnified in the setting of a positive fluid balance.[29,30]

It has been recently shown that performing an SBT using a T-tube (instead of pressure support and PEEP) in difficult to wean patients elicits a different cardiovascular response and when support is added (in the form of pressure support and PEEP), respiratory and cardiovascular function both improve.[31]

In the ICU, there are noninvasive tools (e.g., echocardiography and measurement of plasma B-type natriuretic peptide [BNP]) that help to make the diagnosis of cardiovascular dysfunction. Mekontso-Desap et al.[32] measured BNP levels during weaning trials. In this study, 41% of patients failed the weaning process and high BNP levels were identified as an independent risk factor for weaning failure. In addition, 9 of the 42 patients in whom weaning failed were successfully weaned after the administration of diuretics.

## PREDICTION OF WEANING AND EXTUBATION OUTCOMES

Yang and Tobin[33] studied the predictive power of several weaning indices and showed that the rapid shallow breathing index (f/VT) had the best predictive value. In their study, 95% of patients with a ratio f/VT greater than 105 failed during a test of spontaneous breathing. The rapid shallow breathing index appears to be the most useful method at the bedside to screen a patient for liberation readiness. If the value is less than 105, then 30-120 minutes of an SBT should be used as a confirmation of the capability of breathing spontaneously without assistance. However, since the f/VT has a low specificity (there is a relatively large proportion of weaning failure subjects in whom the test is positive), the f/VT alone is not sufficient to predict weaning failure. From a practical point of view, the information conveyed by weaning indices and clinical judgment should be considered together in making clinically important decisions regarding extubation.

Patients incapable of protecting their airway and clearing secretions with an effective cough are at an increased risk of extubation failure. Traditional assessment has consisted of demonstrating a cough reflex when the airways are stimulated with a suction catheter and by the absence of excessive secretions. Smina et al.[34] found that patients with a peak expiratory flow equal to or below 60 L/min were five times more likely to have an unsuccessful extubation than patients with expiratory flows greater than 60 L/min.

## EXTUBATION FAILURE

Extubation failure can be defined as reintubation and the reinstitution of ventilatory assistance within 24-48 hours of extubation. Data by Esteban et al.[5,35] indicate that the reintubation rate is about 13%-19%.

Mechanisms explaining extubation failure include impending abnormalities not diagnosed at the time that extubation was performed (e.g., pneumonia or ongoing cardiac failure) and the inability to keep the tracheobronchial tree free of copious secretions.[7,36,37] Extubation failure results in a marked increase in the duration of mechanical ventilation, ICU and hospital stay, need for tracheostomy, and hospital mortality.[5,7,38-40] Further studies are needed to understand the pathophysiologic mechanisms of extubation failure.

## PROGRESSIVE WITHDRAWAL OF MECHANICAL VENTILATION

When patients fail SBTs, pressure support ventilation (PSV) is the modality most often used for the progressive withdrawal of mechanical ventilation.[41] Two prospective multicenter randomized clinical trials have shown that the use of synchronized intermittent mandatory ventilation (SIMV) is less efficacious than other techniques.[1,2]

Sedation and analgesia are important components of care for mechanically ventilated patients. An important study revealed that the daily interruption of sedation significantly reduced the duration of mechanical ventilation.[42] Since sedation and weaning from mechanical ventilation cannot be separated from one another, when these two strategies are combined (i.e., daily interruption of sedation and the systematic use of SBTs) to hasten liberation from the ventilator, the results are more effective than if the two strategies are used separately.[43]

### PSV

Clinical experience[1,2] and data obtained from clinical trials[44,45] suggest that the "optimal" initial levels for PSV are those that provide respiratory rates between 25 and 30 breaths/min. In this setting, it is particularly important to rule out the existence of asynchronous breathing or ineffective respiratory effort. A ventilator setting with a high level of pressure support can be the cause of patient-ventilator asynchrony. The patients who show ineffective triggering exhibit a longer time on mechanical ventilation and tracheostomy is more frequent in these patients.[46] A subsequent study found a decrease in the number of ineffective respiratory efforts without changes in the work required for breathing and without modifications in the respiratory rate when pressure support levels were reduced.[47] These studies[46,47] indicate that some patients are receiving excessive levels of mechanical ventilation during the weaning process.

The level of external PEEP used in patients with clinically suspected dynamic hyperinflation and dynamic airway collapse should be adjusted with great caution since the measurement of dynamic intrinsic PEEP in spontaneously breathing patients is not easily performed. To that end, it has been suggested that external PEEP can be titrated according to the changes in airway occlusion pressure.[48]

During weaning, the PSV levels are decreased according to the patient's clinical tolerance, usually by steps of 2-4 cm $H_2O$ at least twice a day. In general, clinical tolerance to a level of PSV of about 8 cm $H_2O$ without PEEP is required before performing extubation, although this level may vary according to a given patient's overall clinical status.

### Spontaneous Breathing with T-Tube

Tolerance to breathing through a T-tube represents a good test to evaluate patients' capacity to maintain autonomous, spontaneous breathing.[49] The optimal duration of a T-tube trial is at least 30 minutes and no more than 120 minutes.

The main disadvantage of the T-tube trial is related to the absence of a connection to a mechanical ventilator. Since the patients are not monitored by the alarms on the ventilator, they need to be closely supervised.

SBTs with pressure support or a T-tube are suitable methods for evaluating the capacity for spontaneous breathing.[5] However, the use of T-tube weaning trials in difficult-to-wean patients should be considered since PSV modifies the breathing pattern, inspiratory muscle effort, and cardiovascular response compared to the T-tube in this group of patients.[31]

### Noninvasive Ventilation

Noninvasive ventilation (NIV) could be used in some clinical scenarios during weaning:

1. Preventive NIV in patients considered high-risk candidates for reintubation.[50] Examples of such patients include those who have hypercapnia at the end of the weaning test and patients with a history of heart problems or chronic hypercapnic respiratory failure.[51-53] One study demonstrated a reduction in the reintubation rate when NIV was used postextubation.[51] Another study showed both a reduction in reintubation and mortality rates with the use of NIV.[52] Finally, the study of Girault et al.[53] found that NIV could improve weaning results in chronic hypercapnic respiratory failure patients by shortening the duration of intubation and reducing the risk of postextubation acute respiratory failure. However, no differences in reintubation and mortality rates were found.
2. NIV for respiratory failure after extubation. A Canadian study examined the use of NIV for respiratory failure after extubation but found no difference regarding reintubation or mortality.[54] In 2004, a study was published questioning the use of NIV for postextubation respiratory failure.[55] The patients were randomized to receive treatment with oxygen and usual care versus NIV treatment and intubation if needed. Although the rate of reintubation was similar

to the Canadian study, the group treated initially with NIV had a higher mortality rate. These results have ended the indiscriminate use of NIV so that NIV is only recommended for specific populations, including those with chronic respiratory problems[56] and selected postoperative patients.[57,58]

The high-flow nasal cannula (HFNC) is a relatively new system that delivers heated and humidified oxygen via nasal prongs with a maximum flow of 60 L/min. HFNC provides a low level of positive airway pressure (<4 cm $H_2O$), which is highly dependent on mouth closing.[59] Several studies have found that HFNC can be used in weaning period. Maggiore et al.[60] conducted a randomized trial on 105 patients with a $PaO_2/FiO_2$ ratio < 300 mm Hg immediately before they were extubated. A total of 52 patients were conventionally treated with Venturi mask, and 53 patients were treated with HFNC during the initial 48 hours after extubation. The HFCN group as compared to those patients randomized to a Venturi mask resulted in significantly better oxygenation, significantly less discomfort associated with the respiratory device, and a significantly lower reintubation rate. Adequately powered randomized studies are needed to confirm or refute the hypothesis for the benefits associated with HFNC.

## New Modalities

Several novel weaning modalities have been examined, including those using closed-loop PSV[61,62] and that provide a continuous adaptation of ventilator assistance to the patient's needs 24 hours a day.[63] Lellouche et al. examined this modality in two groups of patients during the weaning period.[64] In the control group, weaning was performed as per usual care based on written weaning guidelines. In the study group, weaning was performed using a computer-driven weaning protocol. In the study group, weaning time was significantly reduced in comparison to usual weaning (3 days vs. 5 days; $P = 0.01$). The reduction in the weaning time was associated with a decrease in both the total duration of mechanical ventilation (7.5 days vs. 12 days; $P = 0.003$) and the ICU length of stay (12 days vs. 15.5 days; $P = 0.02$).

A subsequent study by Rose et al.,[65] comparing weaning duration with a closed-loop mode versus usual care (weaning managed by experienced critical care specialty nurses using a 1:1 nurse-to-patient ratio) found no differences between the two strategies. Schadler et al.[66] found that the closed-loop system decreased the duration of mechanical ventilation in a specific subgroup of patients (cardiac surgery). Finally, a study by Burns et al.[67] compared automated weaning with closed-loop mode versus a standardized protocol in critically ill patients and found that automated weaning patients had significantly shorter median times to first successful SBT (1 day vs. 4 days; $P < 0.001$) and to successful extubation (4 days vs. 5 days; $P = 0.01$).

# CLASSIFICATION OF WEANING

A Consensus Conference classification[68] defined 3 groups of patients who were weaned: (1) simple weaning (i.e., those patients who proceed from initiation of weaning to successful extubation on the first attempt); (2) difficult weaning (i.e., those patients who fail initial weaning and require up to 7 days from the first SBT to achieve successful weaning); and (3) prolonged weaning (i.e. those patients who require more than 7 days from the first SBT to achieve successful weaning).

The objective of this classification was to provide greater epidemiologic insight in the weaning process and its relationship with outcomes.[68] The simple weaning group represents 60%-70% of ventilated patients, the difficult group includes 20%-25% of patients, and the prolonged group includes the remaining 5%-15% of patients.[69] Several studies[70-74] have evaluated this classification and the distribution among groups is shown in Fig. 63-1, outcomes are shown in Table 63-1, and an overall summary of results shown in Fig. 63-2. These data confirm that simple weaning is the most common scenario and that prolonged weaning is associated with poorer outcomes.

# SUMMARY

The vast majority of intubated mechanically ventilated patients can be successfully liberated from the ventilator after passing an SBT. The best strategy to shorten the total time of mechanical ventilation is based on a simple and daily clinical approach that determines the ability of patients to tolerate unassisted spontaneous breathing. This approach requires that a screening test is performed as early as possible each day and if positive, the patient is continued a confirmatory SBT of 30 to 120 minutes of duration. When patients fail SBTs, techniques for progressive withdrawal of mechanical ventilation can be used. PSV is the

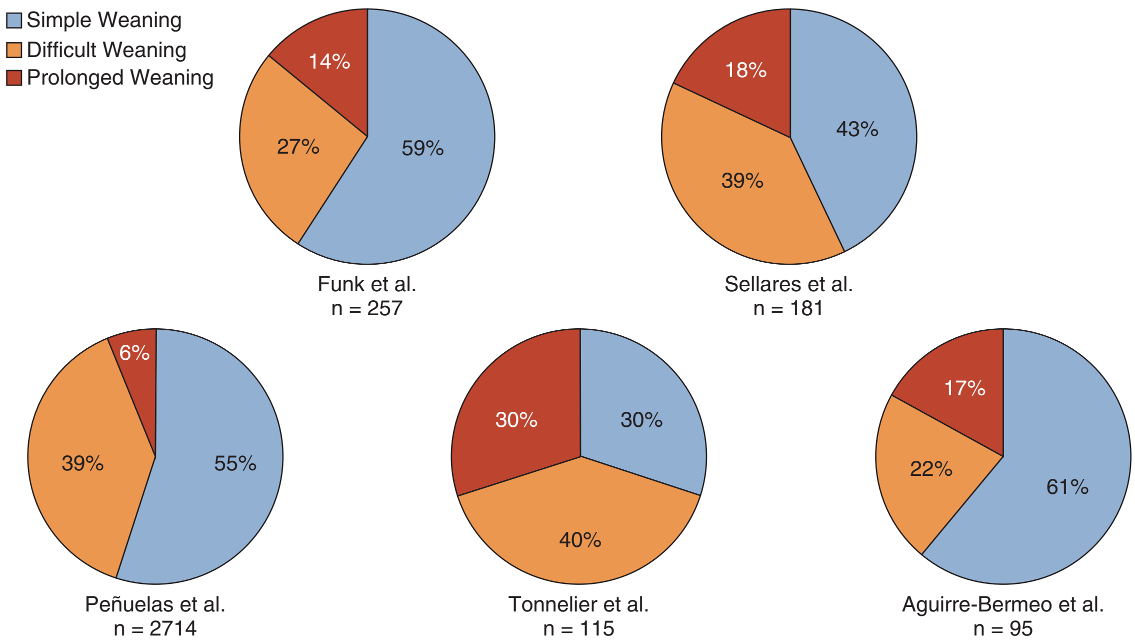


FIGURE 63-1 ■ Patient's distribution in different studies according to the Conference classification.

**TABLE 63-1 Outcomes of the Different Studies According to the Conference Classification**

| VARIABLE | STUDY | SIMPLE WEANING | DIFFICULT WEANING | PROLONGED WEANING |
|---|---|---|---|---|
| Reintubation | Funk et al. (n = 257) | 13% | 7% | 5% |
| | Sellares et al. (n = 181) | 15% | 19% | 33% |
| | Peñuelas et al. (n = 2714) | 10% | 10% | 16% |
| | Tonnelier et al. (n = 115) | 0% | 6% | 15% |
| | Aguirre-Bermeo et al. (n = 95) | 7% | 19% | 73% |
| Tracheotomy | Funk et al. (n = 257) | 7% | 15% | 68% |
| | Sellares et al. (n = 181) | 8% | 9% | 39% |
| | Peñuelas et al. (n = 2714) | 6% | 6% | 10% |
| | Aguirre-Bermeo et al. (n = 95) | 3% | 10% | 50% |
| ICU stay, *(days)** | Funk et al. (n = 257) | 4 (1-9) | 11 (7-20) | 27 (18-37) |
| | Sellares et al. (n = 181) | 11 ± 12 | 12 ± 8 | 21 ± 13 |
| | Peñuelas et al. (n = 2714) | 6 (3-10) | 9 (6-15) | 18 (14-25) |
| | Tonnelier et al. (n = 115) | 10 ± 9 | 16 ± 15 | 30 ± 25 |
| | Aguirre-Bermeo et al. (n = 95) | 10 ± 7 | 17 ± 13 | 24 ± 15 |
| ICU mortality | Funk et al. (n = 257) | 3% | 1% | 22% |
| | Sellares et al. (n = 181) | 13% | 11% | 42% |
| | Peñuelas et al. (n = 2714) | 7% | 7% | 13% |
| | Tonnelier et al. (n = 115) | 0% | 2% | 18% |
| | Aguirre-Bermeo et al. (n = 95) | 3% | 5% | 38% |

*Data are presented as median (percentiles 25%-75%) or means ± SD.

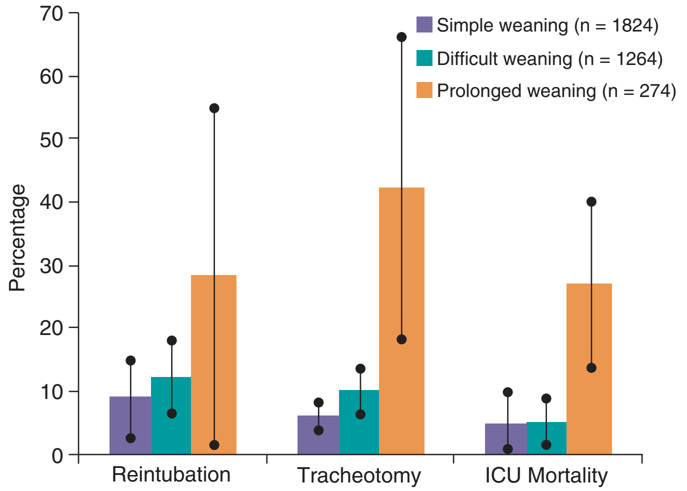


**FIGURE 63-2** ■ Overall summary of study outcomes according to the Conference classification. Data are presented in mean percentage and standard deviation.

modality most often used in this scenario. Automated systems seem to perform at least as well as usual care and perhaps even better. NIV may be useful to hasten the weaning process and avoid reintubation in selected populations. Patients with a long weaning duration (>7 days from the first SBT) have poorer outcomes. Extubation failure is poorly understood and is associated with a high mortality rate.

## KEY POINTS

1. In the vast majority of patients, weaning from mechanical ventilation is a simple process. Patients are extubated at the first SBT attempt. This is associated with favorable outcomes.
2. The implementation of a weaning strategy based on solid clinical and pathophysiologic knowledge improves outcomes regarding the duration of mechanical ventilation and length of stay in the ICU. This effect can be attributed primarily to the fact that patients are screened daily for the capability to maintain spontaneous breathing.
3. A relatively small group of patients require prolonged weaning. This is associated with worsened outcomes. These patients need to be carefully evaluated for neuromuscular and cardiovascular dysfunction and could benefit from adjunctive therapy.
4. Mechanisms explaining extubation failure are still poorly understood and much research is needed in this area. Patients with extubation failure have an increased mortality rate that varies depending on the specific cause of the failure.
5. Noninvasive ventilation is used to facilitate weaning and extubation but with some reservations. Patients should be carefully selected and the NIV administration should be tailored in a patient per patient basis.

## ANNOTATED REFERENCES

Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 1994;150(4):896-903.

*This is the first randomized trial comparing three different methods of weaning. They conclude that the outcome of weaning is influenced by the modality chosen during this period. The weaning duration was shorter with pressure support compared with SIMV or T-tube when pooled together.*

Esteban A, Frutos F, Tobin MJ, et al. A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. N Engl J Med 1995;332(6):345-50.

*This is a randomized multicenter study comparing four different methods of weaning. They show that a once daily spontaneous breathing trial is twice as fast as pressure support and three times more rapid than SIMV. Multiple trials of spontaneous breathing do not reduce the time of weaning compared with the once daily trial.*

Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet 2008;371(9607):126-34.

*This study demonstrated that a strategy combining cessation of sedation followed by spontaneous breathing shortens the duration of mechanical ventilation and improves patient outcome.*

Jubran A, Tobin MJ. Pathophysiologic basis of acute respiratory distress in patients who fail a trial of weaning from mechanical ventilation. Am J Respir Crit Care Med 1997;155(3):906-15.

*This is a physiologic study to determine the mechanisms of acute respiratory distress. They show that COPD patients who failed the spontaneous breathing trial developed rapid shallow breathing with worsening pulmonary mechanics, resulting in an increased* $PaCO_2$.

Thille AW, Richard JC, Brochard L. The decision to extubate in the intensive care unit. Am J Respir Crit Care Med 2013;187(12):1294-302.

*This is a clinical review of extubation in the ICU with an analysis of risk factors and impact of extubation failure. This review discusses the weaning tests and the optimal strategies for weaning in patients at high risk for extubation failure.*

*References for this chapter can be found at expertconsult.com.*

## REFERENCES


1. Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 1994;150(4):896-903.
2. Esteban A, Frutos F, Tobin MJ, et al. A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. N Engl J Med 1995;332(6): 345-50.
3. Ely EW, Baker AM, Evans GW, et al. The prognostic significance of passing a daily screen of weaning parameters. Intensive Care Med 1999;25(6):581-7.
4. Epstein SK. Decision to extubate. Intensive Care Med 2002;28(5):535-46.
5. Esteban A, Alia I, Gordo F, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. Am J Respir Crit Care Med 1997;156(2 Pt 1):459-65.
6. Ely EW, Baker AM, Dunagan DP, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 1996;335(25):1864-9.
7. Vallverdu I, Calaf N, Subirana M, et al. Clinical characteristics, respiratory functional parameters, and outcome of a two-hour T-piece trial in patients weaning from mechanical ventilation. Am J Respir Crit Care Med 1998;158(6):1855-62.
8. Marini JJ. Weaning from mechanical ventilation. N Engl J Med 1991;324(21):1496-8.
9. Mancebo J. Weaning from mechanical ventilation. Eur Respir J 1996;9:1923-31.
10. Vassilakopoulos T, Roussos C, Zakynthinos S. Weaning from mechanical ventilation. J Crit Care 1999;14(1):39-62.
11. McConville JF, Kress JP. Weaning patients from the ventilator. N Engl J Med 2012;367(23):2233-9.
12. Jubran A, Tobin MJ. Pathophysiologic basis of acute respiratory distress in patients who fail a trial of weaning from mechanical ventilation. Am J Respir Crit Care Med 1997;155(3):906-15.
13. Laghi F, Tobin MJ. Disorders of the respiratory muscles. Am J Respir Crit Care Med 2003;168(1): 10-48.
14. Levine S, Nguyen T, Taylor N, et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. N Engl J Med 2008;358(13):1327-35.
15. Hussain SN, Mofarrahi M, Sigala I, et al. Mechanical ventilation-induced diaphragm disuse in humans triggers autophagy. Am J Respir Crit Care Med 2010;182(11):1377-86.
16. Jaber S, Petrof BJ, Jung B, et al. Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans. Am J Respir Crit Care Med 2011;183(3):364-71.
17. Maher J, Rutledge F, Remtulla H, et al. Neuromuscular disorders associated with failure to wean from the ventilator. Intensive Care Med 1995;21(9):737-43.
18. De Jonghe B, Sharshar T, Lefaucheur JP, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA 2002;288:2859-67.
19. Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373(9678): 1874-82.
20. Brochard L. Intrinsic (or auto-) positive end-expiratory pressure during spontaneous or assisted ventilation. Intensive Care Med 2002;28(11):1552-4.
21. Brochard L. Intrinsic (or auto-) PEEP during controlled mechanical ventilation. Intensive Care Med 2002;28(10):1376-8.
22. Feihl F, Broccard AF. Interactions between respiration and systemic hemodynamics. Part I: basic concepts. Intensive Care Med 2009;35(1):45-54.
23. Feihl F, Broccard AF. Interactions between respiration and systemic hemodynamics. Part II: practical implications in critical care. Intensive Care Med 2009;35(2):198-205.
24. Lemaire F, Teboul JL, Cinotti L, et al. Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation. Anesthesiology 1988;69(2):171-9.
25. Chatila W, Ani S, Guaglianone D, et al. Cardiac ischemia during weaning from mechanical ventilation. Chest 1996;109(6):1577-83.
26. Jubran A, Mathru M, Dries D, et al. Continuous recordings of mixed venous oxygen saturation during weaning from mechanical ventilation and the ramifications thereof. Am J Respir Crit Care Med 1998;158(6):1763-9.
27. Gandhi SK, Powers JC, Nomeir AM, et al. The pathogenesis of acute pulmonary edema associated with hypertension. N Engl J Med 2001;344(1):17-22.
28. Poppas A, Rounds S. Congestive heart failure. Am J Respir Crit Care Med 2002;165(1):4-8.
29. Upadya A, Tilluckdharry L, Muralidharan V, et al. Fluid balance and weaning outcomes. Intensive Care Med 2005;31(12):1643-7.
30. Frutos-Vivar F, Ferguson ND, Esteban A, et al. Risk factors for extubation failure in patients following a successful spontaneous breathing trial. Chest 2006;130(6):1664-71.
31. Cabello B, Thille AW, Roche-Campo F, et al. Physiological comparison of three spontaneous breathing trials in difficult-to-wean patients. Intensive Care Med 2010;36(7):1171-9.
32. Mekontso-Dessap A, de Prost N, Girou E, et al. B-type natriuretic peptide and weaning from mechanical ventilation. Intensive Care Med 2006;32(10):1529-36.
33. Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 1991;324(21):1445-50.
34. Smina M, Salam A, Khamiees M, et al. Cough peak flows and extubation outcomes. Chest 2003; 124(1):262-8.
35. Esteban A, Alia I, Tobin MJ, et al. Effect of spontaneous breathing trial duration on outcome of attempts to discontinue mechanical ventilation. Am J Respir Crit Care Med 1999;159(2):512-18.
36. Khamiees M, Raju P, DeGirolamo A, et al. Predictors of extubation outcome in patients who have successfully completed a spontaneous breathing trial. Chest 2001;120(4):1262-70.
37. Thille AW, Boissier F, Ben Ghezala H, et al. Risk factors for and prediction by caregivers of extubation failure in ICU patients: a prospective study*. Crit Care Med 2015;43(3):613-20.
38. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. Chest 1997;112(1):186-92.
39. Lee KH, Hui KP, Chan TB, et al. Rapid shallow breathing (frequency-tidal volume ratio) did not predict extubation outcome. Chest 1994;105(2):540-3.
40. Epstein SK, Ciubotaru RL. Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. Am J Respir Crit Care Med 1998;158(2):489-93.
41. Esteban A, Frutos-Vivar F, Muriel A, et al. Evolution of mortality over time in patients receiving mechanical ventilation. Am J Respir Crit Care Med 2013;188(2):220-30.
42. Kress JP, Pohlman AS, O'Connor MF, et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000;342(20):1471-7.
43. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet 2008;371(9607):126-34.
44. Brochard L, Harf A, Lorino H, et al. Inspiratory pressure support prevents diaphragmatic fatigue during weaning from mechanical ventilation. Am Rev Respir Dis 1989;139(2):513-21.
45. Jubran A, Van de Graaff WB, Tobin MJ. Variability of patient-ventilator interaction with pressure support ventilation in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1995;152(1):129-36.
46. Thille AW, Rodriguez P, Cabello B, et al. Patient-ventilator asynchrony during assisted mechanical ventilation. Intensive Care Med 2006;32(10):1515-22.
47. Thille AW, Cabello B, Galia F, et al. Reduction of patient-ventilator asynchrony by reducing tidal volume during pressure-support ventilation. Intensive Care Med 2008;34(8):1477-86.
48. Mancebo J, Albaladejo P, Touchard D, et al. Airway occlusion pressure to titrate positive end-expiratory pressure in patients with dynamic hyperinflation. Anesthesiology 2000;93(1):81-90.
49. Strauss C, Louis B, Isabey D, et al. Contribution of the endotracheal tube and the upper airway to breathing workload. Am J Respir Crit Care Med 1998;157:23-30.
50. Thille AW, Richard JC, Brochard L. The decision to extubate in the intensive care unit. Am J Respir Crit Care Med 2013;187(12):1294-302.
51. Nava S, Gregoretti C, Fanfulla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. Crit Care Med 2005;33(11):2465-70.
52. Ferrer M, Sellares J, Valencia M, et al. Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: randomised controlled trial. Lancet 2009;374(9695): 1082-8.
53. Girault C, Bubenheim M, Abroug F, et al. Noninvasive ventilation and weaning in patients with chronic hypercapnic respiratory failure: a randomized multicenter trial. Am J Respir Crit Care Med 2011;184(6):672-9.
54. Keenan SP, Powers C, McCormack DG, et al. Noninvasive positive-pressure ventilation for postextubation respiratory distress: a randomized controlled trial. JAMA 2002;287(24):3238-44.
55. Esteban A, Frutos-Vivar F, Ferguson ND, et al. Noninvasive positive-pressure ventilation for respiratory failure after extubation. N Engl J Med 2004;350(24):2452-60.
56. Hilbert G, Gruson D, Portel L, et al. Noninvasive pressure support ventilation in COPD patients with postextubation hypercapnic respiratory insufficiency. Eur Respir J 1998;11(6):1349-53.
57. Auriant I, Jallot A, Herve P, et al. Noninvasive ventilation reduces mortality in acute respiratory failure following lung resection. Am J Respir Crit Care Med 2001;164(7):1231-5.
58. Squadrone V, Coha M, Cerutti E, et al. Continuous positive airway pressure for treatment of postoperative hypoxemia: a randomized controlled trial. JAMA 2005;293(5):589-95.
59. Chanques G, Riboulet F, Molinari N, et al. Comparison of three high flow oxygen therapy delivery devices: a clinical physiological cross-over study. Minerva Anestesiol 2013;79(12):1344-55.
60. Maggiore SM, Idone FA, Vaschetto R, et al. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. Am J Respir Crit Care Med 2014;190(3):282-8.
61. Dojat M, Harf A, Touchard D, et al. Evaluation of a knowledge-based system providing ventilatory management and decision for extubation. Am J Respir Crit Care Med 1996;153(3):997-1004.
62. Dojat M, Harf A, Touchard D, et al. Clinical evaluation of a computer-controlled pressure support mode. Am J Respir Crit Care Med 2000;161(4 Pt 1):1161-6.
63. Bouadma L, Lellouche F, Cabello B, et al. Computer-driven management of prolonged mechanical ventilation and weaning: a pilot study. Intensive Care Med 2005;31(10):1446-50.
64. Lellouche F, Mancebo J, Jolliet P, et al. A multicenter randomized trial of computer-driven protocolized weaning from mechanical ventilation. Am J Respir Crit Care Med 2006;174(8):894-900.
65. Rose L, Presneill JJ, Johnston L, et al. A randomised, controlled trial of conventional versus automated weaning from mechanical ventilation using SmartCare/PS. Intensive Care Med 2008;34(10): 1788-95.
66. Schadler D, Engel C, Elke G, et al. Automatic control of pressure support for ventilator weaning in surgical intensive care patients. Am J Respir Crit Care Med 2012;185(6):637-44.
67. Burns KE, Meade MO, Lessard MR, et al. Wean earlier and automatically with new technology (the WEAN study). A multicenter, pilot randomized controlled trial. Am J Respir Crit Care Med 2013;187(11):1203-11.
68. Boles JM, Bion J, Connors A, et al. Weaning from mechanical ventilation. Eur Respir J 2007;29(5): 1033-56.
69. Brochard L, Thille AW. What is the proper approach to liberating the weak from mechanical ventilation? Crit Care Med 2009;37(Suppl. 10):S410-15.
70. Funk GC, Anders S, Breyer MK, et al. Incidence and outcome of weaning from mechanical ventilation according to new categories. Eur Respir J 2010;35(1):88-94.
71. Sellares J, Ferrer M, Cano E, et al. Predictors of prolonged weaning and survival during ventilator weaning in a respiratory ICU. Intensive Care Med 2011;37(5):775-84.
72. Peñuelas O, Frutos-Vivar F, Fernandez C, et al. Characteristics and outcomes of ventilated patients according to time to liberation from mechanical ventilation. Am J Respir Crit Care Med 2011;184(4):430-7.
73. Tonnelier A, Tonnelier JM, Nowak E, et al. Clinical relevance of classification according to weaning difficulty. Respir Care 2011;56(5):583-90.
74. Aguirre-Bermeo H, Bottiroli M, Cuartero M, et al. Outcomes of weaning from mechanical ventilation. Intensive Care Med 2011;37(1):S189.