

REVIEW ARTICLE

CURRENT CONCEPTS

Weaning Patients from the Ventilator

John F. McConville, M.D., and John P. Kress, M.D.

IN THE UNITED STATES, ALMOST 800,000 PATIENTS WHO ARE HOSPITALIZED each year require mechanical ventilation.¹ This estimate excludes neonates, and there is little doubt that mechanical ventilation will be increasingly used as the number of patients 65 years of age or older continues to increase.^{2,3} The majority of patients who receive mechanical ventilation have acute respiratory failure in the postoperative period, pneumonia, congestive heart failure, sepsis, trauma, or the acute respiratory distress syndrome (ARDS).⁴

Our discussion below assumes that physicians have addressed metabolic, inflammatory, and infectious conditions that may be present and have corrected them to the extent possible. As soon as the condition that caused respiratory failure has started to improve, the transition from full ventilatory support to spontaneous breathing may be initiated. This transition requires sufficient respiratory-muscle strength to sustain breathing and maintain acceptable gas exchange. In most patients, this transition also includes the removal of the endotracheal tube. In patients with prolonged respiratory failure, the term “weaning” may be apropos, since it describes a gradual process of improving the strength-to-load ratio of the respiratory system to enable spontaneous respiration. Unfortunately, although this term is widely used, it is somewhat misleading in the vast majority of patients with acute respiratory failure. “Liberation” from mechanical ventilation is a better description, since it implies rapid removal of a burden that is no longer necessary.

Figure 1 shows a typical algorithm used by clinicians to discontinue mechanical ventilation. Patients are assessed daily for their readiness to undergo a trial of spontaneous breathing. In many intensive care units (ICUs), protocol-driven assessments of readiness are carried out by nurses or respiratory therapists. Typical readiness criteria include hemodynamic stability, a ratio of the partial pressure of arterial oxygen (measured in millimeters of mercury) to the fraction of inspired oxygen (which is unitless) of more than 200 with the ventilator set to deliver a positive end-expiratory pressure of 5 cm of water or less, and some improvement in the underlying condition that caused the respiratory failure.

Trials of spontaneous breathing assess a patient’s ability to breathe while receiving minimal or no respiratory support. To accomplish this, ventilators are switched from full respiratory support modes such as volume-assist control or pressure control to ventilatory modes such as pressure support, continuous positive airway pressure (CPAP), or ventilation with a T-piece (in which there is no positive end-expiratory pressure). Ideally, a trial of spontaneous breathing is initiated while the patient is awake and not receiving sedative infusions.⁵

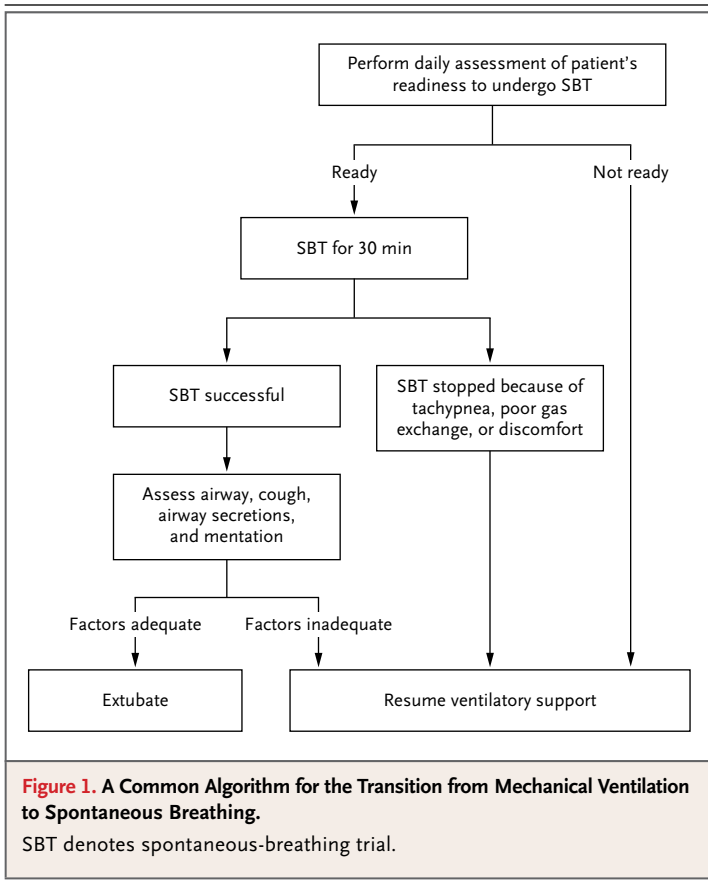
For a spontaneous-breathing trial to be successful, a patient must breathe spontaneously with little or no ventilator support for at least 30 minutes without any of the following: a respiratory rate of more than 35 breaths per minute for more than 5 minutes, an oxygen saturation of less than 90%, a heart rate of more than 140 beats per minute, a sustained change in the heart rate of 20%, systolic blood pressure of more than 180 mm Hg or less than 90 mm Hg, increased anxiety, or diaphoresis.

From the Department of Medicine, Section of Pulmonary and Critical Care, University of Chicago, Chicago. Address reprint requests to Dr. Kress at the University of Chicago, Department of Medicine, Section of Pulmonary and Critical Care, 5841 S. Maryland Ave., MC 6026, Chicago, IL 60637, or at jkress@medicine.bsd.uchicago.edu.

N Engl J Med 2012;367:2233-9.

DOI: 10.1056/NEJMra1203367

Copyright © 2012 Massachusetts Medical Society.



If a trial of spontaneous breathing is successful, several additional factors need to be assessed before removal of the endotracheal tube, including the ability to protect the airway once the tube is removed, the quantity of airway secretions, the strength of cough, and mentation. If these factors are deemed adequate, then the endotracheal tube should be removed. Alternatively, an unsuccessful trial of spontaneous breathing, excessive airway secretions, or inadequate cough and mentation should prompt reinitiation of support with a mechanical ventilator. The mechanism underlying the respiratory failure and the inability of the patient to breathe spontaneously should be determined and addressed daily while the patient continues to receive mechanical ventilation.

STRATEGIES TO REDUCE THE DURATION OF MECHANICAL VENTILATION

Several studies suggest that the process of discontinuing ventilation after the underlying cause of respiratory failure has been addressed accounts for

more than half the total duration of mechanical ventilation.^{6,7} Minimizing the duration of mechanical ventilation is an important consideration for all clinicians who care for critically ill patients. The first textbook on mechanical ventilation, published in 1965, stated, “To know the proper timing and rate of weaning from the respirator requires considerable judgment and experience. As a rule, weaning should start as soon as possible.”⁸ There is support in the literature for this notion that quick discontinuation of mechanical ventilation is beneficial. In a prospective observational study involving patients with brain injuries, Coplin et al.⁹ compared discontinuation of mechanical ventilation within 48 hours after readiness criteria had been met with more than a 48-hour delay in discontinuation. There was higher mortality, an increased risk of pneumonia, and a longer hospital stay in the group with delayed discontinuation than in the group in which ventilation was discontinued in a more timely fashion. Thus, clinicians should be motivated to minimize the duration of mechanical ventilation. Table 1 outlines evidence-based treatment strategies to prevent the need for mechanical ventilation as well as interventions to reduce the duration of mechanical ventilation once it has been initiated.

Several studies have investigated whether particular methods of ventilatory assistance were associated with earlier discontinuation of mechanical ventilation. Brochard et al.²¹ and Esteban et al.²² conducted studies that compared a gradual reduction of ventilatory support with spontaneous-breathing trials in patients in medical-surgical ICUs in whom initial spontaneous-breathing trials had been unsuccessful. Although these studies came to different conclusions about which method led to earlier discontinuation of mechanical ventilation, both suggested that subsequent trials of spontaneous breathing were successful in most patients — nearly 76%. These findings provide support for the notion that most patients with acute respiratory failure are quickly able to resume spontaneous respiration if their physicians afford them the opportunity to do so.

Efforts to decrease the duration of mechanical ventilation can be divided into two categories: earlier appreciation of readiness for spontaneous-breathing trials and a shorter process of discontinuing mechanical ventilation. Many studies have tried to identify simple measurements that can help clinicians predict which patients are ready for a spontaneous-breathing trial and in which

Table 1. Strategies to Prevent the Need for Mechanical Ventilation and to Reduce Its Duration.

Strategy	Source
Evidence-based approaches to reduce the need for mechanical ventilation	
Early goal-directed therapy in the initial treatment of sepsis	Rivers et al. ¹⁰
Use of noninvasive ventilation in selected patients with an acute exacerbation of chronic obstructive pulmonary disease or acute cardiogenic pulmonary edema	Brochard et al., ¹¹ Ram et al., ¹² Masip et al., ¹³ Gray et al. ¹⁴
Ventilator management and associated care to reduce the duration of mechanical ventilation	
Use of small tidal volumes (6 ml/kg of ideal body weight) in patients with the acute respiratory distress syndrome	The Acute Respiratory Distress Syndrome Network ¹⁵
Daily interruption of sedative infusion	Kress et al. ¹⁶
Interruption of sedative infusion before spontaneous-breathing trial	Girard et al. ⁵
Early physical and occupational therapy	Schweickert et al. ¹⁷
No use of sedatives in patients receiving mechanical ventilation	Strøm et al. ¹⁸
Conservative strategy of fluid management in patients with acute lung injury	ARDS Clinical Trials Network ¹⁹
Strategies to reduce ventilator-associated pneumonia	Dezfulian et al. ²⁰

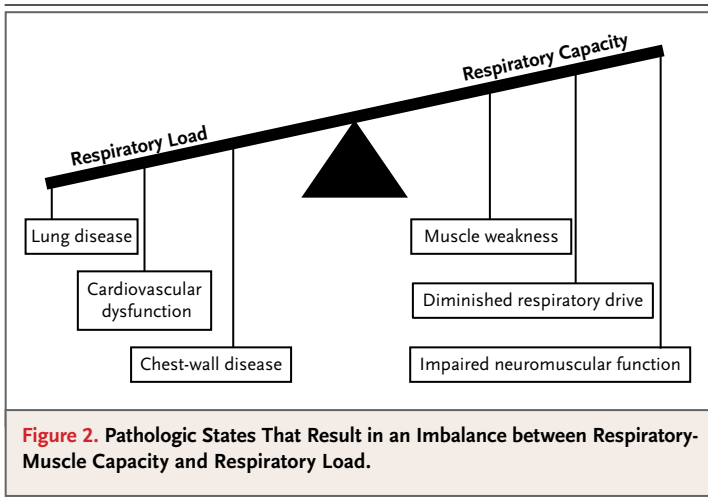
patients these trials are most likely to be successful. Yang and Tobin²³ found that a ratio of the respiratory rate (expressed in breaths per minute) to tidal volume (expressed in liters) (f:Vt) of 105 breaths per minute per liter or less during a 1-minute trial with the use of a T-piece was quite accurate in identifying patients in whom a subsequent spontaneous-breathing trial would be successful (positive predictive value, 78%; negative predictive value, 95%). However, most experts agree that the best method of determining whether patients are ready to breathe on their own is to perform a trial of spontaneous breathing once they have met readiness criteria.²⁴

Many ICUs use protocols to guide the transition from assisted ventilation to spontaneous breathing and subsequent discontinuation of mechanical ventilation. Most protocols include three components: objective criteria to determine whether a patient is ready to breathe with reduced ventilatory support, structured guidelines for reducing ventilatory support, and a list of criteria to determine whether a patient is ready for extubation. There is also growing consensus that the use of systematic protocols for discontinuation of mechanical ventilation, as compared with usual care, may reduce the duration of mechanical ventilation.²⁵ However, not all studies that use protocols for these strategies have shown improvement over usual care.²⁶⁻²⁹ Because there are differences between readiness criteria for spontaneous-breathing trials and algorithms for discontinuation of mechanical ventilation, it is difficult

to definitively state which aspect or aspects of these protocols are responsible for a reduction in the duration of mechanical ventilation. Nevertheless, the reproducible benefit shown in studies of various protocols in multiple ICUs suggests that it is the standardized approach to management rather than any specific method of ventilator support, prespecified readiness, or criteria for discontinuation of mechanical ventilation that reduces the duration of mechanical ventilation and improves outcomes. Thus, most guidelines recommend that patients who are receiving mechanical ventilation be assessed daily for their readiness to breathe spontaneously and afforded the opportunity to do so if they meet prespecified criteria.²⁴

APPROACHES TO SPONTANEOUS-BREATHING TRIALS

Trials of spontaneous breathing do not succeed for a variety of reasons. Often, respiratory mechanics worsen during a spontaneous-breathing trial, causing increased work in breathing that cannot be maintained in critically ill patients.³⁰ Deterioration of respiratory mechanics can result from the following: increased respiratory resistance such as that which occurs in status asthmaticus and other obstructive pulmonary conditions; decreased lung compliance in diseases such as pulmonary fibrosis, pulmonary edema, acute lung injury, or ARDS; and air trapping that can occur in chronic obstructive pulmonary dis-



ease. Trials of spontaneous breathing also challenge the circulation; thus, unsuccessful spontaneous-breathing trials are often the result of cardiac dysfunction.³¹ Figure 2 shows many of the pathologic states that result in an imbalance between respiratory-muscle strength and respiratory load. This imbalance can lead to an unsuccessful spontaneous-breathing trial.

To better describe the transition from mechanical ventilation to spontaneous breathing, a classification scheme based on the results of spontaneous-breathing trials has been developed.³² A simple transition to spontaneous breathing is defined as a successful first trial, followed by discontinuation of mechanical ventilation. A difficult transition involves up to three spontaneous-breathing trials but fewer than 7 days between the first unsuccessful trial and successful discontinuation of mechanical ventilation. A prolonged transition is defined as at least three unsuccessful spontaneous-breathing trials or 7 days or more of mechanical ventilation after the initial unsuccessful trial.

There is emerging evidence that in-hospital mortality and possibly overall mortality are increased among patients who have a prolonged transition to spontaneous breathing, as compared with patients with a simple or difficult transition.³³ Although 10 to 20% of patients receiving mechanical ventilation require a prolonged process of discontinuation, data are lacking to guide this process.³³⁻³⁵

Treatment approaches include a progressive reduction of ventilator assistance, typically with diminishing levels of pressure support, and a progressive increase in the duration of spontane-

ous-breathing trials. Increasingly, tracheostomy is performed in patients who require prolonged weaning.³⁶ However, the timing of tracheostomy remains controversial. Potential advantages of tracheostomy include easier airway suctioning and improvements in the patient's comfort and ability to communicate. Although some studies have suggested that early tracheostomy might reduce short-term mortality, the length of stay in the ICU, and the incidence of pneumonia,^{37,38} other studies have not shown such benefits.^{39,40} A recent meta-analysis led to the conclusion that there is insufficient evidence of improved outcomes to warrant a recommendation for early tracheostomy.⁴¹

UNSUCCESSFUL WEANING FROM THE VENTILATOR

Approximately 15% of patients in whom mechanical ventilation is discontinued require reintubation within 48 hours.⁴²⁻⁴⁴ Rates of extubation failure vary considerably among ICUs. For example, the average rate of failed extubation in surgical ICUs ranges from 5 to 8%, whereas it is often as high as 17% in medical or neurologic ICUs.⁴⁵ Patients who require reintubation have an increased risk of death, a prolonged hospital stay, and a decreased likelihood of returning home, as compared with patients in whom discontinuation of mechanical ventilation is successful.⁴² Thus, it is essential that critical care physicians identify risk factors for failure of extubation despite successful spontaneous-breathing trials.

Several studies have started to elucidate the difference between readiness for discontinuation of ventilation and successful spontaneous-breathing trials. Salam and colleagues⁴⁶ measured peak cough flow, quantified endotracheal secretions, and assessed mental status in 88 patients in whom discontinuation of mechanical ventilation was attempted after a spontaneous-breathing trial that was successful. All the patients with inadequate cough, excessive secretions, and poor mental status required reintubation after discontinuation of mechanical ventilation; in contrast, only 3% of the patients with adequate cough, minimal secretions, and good mental status required reintubation. These findings suggest that it may be wise to delay extubation in patients who have had a successful trial of spontaneous breathing but do not meet these three criteria. A study using logistic-regression analysis showed that an increased fVt ratio at the end of a spontaneous-breathing trial, a positive fluid balance

before discontinuation of ventilation, and a diagnosis of pneumonia were additional risk factors for reintubation in patients who had a successful spontaneous-breathing trial.⁴⁷ Although these studies involved small numbers of patients, the results reinforce the view that the physician's judgment and experience are essential components in successful extubation after an apparently successful trial of spontaneous breathing.

TREATMENT OF RESPIRATORY DISTRESS AFTER EXTUBATION

Several studies have assessed noninvasive positive-pressure ventilation in patients in whom respiratory distress develops within 48 hours after extubation. Two studies randomly assigned patients with respiratory distress that developed after discontinuation of mechanical ventilation to standard care (primarily oxygen and bronchodilators) or noninvasive positive-pressure ventilation.^{48,49} Neither study showed a significant between-group difference in the number of patients who required reintubation, and there was a suggestion of increased mortality in one of the studies. However, two additional studies prospectively identified factors that placed patients at increased risk for extubation failure and randomly assigned these patients to usual care or preemptive noninvasive positive-pressure ventilation in the immediate postextubation period.^{50,51} Both studies showed that the groups receiving noninvasive positive-pressure ventilation had a reduced need for reintubation, as compared with the standard-care groups. Thus, the preemptive use of noninvasive positive-pressure ventilation in the early period after discontinuation of mechanical ventilation in patients deemed to be at increased risk for extubation failure appears to be effective in reducing the need for reintubation. However, patients who have respiratory distress in the postextubation period may not benefit from noninvasive positive-pressure ventilation if it is started after respiratory distress begins; in fact, it may be harmful for some patients. Risk factors for unsuccessful discontinuation of mechanical ventilation are listed in Table 2.

OUR APPROACH

We attempt to discontinue mechanical ventilation in patients as soon as possible. This aggressive approach includes assessing all patients in hemodynamically stable condition to determine

Table 2. Risk Factors for Unsuccessful Discontinuation of Mechanical Ventilation.

Failure of two or more consecutive spontaneous-breathing trials
Chronic heart failure
Partial pressure of arterial carbon dioxide >45 mm Hg after extubation
More than one coexisting condition other than heart failure
Weak cough
Upper-airway stridor at extubation
Age ≥65 yr
APACHE II score >12 on day of extubation*
Patient in medical, pediatric, or multispecialty ICU
Pneumonia as cause of respiratory failure

* Scores on the Acute Physiology and Chronic Health Evaluation (APACHE II) range from 0 to 71, with higher scores indicating greater impairment.

their readiness for extubation and then performing a 30-minute spontaneous-breathing trial with the use of CPAP of 5 cm of water or less in eligible patients while they are awake and not receiving continuous sedation. However, we routinely break these rules if the underlying disease process is starting to improve. We will, for example, initiate a spontaneous-breathing trial in a patient with sepsis and bacteremia at 8 p.m. if the infectious source has been identified and the dose of intravenous norepinephrine required to achieve hemodynamic stability is decreasing. If the patient is awake and has minimal airway secretions, and if the spontaneous-breathing trial is successful at 8:30 p.m., then we would advocate immediate discontinuation of mechanical ventilation.

This type of aggressive approach is intended to minimize the duration of ventilatory support and prevent complications of mechanical ventilation. However, the rate of unsuccessful discontinuation of mechanical ventilation is probably increased when the primary focus of the treatment team is to minimize the duration of such ventilation. Conversely, a conservative approach that is intended to minimize the frequency and consequences of unsuccessful discontinuation of mechanical ventilation will undoubtedly increase the duration of ventilation in some patients. In our patient with bacteremia, this conservative approach might involve continued tapering of intravenous norepinephrine at 8 p.m. rather than initiation of a spontaneous-breathing trial. If the patient is in a hemodynamically stable condition the next morning and is not receiving an infusion of a vasoactive drug, then a spontaneous-breathing trial can be initiated.

There are no data from randomized trials to indicate which approach is superior, but we believe a universally applied aggressive approach to discontinuation of mechanical ventilation that emphasizes early spontaneous breathing and seeks to minimize the duration of mechanical ventilation results in fewer ICU-related complications. We recommend extubation and the use of preemptive noninvasive positive-pressure ventilation in patients who have had a successful spontaneous-breathing trial but are at risk for unsuccessful discontinuation of mechanical ventilation. In these situations, we reassess the patient within 30 minutes after initiating noninvasive positive-pressure ventilation. If respiratory effort is normal and the patient is comfortable, then we will continue noninvasive positive-pressure ventilation as long as necessary. However, if the respiratory rate is elevated or the patient is in mild distress, then we advocate immediate reintubation. We believe that extubation and the prespecified use of noninvasive positive-pressure ventilation in patients with a borderline performance during a spontaneous-breathing trial lead to earlier discontinuation of ventilation in many patients. This approach is coupled with an early decision regarding the need for reintubation. Because delayed time to reintubation has been associated with increased mortality among patients in whom discontinuation of ventilation has been unsuccessful, it is essential to determine quickly whether noninvasive positive-pressure ventilation is adequately addressing res-

piratory distress in the period after discontinuation of ventilation.^{49,52} Although this aggressive approach may lead to higher rates of reintubation, we believe that the benefits of earlier discontinuation of ventilation outweigh the risks associated with waiting another 12 to 24 hours for continued clinical improvement before assessing a patient's ability to breathe spontaneously.

FUTURE RESEARCH

Ongoing research is likely to alter our approach to the discontinuation of mechanical ventilation in the near future. Currently, computerized systems automatically adjust ventilatory support on the basis of frequent monitoring of a patient's respiratory rate, tidal volume, and gas exchange. Early studies of these automated weaning systems have had conflicting results. Nevertheless, a system that can automatically assess a patient's ability to receive reduced levels of ventilatory support without adverse effects has the potential to more quickly identify patients who are ready for spontaneous breathing. Additional studies are also likely to identify treatment algorithms that shorten the duration of mechanical ventilation or that reduce risk factors for unsuccessful discontinuation of ventilation after a successful spontaneous-breathing trial.

Dr. Kress reports receiving lecture fees from Hospira and the France Foundation. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

REFERENCES

1. Wunsch H, Linde-Zwirble WT, Angus DC, Hartman ME, Milbrandt EB, Kahn JM. The epidemiology of mechanical ventilation use in the United States. *Crit Care Med* 2010;38:1947-53.
2. Carson SS, Cox CE, Holmes GM, Howard A, Carey TS. The changing epidemiology of mechanical ventilation: a population-based study. *J Intensive Care Med* 2006;21:173-82.
3. Needham DM, Bronskill SE, Calinawan JR, Sibbald WJ, Pronovost PJ, Laupacis A. Projected incidence of mechanical ventilation in Ontario to 2026: preparing for the aging baby boomers. *Crit Care Med* 2005;33:574-9.
4. Esteban A, Anzueto A, Frutos F, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002;287:345-55.
5. 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;371:126-34.
6. Esteban A, Alia I, Ibañez J, Benito S, Tobin MJ. Modes of mechanical ventilation and weaning: a national survey of Spanish hospitals. *Chest* 1994;106:1188-93.
7. Esteban A, Ferguson ND, Meade MO, et al. Evolution of mechanical ventilation in response to clinical research. *Am J Respir Crit Care Med* 2008;177:170-7.
8. Bendixen HH, Egbert LD, Hedley-Whyte J, Laver MB, Pontoppidan H. *Respiratory care*. St. Louis: Mosby, 1965: 149-50.
9. Coplin WM, Pierson J, Cooley KD, Newell DW, Rubenfeld GD. Implications of extubation delay in brain-injured patients meeting standard weaning criteria. *Am J Respir Crit Care Med* 2000;161:1530-6.
10. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001;345:1368-77.
11. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;333: 817-22.
12. Ram FSF, Picot J, Lightowler J, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2004;3:CD004104.
13. Masip J, Roque M, Sánchez B, Fernández R, Subirana M, Expósito JA. Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and meta-analysis. *JAMA* 2005;294:3124-30.
14. Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J. Noninvasive ventilation in acute cardiogenic pulmonary edema. *N Engl J Med* 2008;359:142-51.

15. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000;342:1301-8.
16. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000;342:1471-7.
17. 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;373:1874-82.
18. Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. *Lancet* 2010;375:475-80.
19. The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 2006;354:2564-75.
20. Dezfulian C, Shojania K, Collard H, Kim HM, Matthay MA, Saint S. Subglottic secretion drainage for preventing ventilator-associated pneumonia: a meta-analysis. *Am J Med* 2005;118:11-8.
21. Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawal from ventilator support during weaning from mechanical ventilation. *Am J Respir Crit Care Med* 1994;150:896-903.
22. Esteban A, Frutos F, Tobin MJ, et al. A comparison of four methods of weaning patients from mechanical ventilation. *N Engl J Med* 1995;332:345-50.
23. Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *N Engl J Med* 1991;324:1445-50.
24. MacIntyre NR, Cook DJ, Ely EW Jr, et al. Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians, the American Association for Respiratory Care, and the American College of Critical Care Medicine. *Chest* 2001;120:Suppl:375S-395S.
25. Blackwood B, Alderdice F, Burns KEA, Cardwell CR, Lavery G, O'Halloran P. Protocolized versus non-protocolized weaning for reducing the duration of mechanical ventilation in critically ill adult patients. *Cochrane Database Syst Rev* 2010;5:CD006904.
26. Krishnan JA, Moore D, Robeson C, Rand CS, Fessler HE. A prospective, controlled trial of a protocol-based strategy to discontinue mechanical ventilation. *Am J Respir Crit Care Med* 2004;169:673-8.
27. Namen AM, Ely EW, Tatter SB, et al. Predictors of successful extubation in neurosurgical patients. *Am J Respir Crit Care Med* 2001;163:658-64.
28. Randolph AG, Wypij D, Venkataraman ST, et al. Effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children: a randomized controlled trial. *JAMA* 2002;288:2561-8.
29. Rose L, Presneill JJ, Johnston L, Cade JF. A randomised, controlled trial of conventional versus automated weaning from mechanical ventilation using SmartCare/PS. *Intensive Care Med* 2008;34:1788-95.
30. Jubran A, Tobin JM. Pathophysiologic basis of acute respiratory distress in patients who fail a trial of weaning from mechanical ventilation. *Am J Respir Crit Care Med* 1997;155:906-15.
31. Lemaire F, Teboul JL, Cinotti L, et al. Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation. *Anesthesiology* 1988;69:171-9.
32. Boles J-M, Bion J, Connors A, et al. Weaning from mechanical ventilation. *Eur Respir J* 2007;29:1033-56.
33. Funk G-C, Anders S, Breyer M-K, et al. Incidence and outcome of weaning from mechanical ventilation according to new categories. *Eur Respir J* 2010;35:88-94.
34. Seneff MG, Zimmerman JE, Knaus WA, Wagner DP, Draper EA. Predicting the duration of mechanical ventilation: the importance of disease and patient characteristics. *Chest* 1996;110:469-79.
35. Kurek CJ, Cohen IL, Lambrinos J, Minatoya K, Booth FV, Chalfin DB. Clinical and economic outcome of patients undergoing tracheostomy for prolonged mechanical ventilation in New York State during 1993: analysis of 6,353 cases under diagnosis-related group 483. *Crit Care Med* 1997;25:983-8.
36. Cox CE, Carson SS, Holmes GM, Howard ABS, Carey TS. Increase in tracheostomy for prolonged mechanical ventilation in North Carolina, 1993-2002. *Crit Care Med* 2004;32:2219-26.
37. Arabi Y, Haddad S, Shirawi N, Al Shimemeri A. Early tracheostomy in intensive care trauma patients improves resource utilization: a cohort study and literature review. *Crit Care* 2004;8:R347-R352.
38. Rumbak MJ, Newton M, Truncala T, Schwartz SW, Adams JW, Hazard PB. A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. *Crit Care Med* 2004;32:1689-94. [Erratum, *Crit Care Med* 2004;32:2566.]
39. Trouillet JL, Luyt CE, Guiguet M, et al. Early percutaneous tracheotomy versus prolonged intubation of mechanically ventilated patients after cardiac surgery: a randomized trial. *Ann Intern Med* 2011;154:373-83.
40. Patel SB, Kress JP. Early tracheotomy after cardiac surgery: not ready for prime time. *Ann Intern Med* 2011;154:434-5.
41. Gomes Silva BN, Andriolo RB, Saconato H, Atallah AN, Valente O. Early versus late tracheostomy for critically ill patients. *Cochrane Database Syst Rev* 2012;3:CD007271.
42. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. *Chest* 1997;112:186-92.
43. Esteban A, Alía 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;159:512-8.
44. Esteban A, Alía 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;156:459-65. [Erratum, *Am J Respir Crit Care Med* 1997;156:2028.]
45. Epstein SK. Noninvasive ventilation to shorten the duration of mechanical ventilation. *Respir Care* 2009;54:198-208.
46. Salam A, Tilluckdharry L, Amoateng-Adjepong Y, Manthous CA. Neurologic status, cough, secretions and extubation outcomes. *Intensive Care Med* 2004;30:1334-9.
47. Frutos-Vivar F, Ferguson ND, Esteban A, et al. Risk factors for extubation failure in patients following a successful spontaneous breathing trial. *Chest* 2006;130:1664-71.
48. Keenan SP, Powers C, McCormack DG, Block G. Noninvasive positive-pressure ventilation for postextubation respiratory distress: a randomized controlled trial. *JAMA* 2002;287:3238-44.
49. Esteban A, Frutos-Vivar F, Ferguson ND, et al. Noninvasive positive-pressure ventilation for respiratory failure after extubation. *N Engl J Med* 2004;350:2452-60.
50. Nava S, Gregoretti C, Fanfulla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. *Crit Care Med* 2005;33:2465-70.
51. Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. *Am J Respir Crit Care Med* 2006;173:164-70.
52. 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;158:489-93.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.