Weaning from Mechanical Ventilation

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Abstract

For many critically ill patients admitted to an intensive care unit, the insertion of an endotracheal tube and the initiation of mechanical ventilation (MV) can be lifesaving procedures. Subsequent patient care often requires intensivists to manage the complex interaction of multiple failing organ systems. The shift in the intensivists' focus toward the discontinuation of MV can thus occur late in the course of critical illness. The dangers of MV, however, make it imperative to wean patients at the earliest possible time. Premature weaning trials, however, trigger significant respiratory distress, which can cause setbacks in the patient's clinical course. Premature extubation is also risky. To reduce delayed weaning and premature extubation, a three-step diagnostic strategy is suggested: measurement of weaning predictors, a trial of unassisted breathing (T-tube trial), and a trial of extubation. Since each step constitutes a diagnostic test, clinicians must not only command a thorough understanding of each test but must also be aware of the principles of clinical decision making when interpreting the information generated by each step. Many difficult aspects of pulmonary pathophysiology encroach on weaning management. Accordingly, weaning commands sophisticated, individualized care. Few other responsibilities of an intensivist require a more analytical effort and carry more promise for improving patient outcome than the application of physiologic principles in the weaning of patients.

Keywords
- mechanical ventilation
- weaning
- monitoring
- diagnostic tests
- screening
- extubation

Although often lifesaving, mechanical ventilation (MV) can be associated with life-threatening complications.[1] Accordingly, when it can be done safely, it is essential to discontinue MV at the earliest possible time. The process of discontinuing MV is known as *weaning*. Of patients who are deemed ready for a weaning trial, approximately 20 to 30% will develop severe distress during the first trial of spontaneous breathing and require the resumption of MV.[2]

Pathophysiology of Weaning Failure

The mechanisms that cause weaning failure can be divided into those occurring at the level of control of breathing, the mechanics of the lung and chest wall, the respiratory muscles, and the cardiovascular system.[1] In some patients, psychological factors may also contribute to weaning failure.[3]

Control of Breathing

Many weaning-failure patients develop hypercapnia. In most of these patients, hypercapnia is accompanied by an increase in respiratory drive and marked shortening of inspiratory time (T_I) coupled with shortening of expiratory time (T_E). The shortening of T_I and T_E results in an elevation in the respiratory frequency (f) and a marked decrease of tidal volume (V_T).[2] The combined elevation in f and decrease in V_T is referred to as *rapid shallow breathing* and has been recognized as the physiologic hallmark of weaning failure (►**Fig. 1**).[1]

Respiratory Mechanics

Resistance, elastance, and intrinsic positive end-expiratory pressure (PEEPi) measured immediately before the start of a trial of unassisted breathing are equivalent in patients who go on to

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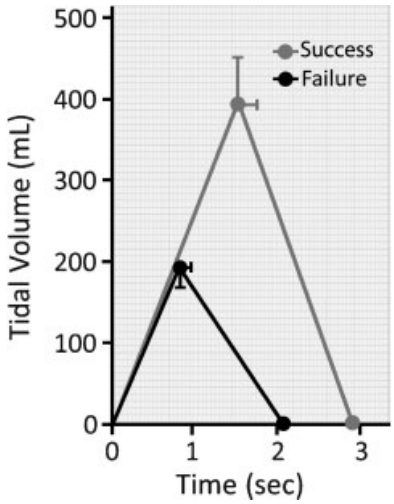


Fig. 1 The mean respiratory cycle during spontaneous breathing in 7 weaning-failure patients and 10 weaning-success patients. The early termination of inspiratory time in the weaning-failure patients lead to a decrease in tidal volume (V_T). The decrease in inspiratory time, coupled with a decrease in expiratory time, resulted in a faster respiratory frequency. (Bars represent one standard error). (Redrawn from Tobin et al.[30])

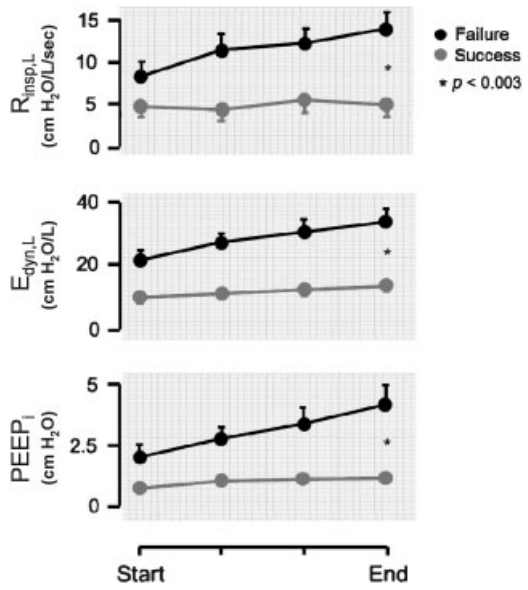


Fig. 2 Inspiratory resistance of the lung ($R_{insp,L}$), dynamic lung elastance ($E_{dyn,L}$), and intrinsic positive end-expiratory pressure (PEEPi) in 17 weaning failure patients and 14 weaning success patients. Data displayed were obtained during the second and last minute of a T-tube trial, and at one-third and two-thirds of the trial duration. Between the onset and end of the trial, the failure group developed increases in $R_{insp,L}$ ($p < 0.009$), $E_{dyn,L}$($p < 0.0001$), and PEEPi ($p < 0.0001$) and the success group developed increases in $E_{dyn,L}$ ($p < 0.006$) and PEEPi ($p < 0.02$). Over the course of the trial, the failure group had higher values of $R_{insp,L}$ ($p < 0.003$), $E_{dyn,L}$ ($p < 0.006$), and PEEPi ($p < 0.009$) than the success group. (Reprinted with permission from Jubran and Tobin.[5])

tolerate or to fail the trial.[4] Over the course of the trial, however, all of these variables become more abnormal in the weaning-failure patients than in the weaning-success patients (►**Fig. 2**).[5,6] These observations indicate that some mechanism associated with the act of spontaneous breathing results in the worsening of respiratory mechanics that leads to weaning failure.[2] This worsening is accompanied by greater inspiratory effort in weaning-failure than in weaning-success patients.[1]

Respiratory Muscles

Inspiratory pressure recorded at the airway during maximal voluntary inspiratory efforts (PI_{max}) and airway and transdiaphragmatic pressures elicited by single stimulation of the phrenic nerves (►**Fig. 3**) are equally—and profoundly—decreased in weaning-failure and weaning-success patients.[7–10] These findings raise several considerations. First, measurements of respiratory muscle strength cannot discriminate between weaning-success and weaning-failure patients.[7,8] Second, it is likely that the profound respiratory muscle weakness combined with greater inspiratory effort in the weaning-failure patients is mechanistically linked to weaning outcome.[11] Third, this imbalance between effort and strength raises the possibility that respiratory muscle fatigue could contribute to weaning failure.[12,13] To assess the latter possibility, Laghi et al[8] recorded transdiaphragmatic twitch pressures elicited by magnetic stimulation of the phrenic nerves in 11 weaning-failure and 8 weaning-success patients before and after a trial of unassisted breathing (T-tube trial). No patient in either group exhibited a fall in twitch pressure. This result was surprising. Related analyses disclosed why. Weaning-failure patients became progressively distressed during the trial, leading clinicians to reinstate ventilator support before patients had breathed long enough to develop fatigue (►**Fig. 4**).[8,14] In other words, monitoring clinical signs of distress provides sufficient warning to avoid respiratory muscle fatigue.

Cardiovascular Performance

In the acute setting, oxygen consumption at the completion of a weaning trial is equivalent in weaning-success and weaning-failure patients (►**Fig. 5**, *upper panel*).[15] The manner in which the cardiovascular system meets oxygen demands, however, differs between the two groups. In weaning successes, oxygen transport increases, resulting mainly from an increase in cardiac index; in weaning failures, the increase in demand is met by an increase in oxygen extraction, resulting in a decrease in mixed venous oxygen saturation (►**Fig. 5**, *lower panel*). A decrease in mixed venous oxygen saturation is consistent with a failing cardiovascular response to an increased metabolic demand.[3] High variability in hemodynamic response during failure to wean has been reported by Zakynthinos et al.[16] It is unclear whether the absent interaction between weaning failure and oxygen consumption in some of the patients studied by Zakynthinos et al[16] was due to depression of the respiratory centers, limited capacity to extract oxygen, or limited cardiac reserve[3] including diastolic dysfunction caused by impairment of left ventricular relaxation.[17]

Psychological Factors

Overall, 50 to 80% of patients receiving MV in adult intensive care units (ICUs) develop delirium at some point during the

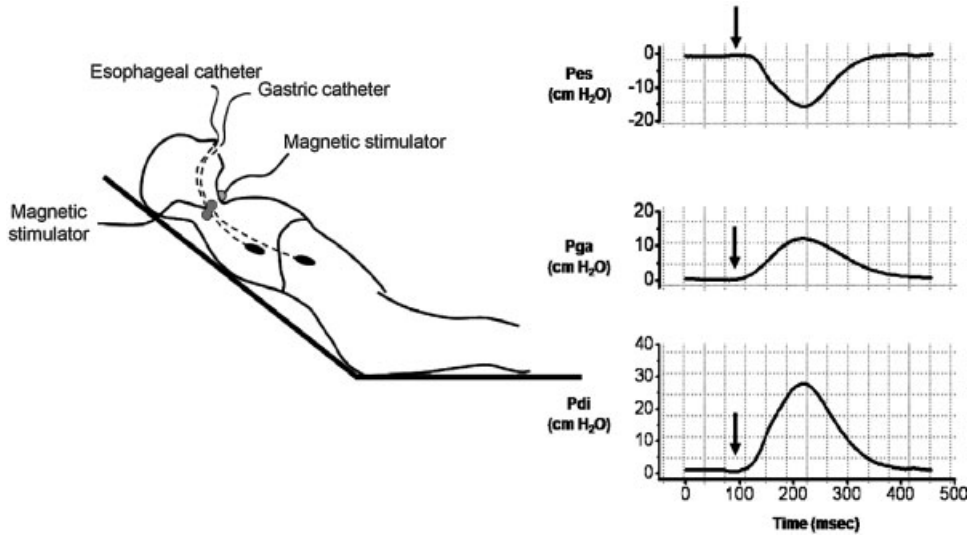


Fig. 3 Recording of transdiaphragmatic twitch pressure. (Left panel) An esophageal balloon and a gastric balloon are passed through the nares. Magnetic stimulation of the phrenic nerves elicits diaphragmatic contraction. (Right panel) Continuous recordings of esophageal (Pes) and gastric pressures (Pga) and transdiaphragmatic pressure (Pdi)—calculated by subtracting Pes from Pga. Phrenic nerve stimulation (arrows) results in contraction of the diaphragm with consequent fall in intrathoracic pressure (negative defection of Pes) and rise in intra-abdominal pressure (positive deflection of Pga). These swings in pressure are responsible for the transdiaphragmatic twitch pressure. The smaller the transdiaphragmatic twitch pressure, the smaller the force generation capacity of the diaphragm. (Adapted from Laghi.[10])

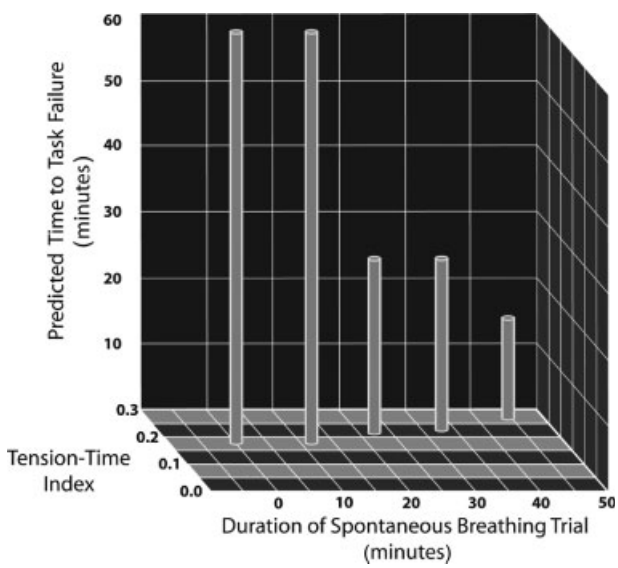


Fig. 4 Interrelationship between the duration of a spontaneous breathing trial, tension-time index of the diaphragm, and predicted time to task failure in nine patients who failed a trial of weaning from mechanical ventilation. The patients breathed spontaneously for an average of 44 minutes before a physician terminated the trial. At the start of the trial, the diaphragm effort, quantified in terms of tension-time index, was 0.17. According to a formula developed by Bellemare and Grassino,[14] this effort could have been sustained for a total of 59 minutes before developing task failure. As the trial progressed, the tension-time index increased and the predicted time to development of task failure decreased. At the end of the trial, the tension-time index reached 0.26. That patients were predicted to sustain spontaneous breathing for another 13 minutes before developing task failure clarifies why patients did not develop a decrease in diaphragmatic twitch pressure. In other words, physicians interrupted the trial on the basis of clinical manifestations of respiratory distress, before patients had sufficient time to develop contractile fatigue. (Used with permission from Laghi and Tobin.[12])

ICU stay.[18,19] Delirium is independently associated with a longer duration of MV, longer post-ICU stay, fewer median days alive, and a higher incidence of cognitive impairment at hospital discharge.[18] As with delirium, posttraumatic stress disorder (PTSD) too is common in acutely and chronically ventilated patients.[20,21] Duration of MV, use of sedative agents, and presence and severity of PTSD appear causally linked.[22] The presence of PTSD may influence duration of MV and psychological function after discharge.[22] Finally, the rate of weaning failure is higher in patients with anxiety or depression than in those without such disorders.[23,24] The possible (causal) association between anxiety and depression and weaning outcome likely rests on the known link between these psychological disorders and decreases in motivation, interference with the execution of simple tasks, and a decrease in self-esteem.[22]

Possible mechanisms for psychological dysfunction in mechanically ventilated patients include respiratory discomfort, severity of illness, sleep deprivation, sensory deprivation (►**Fig. 6**), and medication side effects.[22] The delivery of MV itself may cause psychological dysfunction by limiting mobility, fostering isolation, impairing communication, and interfering with the patient's control of the act of breathing.[25]

Prediction of Weaning Outcome

Most patients deemed clinically stable with satisfactory oxygenation (e.g., $Pa_{O_2} > 60$ mm Hg on $F_{IO_2} \leq 0.4$) after receiving MV for a week or longer and who are recruited in randomized controlled trials (RCTs) of different weaning techniques often are able to tolerate ventilator discontinuation on the 1st day of active weaning.[26] This means that many of these patients would have likely tolerated extubation a day

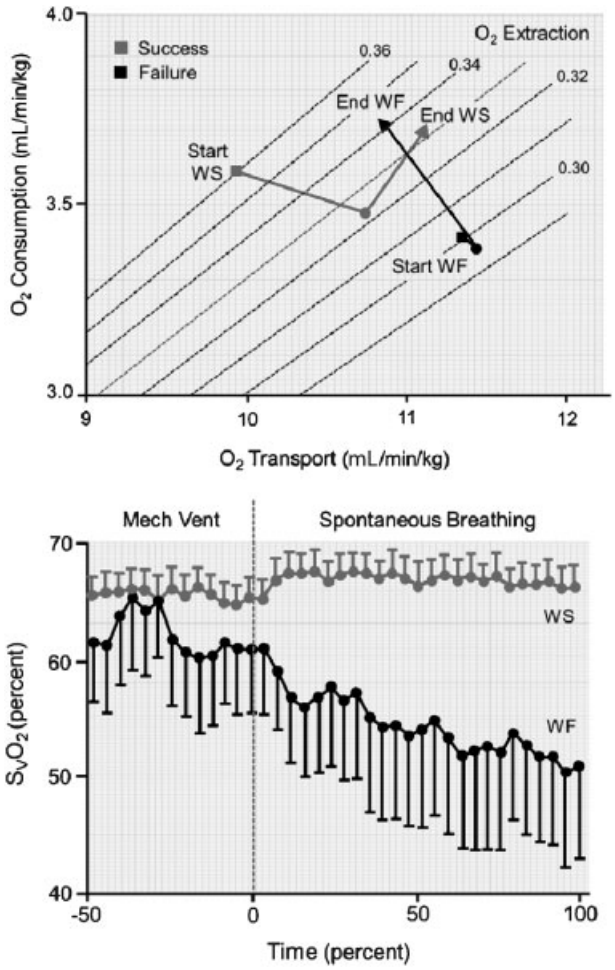


Fig. 5 *Upper panel*: Oxygen transport, oxygen consumption, and isopleths of oxygen extraction ratio in the success (WS, *grey symbols*) and failure (WF, *black symbols*) groups during mechanical ventilation (*squares*) and at the onset (*circles*) and end (*triangles*) of a spontaneous breathing trial. *Lower panel*: Mixed venous oxygen saturation (SVO_2) during mechanical ventilation and a trial of spontaneous breathing in 11 weaning-success patients (WS, *grey symbols*) and in 8 weaning-failure patients (WF, *black symbols*). During mechanical ventilation, SVO_2 was similar in the two groups ($p = 0.28$). Between the onset (*dashed line*) and the end of the trial, SVO_2 decreased in the failure group ($p < 0.01$), whereas it remained unchanged in the success group ($p = 0.48$). Over the course of the trial, SVO_2 was lower in the failure group than in the success group ($p < 0.02$). Bars indicate standard error. See text for details. (Redrawn from Jubran et al.[15])

or so earlier. In other words, one of the leading sources of weaning delay is the failure of the physician to recognize the possibility that the patient just might come off the ventilator. Accordingly, when taking care of a ventilator-supported patient, physicians must employ screening tests to recognize a patient's readiness for weaning at the earliest possible time. By warning an unsuspicious physician to a patient's readiness for unassisted ventilation—hours or days before he or she would otherwise order a weaning trial—weaning-predictor tests avoid the cognitive errors intrinsic in clinical decision making.[26] Research on weaning-predictor tests employs the tools of medical decision analysis. Therefore, before discussing weaning predictor tests, it is useful to review the principles of medical decision analysis.

Medical Decision Analysis

Diagnostic tests are designed to screen for a condition and to confirm the condition. The characteristics of screening tests and confirmatory tests differ and, rarely, a single diagnostic test fulfills both functions.[27] The primary goal of weaning-predictor tests is screening (►**Fig. 7**).[28] A good weaning-predictor test, like any good screening test, should miss no patient who has the condition under consideration, that is, to be ready for a weaning trial. This means that a good weaning-predictor test must have a low rate of false-negative results—high sensitivity.[27,28] A high rate of false-positive results (low specificity) is acceptable.[27,28]

The process of weaning entails measurement of weaning predictors, a trial of weaning, and a trial of extubation.[28] Each step in this sequence is a diagnostic test (►**Fig. 8**). Measurements of weaning predictors (screening tests) are used to diagnose readiness for a weaning trial. The trial of weaning (confirmatory test of the screening tests) itself is used to screen for readiness to extubate. Extubation (confirmatory test of the weaning trial) is used to diagnose/screen for readiness to maintain spontaneous respiration. To apply diagnostic tests (screening or confirmatory) in sequence introduces critical confounders in the interpretation of studies designed to assess the reliability of a (pre-existing) predictor test. These confounders are: spectrum bias, test-referral bias, and base-rate fallacy.[27,29] In the case of weaning, spectrum bias arises when the study population in a new investigation contains more (or fewer) sick patients than the population in which the diagnostic test was first developed.[27,29] Test-referral bias arises when the results of the weaning-predictor test being assessed are used to choose patients for a reference-standard test, that is, passing a weaning trial that leads to extubation.[27,29] Base-rate fallacy occurs when physicians fail to take into account the pretest probability of the disorder.[29]

Pretest probability is a physician's estimate of the likelihood of a particular condition (weaning outcome) before a diagnostic test is undertaken.[28] Posttest probability (typically expressed as positive- or negative-predictive value) is the new likelihood after the test results are obtained. A good diagnostic test achieves a marked increase (or decrease) in the posttest probability (over pretest probability). For every test in every medical subspecialty, the magnitude of change between pretest probability and posttest probability is determined by Bayes' theorem.[29] Three factors alone determine the magnitude of the pre- to posttest change: sensitivity, specificity, and pretest probability. It is commonly assumed that sensitivity and specificity remain constant for a test. In truth, test-referral bias, a common occurrence in studies of weaning tests, leads to major changes in sensitivity and specificity.[27] Likewise, major changes in pretest probability arise as a consequence of spectrum bias.[27] All of these factors need to be carefully considered when reading a study that evaluates the reliability of a weaning-predictor test.

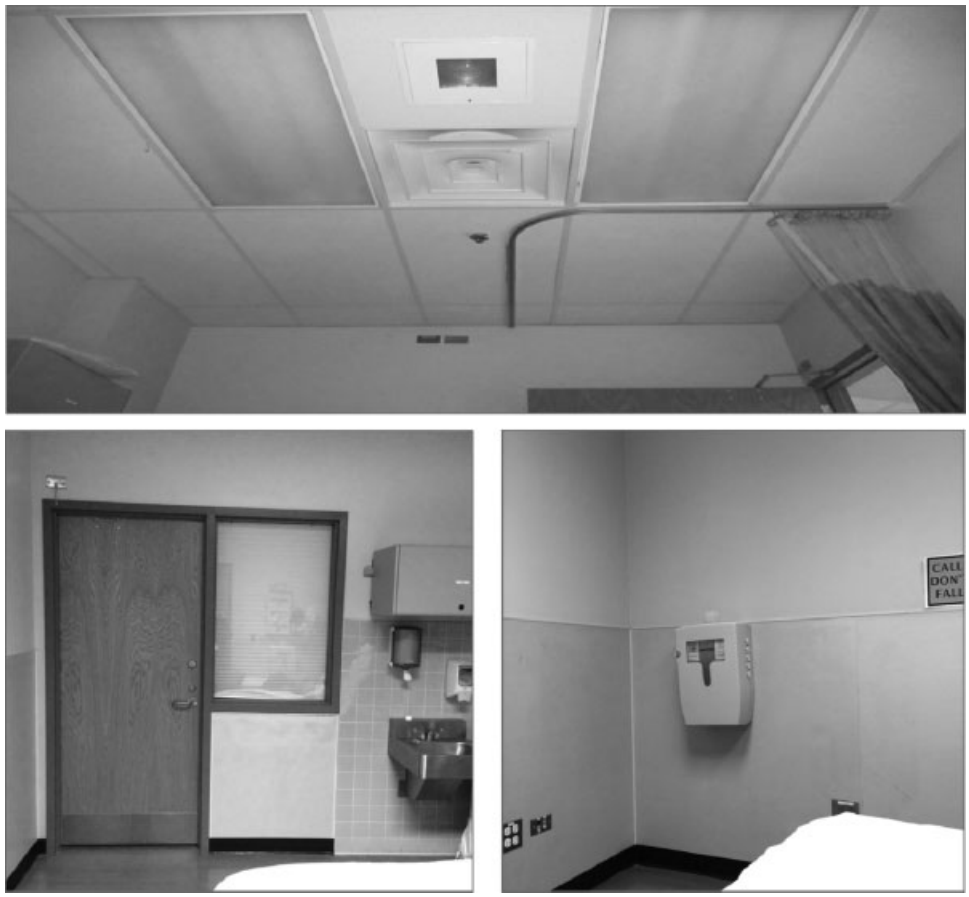


Fig. 6 The environment where ventilated patients are being cared for can promote sensory deprivation through the lack of windows with a view (*left lower panel*), bare walls (*right lower panel*), and tedious ceiling (*upper panel*).

Weaning-Predictor Tests

Several weaning-predictor tests have been proposed and studied over the years. These tests include measurements of breathing pattern, muscle strength and, recently, B-type natriuretic peptides and diaphragm ultrasonography.

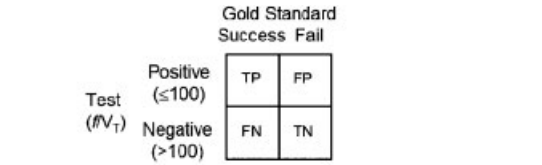
Respiratory Frequency-to-Tidal Volume Ratio

The ratio of respiratory frequency to tidal volume (f/V_T) is measured during 1 minute of spontaneous breathing.[30] The f/V_T can be recorded with a handheld spirometer after disconnecting the patient's endotracheal tube from the ventilator circuit[7] (►**Fig. 9**). Alternatively, f/V_T can be recorded with the use of the pneumotachograph within the ventilator.[31] In this case, the physician has at least three settings to choose from: 0 cm H_2O of pressure support ventilation (PSV), or 0 cm H_2O of continuous positive airway pressure (CPAP), or tube compensation with lowest possible compensatory parameters. In addition, the clinician must select a PEEP of 0 cm H_2O and, preferably, flow triggering.* These steps are necessary to avoid the inaccurate prediction of weaning outcome.[28,32] For instance, the use of PSV of 5 or 10 cm H_2O decreases f/V_T by 20 to 80% as compared with unassisted breathing.[32–35] The use of CPAP of 5 cm H_2O decreases f/V_T by 20 to 50% as compared with unassisted breathing[31,36,37] (►**Fig. 10**).

The higher the f/V_T ratio, the more severe the rapid shallow breathing, and the greater the likelihood of unsuccessful weaning. An f/V_T ratio of 100 recorded with a handheld spirometer best discriminates between successful and unsuccessful attempts at weaning[7] (►**Fig. 11**). The initial evaluation of f/V_T during 1 minute of spontaneous breathing was reported in 1991.[7] Since then, this test has been evaluated in more than 25 studies. Reported sensitivity ranges from 0.35 to 1.00.[29] Specificity ranges from 0.00 to 0.89.[29] At first glance, this wide scatter suggests that f/V_T is an unreliable predictor of weaning outcome. Many of the investigators, however, ignored the possibility of test-referral bias and spectrum bias.[28,29] These problems were compounded by an evidence-based medicine task force set up by the American College of Chest Physicians,[38] which in 2001 undertook a meta-analysis primarily based on work performed by the McMaster University Evidence-based Practice Centre.[39]

The task force calculated pooled likelihood ratios for f/V_T, and judged the summated values to signify that f/V_T was not a reliable predictor of weaning success, and recommended that clinicians should start the weaning process with a spontaneous breathing trial (a confirmatory test), and use the initial

* Of interest, even if a clinician uses flow triggering with PSV set at 0 cm H_2O, ventilators manufactured by some companies (e.g., Nellcor Puritan Bennett, Boulder, CO and Siemens, Munich, Germany) will still provide 1.5 cm H_2O assistance during inhalation.



TP = Test predicts weaning success and patient actually succeeds
TN = Test predicts weaning failure and patient actually fails
FP = Test predicts weaning success and patient actually fails
FN = Test predicts weaning failure and patient actually succeeds

$$\text{Sensitivity} = \frac{TP}{TP+FN} = TPR = [1 - FNR]$$

$$\text{Specificity} = \frac{TN}{TN+FP} = TNR = [1 - FPR]$$

$$PPV = \frac{TP}{TP+FP}$$

$$NPV = \frac{TN}{TN+FN}$$

FN Rate = 1 - Sensitivity

FP Rate = 1 - Specificity

Likelihood ratio for a positive test = TPR / FPR = sensitivity / (1 - specificity)

Likelihood ratio for a negative test = FNR / TNR = (1 – sensitivity) / specificity

Prevalence = TP + FN / (TP + TN + FP + FN)

Diagnostic accuracy = [TP + TN] / [TP + TN + FP + FN]

Fig. 7 A 2 × 2 tabular display of the characteristics of diagnostic tests. The vertical columns represent the results of the gold standard test. The horizontal rows represent the results of the index test. Readings of the ratio of respiratory frequency to tidal volume (f/V_T) ≤100 are classified as positive test results and readings >100 are classified as negative test results. The relationship of these binary results to the outcome of a T-tube weaning trial forms a decision matrix that has four possible combinations. The result of an f/V_T reading is used to predict the outcome of a weaning trial (confirmatory test of the weaning predictor f/V_T) *but not the outcome of extubation* (confirmatory test of the weaning trial). (Used with permission from Tobin and Jubran.[1])

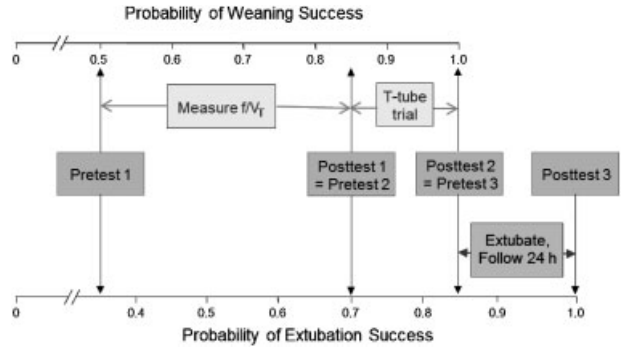


Fig. 8 Interpreting the sequence of diagnostic testing in a patient who is weaned from mechanical ventilation and then extubated, with successful outcome defined as the ability to breathe spontaneously without ventilator assistance for 24 hours after extubation. Pretest 1 is the pretest probability of extubation success before measurement of the ratio of respiratory frequency to tidal volume (f/V_T). The f/V_T reading constitutes the posttest results of the first diagnostic test, and also pretest probability of extubation success for the second diagnostic test, a T-tube trial. The outcome of the T-tube trial constitutes the posttest results of the second diagnostic test, and also the pretest probability of extubation success for the third diagnostic test, a trial of extubation. The outcome of the trial of extubation constitutes the posttest result of the third diagnostic test. In this hypothetical example, pretest probability of weaning success for the first diagnostic test is set arbitrarily at 0.50; the extent of the change for each subsequent step is based on average changes reported in published studies. (Used with permission from Tobin and Jubran.[1])

few minutes of the trial as a screening test.[38,39] This recommendation, however, is untenable because the studies included in the meta-analysis exhibited significant heterogeneity in pretest probability of successful outcome.[29] Such marked heterogeneity prohibits the undertaking of a reliable meta-analysis.[40,41] When data from the studies included in the meta-analysis were entered into a Bayesian model with pretest probability as the operating point, the reported positive-predictive values were significantly correlated with the values predicted by the original report on f/V_T,[7] $r = 0.86$ ($p < 0.0001$); likewise, reported negative-predictive values were correlated with the values predicted, $r = 0.82$ ($p < 0.0001$) (►**Figs. 12** and **13**).[29]

Maximum Inspiratory Pressure

The use of $P_I$max as a weaning predictor stems from a study by Sahn and Lakshminarayan.[42] They found that all patients with a $P_I$max value more negative than – 30 cm H_2O were successfully weaned, whereas all patients with a $P_I$max less negative than – 20 cm H_2O failed a weaning trial. In most successive investigations, these threshold values have shown poor sensitivity and specificity.[7,8,16]

B-Type Natriuretic peptides

The mechanical stretch of cardiomyocytes caused by atrial or ventricular pressure overload or volume overload or both triggers the release of probrain natriuretic peptide (pro-BNP), a prohormone. Pro-BNP is rapidly cleaved into a biologically active 32-amino acid carboxyl-terminal peptide (BNP) and its inactive 76-amino acid amino terminal (N-terminal) fragment (NT-proBNP).[43] Several investigators have evaluated the accuracy of BNP and NT-proBNP in identifying the likelihood and presence of cardiac causes of weaning failure. To this date, however, there is substantial discrepancy in the results of studies assessing the capacity of natriuretic peptides to predict weaning outcome. For some investigators, the change in a peptide concentration over the course of a weaning trial has the greatest predictive power[44]; while for others baseline, values are more reliable.[45] Some report that BNP is more dependable than NT-proBNP[46]; while others report the opposite.[44] The threshold values that differentiate between weaning-success and weaning-failure patients diverge greatly among the investigations.

Diaphragm Ultrasonography

Diaphragmatic dysfunction is common in mechanically ventilated patients.[8,47] M-mode ultrasonography is a promising and noninvasive technique to identify diaphragmatic dysfunction in these patients. Recently, Kim et al[48] assessed the impact of diaphragmatic dysfunction in 88 patients deemed

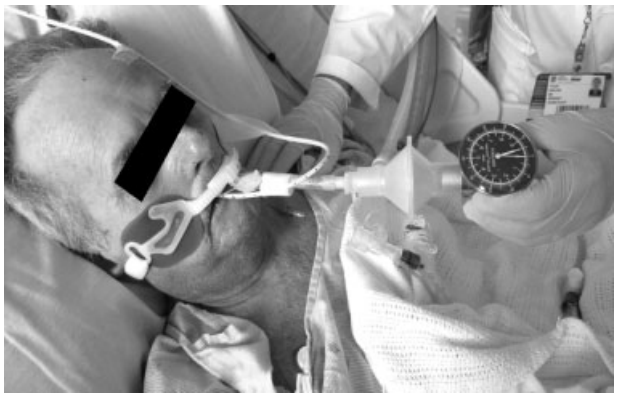


Fig. 9 Technique to record the ratio of respiratory frequency to tidal volume (f/V_T) with a handheld spirometer. The endotracheal tube is disconnected from the ventilator. A handheld spirometer connected to a filter is attached to the end of the endotracheal tube. When recording f/V_T, it is important that the patient's breathing pattern achieves equilibrium before starting the measurement as mechanical ventilation can depress respiratory motor output and, thus, apneic pauses and shallow breaths can occur during the 1st minute after disconnecting a patient from the ventilator. To avoid this pitfall, the clinician must wait until the patient has established a regular respiratory rhythm, a process that can take about 1 minute. When regular respiratory rhythm has been established the clinician will be able to measure 0 f/V_T over the subsequent minute.

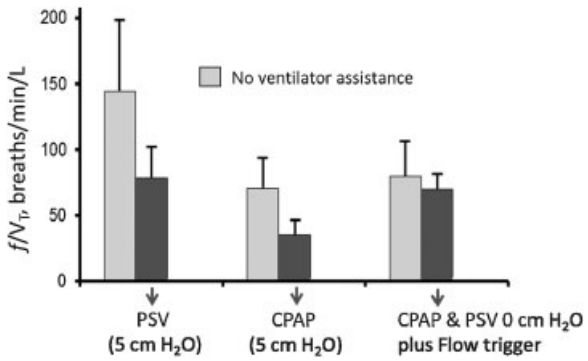


Fig. 10 Effect of pressure support ventilation (PSV), continuous positive airway pressure (CPAP), and flow trigger on frequency-to-tidal volume ratio (f/V_T). *Left panel*: In 21 patients with chronic obstructive pulmonary disease, f/V_T recorded with a handheld spirometer while patients received no ventilator assistance was 145 ± 121 (standard deviation [SD]); the addition of PSV 5 cm H_2O caused f/V_T to decrease to 79 ± 53 (45% decrease).[13,32,56] *Middle panel*: In 33 postoperative patients, the f/V_T recorded with a handheld spirometer while patients received no ventilator assistance was 71 ± 23 (SD); the addition of CPAP 5 cm H_2O caused f/V_T to decrease to 36 ± 14 (49% decrease).[37] *Right panel*: In 80 patients cared for in a medical intensive care unit, f/V_T recorded with a handheld spirometer while patients received no ventilator assistance was 80 ± 30 (SD). The corresponding value of f/V_T recorded while patients were connected to the ventilator with CPAP and PSV both set at 0 cm H_2O plus flow trigger decreased to 70 ± 26 (12% decrease).[135]

ready for a trial of spontaneous respiration, and with no history of diaphragmatic disease. Diaphragmatic dysfunction was defined as either a vertical excursion of the muscle of less than 10 mm or as paradoxical movements. Twenty-four patients (29%) had evidence of diaphragmatic dysfunction.

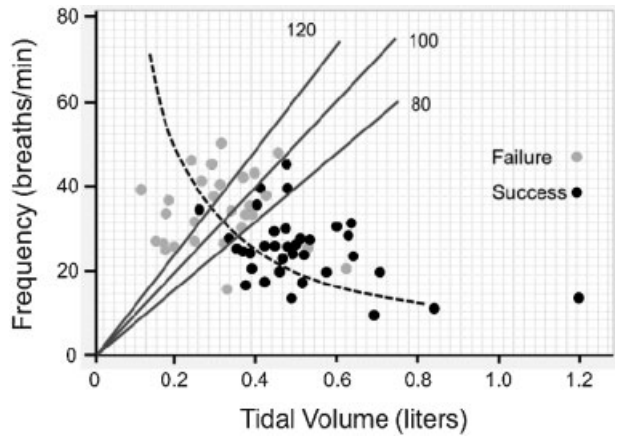


Fig. 11 Isopleths for the ratio of respiratory frequency to tidal volume (f/V_T) recorded reported by Yang and Tobin[7] in clinically stable patients considered ready to undergo a weaning trial by their primary physicians. The isopleths represent different degrees of rapid shallow breathing. For the patients indicated by the points to the left of the isopleth representing 100 breaths per minute per liter, the likelihood that a weaning trial would fail was 95%, whereas for the patients indicated by the points to the right of this isopleth, the likelihood of a successful weaning outcome was 80%. The hyperbola represents a minute ventilation of 10 L per minute, a criterion commonly used to predict weaning outcome; this criterion was of little value in discriminating between the successfully weaned patients (open circles) and the patients in whom weaning failed (solid circles). (Modified from Yang and Tobin.[7])

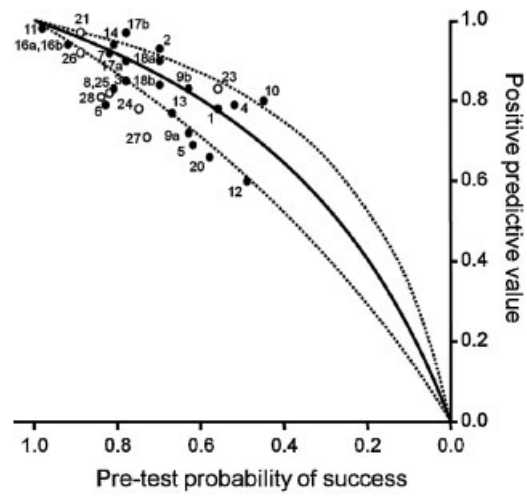


Fig. 12 Positive-predictive value (posttest probability of successful outcome) for f/V_T plotted against pretest probability of successful outcome. Studies included in the ACCP Task Force's meta-analysis are indicated by closed symbols; studies undertaken after publication of the Task Force's report are indicated by open symbols. The curve is based on the sensitivity and specificity originally reported by Yang and Tobin[7] and Bayes' formula for 0.01-unit increments in pretest probability between 0.00 and 1.00. The lines represent the upper and lower 95% confidence intervals for the predicted relationship of the positive predictive values against pretest probability. The observed positive-predictive value in a study is plotted against the pretest probability of weaning success (prevalence of successful outcome). Studies 5, 6, 11, 18a, 18b, and 24 include measurements of f/V_T obtained during pressure support. Studies 14 and 21 include measurements obtained in pediatric patients. Studies 7, 18a, 18b, and 28 used f/V_T threshold values < 65. (Modified from Tobin and Jubran.[29])

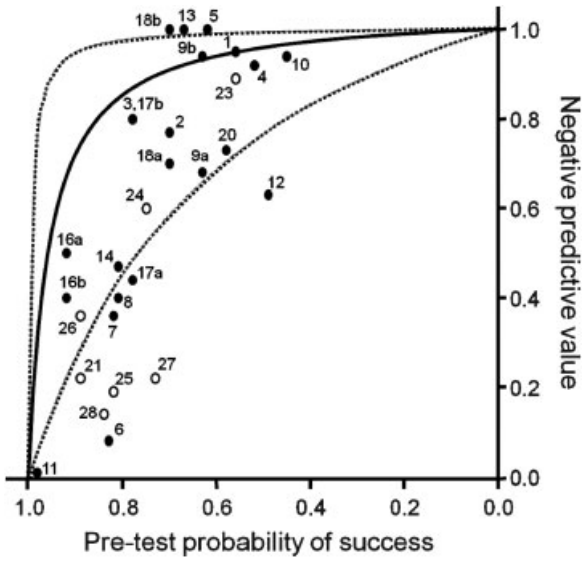


Fig. 13 Negative-predictive value (posttest probability of unsuccessful outcome) for f/V_T. Studies included in the ACCP Task Force's meta-analysis are indicated by closed symbols; studies undertaken after publication of the Task Force's report are indicated by open symbols. The curve, its 95% confidence intervals, and placement of a study on the plot are described in the legend to ►**Fig. 12**. The observed negative-predictive value in a study is plotted against the pretest probability of weaning success (prevalence of successful outcome). Of note, study 11 has a negative-predictive value of 0.00 and specificity of 0.00, which are predictable given its pretest probability of weaning success of 98.2% (i.e., spectrum bias). The large number of subjects in study 11 ($n = 163$) means that this study made a substantial contribution to the pooled likelihood ratio calculated in the meta-analysis of the ACCP Task Force. (Modified from Tobin and Jubran.[29])

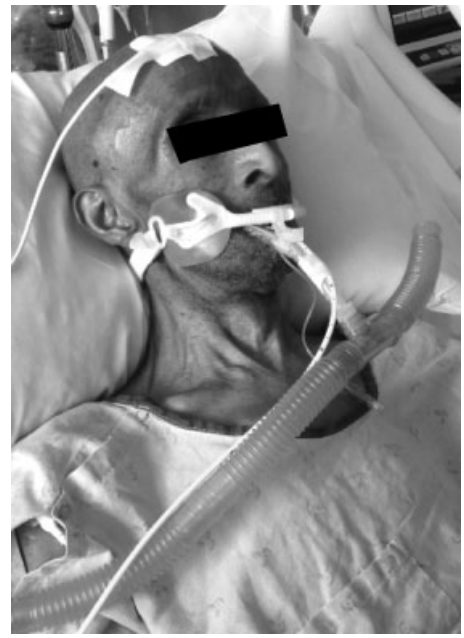


Fig. 14 Unassisted breathing through a T-tube circuit. During a weaning trial of unassisted breathing the patient is disconnected from the ventilator and breathes through a T-tube circuit without continuous positive airway pressure. The T-tube is connected to an oxygen source with an F_{IO_2} usually set at 0.40. During the trial, we monitor transcutaneous oxygen saturation, cardiac activity, and blood pressure. Concurrently, we observe the patient for development of respiratory distress. Patients who tolerate the T-tube trial for at least 30 minutes are considered for a trial of extubation. Only in selected patients do we perform arterial blood gas analysis before extubation. Patients who do not tolerate the trial are reconnected to the ventilator and are usually reassessed the following day.

Compared with patients without dysfunction, those with dysfunction had longer weaning time (17 vs. 4 days, $p < 0.01$) and total ventilation time (24 vs. 9 days, $p < 0.01$). Future studies are necessary to assess the role of diaphragm ultrasonography in identifying patients at high risk of difficulty weaning.

Weaning Trials

When a screening test is positive (e.g., low f/V_T), the clinician proceeds to a confirmatory test,[27] for example, PSV of 6 to 8 cm H_2O or spontaneous respiration through a T-tube circuit (►**Fig. 14**). The goal of a positive result on a confirmatory test (no respiratory distress at the conclusion of the PSV trial or T-tube trial) is to rule in a condition—in this case, high likelihood that a patient will tolerate a trial of extubation.[27] An ideal confirmatory test has a very low rate of false-positive results, that is, a high specificity.[27] To determine the specificity of a spontaneous breathing trial, it is required to extubate all patients who fail a weaning trial and to count how many require reintubation.[28] Unfortunately, the specificity of a spontaneous breathing trial is not known. Indeed, its specificity will never be known because its determination would require an unethical experiment: extubating all patients who fail a weaning trial and counting how many require reintubation without introducing confounders such as the use of noninvasive positive pressure ventilation (NIPPV) for postextubation respiratory distress.[49]

The major weaning techniques used include synchronized intermittent mandatory ventilation (SIMV), T-tube trial, PSV and, in selected patients, NIPPV.

Synchronized Intermittent Mandatory Ventilation

When SIMV is used for weaning, the ventilator's mandatory rate is reduced in steps of 1 to 3 breaths per minute, and an arterial blood gas is obtained approximately 30 minutes after each rate change.[50] Unfortunately, titrating the ventilator's mandatory rate according to the results of arterial blood gases can produce a false sense of security. As little as 2 to 3 SIMV breaths per minute can achieve acceptable blood gases, but these values provide no information regarding the patient's work of breathing.[28] Moreover, at SIMV rates of 14 breaths per minute or less, the patient's work of breathing may be excessive.[51,52] By providing inadequate respiratory muscle rest, SIMV is likely to delay rather than facilitate weaning.[53]

Pressure Support Ventilation

When PSV is used for weaning, the level of pressure is reduced gradually and titrated on the basis of the patient's respiratory

frequency.[54] When the patient tolerates a PSV of approximately 6 to 8 cm H_2O (and PEEP 5 cm H_2O), he or she is extubated.[55,56] This strategy is based on the belief that such "minimal levels" of support are solely overcoming the resistance produced by the endotracheal tube and ventilator circuit.[55] This belief, however, disregards the edema and inflammation that develops in the upper airways after an endotracheal tube has been in place for a day or more.[57] On removal of the tube, the work produced by breathing through the swollen airway is about the same as that caused by breathing through an endotracheal tube[57]—this should hold true as long as the internal diameter of the endotracheal tube is not too small and there is no accumulation of dense secretions within it.[58] In other words, in most cases, any level of PSV overcompensates and may give misleading information about the likelihood that a patient can tolerate extubation.[59] The addition of a small amount of PSV produces surprisingly large reductions in inspiratory work in ventilated patients: 5 cm H_2O can decrease inspiratory work by 31 to 38% and 10cm H_2O can decrease work by 46 to 60%.[55] Independently, the addition of 5 cm H_2O of PEEP can decrease the work of breathing by as much as 40% in ventilated patients.[55]

T-Tube Trials

The use of *repeated* T-tube trials several times a day is the oldest method for conducting a weaning trial.[60] The patient receives an enriched supply of oxygen through a T-tube circuit (►**Fig. 14**). Initially 5 to 10 minutes in duration, T-tube trials are extended and repeated several times a day until the patient can sustain spontaneous ventilation for several hours. This approach has become unpopular because it requires considerable time on the part of intensive care staff.

Today, it is usual to perform a *single* daily T-tube trial, lasting for 30 to 120 minutes.[61] Performing single daily T-tube trials is as effective as performing such trials several times a day,[53] but much simpler. If the trial is successful, the patient is extubated. If the trial is unsuccessful, the patient is given at least 24 hours of respiratory muscle rest with full ventilator support before another trial is performed.

Patients are judged to have failed a T-tube trial when they develop severe tachypnea, increased accessory muscle activity, diaphoresis, facial signs of respiratory distress, oxygen desaturation, tachycardia, arrhythmias, or hypotension. The degree of change in these variables, however, varies from report to report. A standardized approach to patient monitoring during a T-tube trial does not exist. Indeed, there is no agreement as to whether the monitoring of any variable helps in deciding whether to continue a T-tube trial for an initially planned duration, prolong it, or curtail it.[28]

Noninvasive Positive Pressure Ventilation in Weaning

Several RCTs have been conducted to assess the role of NIPPV to facilitate weaning and extubation in difficult-to-wean patients.[62] These studies favor the use of NIPPV as long as the following caveats are borne in mind[63]: (1) NIPPV for weaning and extubation must be reserved mainly for patients with chronic obstructive pulmonary disease—particularly those who are hypercapnic; (2) patients must be good candidates for NIPPV (►**Table 1**); (3) patients should have been easy to intubate; (4) before extubation, patients must be comfortable and well oxygenated on levels of PSV and F_{IO_2} that can used via mask after extubation, for example, PSV < 15 to 20 cm H_2O and $F_{IO_2} < 0.40$ to 0.50. (See also article "Non-invasive ventilation in withdrawal of mechanical ventilation" by Miquel Ferrer et al of this issue.)

Comparison of Weaning Methods

Weaning methods are not equally effective. For example, the period of weaning is as much as three times as long with SIMV as

Table 1 Indications and contraindications for noninvasive ventilation in patients with COPD who fail extubation

Indications
Clinical observations
Moderate to severe dyspnea
Tachypnea
Accessory muscle use, abdominal paradox
Impaired gas exchange
Acute or acute-on-chronic hypercapnic respiratory failure ($Pa_{CO_2} > 45$ mm Hg, pH < 7.35)
Hypoxemia ($Pa_{O_2}/F_{IO_2} \leq 200$)[a]
Contraindications
Absolute
Bradypnea, respiratory arrest, immediate need for intubation
Life-threatening hypoxemia
Unable to fit mask
Upper airway obstruction
Undrained pneumothorax
Vomiting/severe upper gastrointestinal bleed
Relative
Agitated, uncooperative
Severe hypercapnic encephalopathy (Glasgow coma scale score < 10)
Inability to protect the airway
Impaired swallowing or cough
Excessive secretions
Recent upper airway or upper gastrointestinal surgery
Multiple organ failure
Medically unstable
Uncontrolled cardiac ischemia or arrhythmia
Hypotensive shock

Abbreviation: COPD, chronic obstructive pulmonary disease.
Source: Modified from Laghi.[81]
[a]Noninvasive ventilation should be used with caution in exacerbations of COPD accompanied with hypoxemia.

with T-tube trials[53] or PSV[64] trials. In a study involving patients with respiratory difficulties during weaning, T-tube trials halved the weaning time as compared with PSV[53]; in another study, the weaning time was similar to the two methods.[64]

Weaning by Protocol versus Usual Care

The use of human-driven protocols for weaning versus usual care has been compared in at least six RCTs.[65–70] The reports of Namen et al,[65] Randolph et al,[66] and Krishnan et al[67] show no benefit for a protocol approach. The reports of Kollef et al,[68] Marelich et al,[69] and Ely et al[70] are viewed as evidence for the superiority of a protocol approach to weaning.

In the trial of Kollef et al,[68] however, no advantage for weaning by protocol was observed in three of the four study ICUs. In the fourth unit, where a significant advantage for a protocol approach to weaning was observed, patients assigned to usual care were significantly sicker than the patients assigned to protocol management in that ICU; this confounding factor markedly weakens (if not destroys) any assertion that protocol weaning was superior.

Marelich et al[69] studied weaning by protocol in two ICUs, and found no significant advantage in one. The study of Ely et al[70] does not consist of a straightforward comparison of protocol versus non-protocol care. All of the patients in the intervention arm were weaned by T-tube or flow-by trials, whereas 76% of the patients in the non-intervention arm were managed by SIMV alone or in combination with PSV. Physiological studies and randomized trials have repeatedly shown that SIMV is the least effective weaning modality.[51–53,64] With this fundamental difference in techniques, it is impossible to use data from this study to form a judgment about the efficacy of a protocol per se. Instead, the report of Ely et al[70] can be viewed primarily as another study of SIMV,[28] confirming the reports of Brochard et al[64] and Esteban et al[53] that SIMV slows weaning.

That the use of a protocol does not improve weaning outcome should not be surprising.[28,71] One needs to make a distinction between the use of algorithms in research protocols and their subsequent application in everyday practice. As noted above, the algorithm in a research protocol is specified with exacting precision. For example, if $f/V_T \leq 100$ is the nodal point for advancement to a T-tube trial, then patients with an f/V_T of 100 will undergo the trial whereas patients with an f/V_T of 101 will return to MV for another 24 hours. An experienced clinician, however, would think it silly to comply with a protocol that decided an entire day of ventilator management on a one-unit difference in a single measurement of f/V_T (or any other weaning predictor).[71] Instead, an intelligent physician customizes the knowledge generated by research to the particulars of each patient. The intelligent application of physiological principles is likely to outperform an inflexible application of a protocol.

Computerized Approaches to Weaning

A novel strategy of weaning entails the use of modified ventilators equipped with computer-driven closed-loop knowledge-based algorithms.[72–74] These modified ventilators continuously monitor f, V_T, and end-tidal CO_2 tension, and repeatedly alter the level of delivered pressure support based on iterative changes in these three variables.[72] The pace of pressure support reduction is tailored according to the needs and performance of the patient. Once a predesignated minimal level of pressure support is reached, the ventilator automatically subjects the patient to a weaning trial, conducted at a low level of PS. If the patient develops no distress, a message is displayed on the screen recommending the removal of the ventilator.

Lellouche et al[75] were the first to perform a large RCT in Europe comparing the computerized ventilator (SmartCare, Lubeck, Germany) against standardized written instructions. They concluded that, compared with usual care, the computerized system decreased weaning duration from a median of 5 to 3 days ($p = 0.01$) and decreased total duration of MV from 12 to 7.5 days ($p = 0.003$) (►**Fig. 15**, *left panel*). These positive results have been confirmed by Burns et al[76] in a recent Canadian study (the *WEAN* study) conducted in collaboration with the research team of Lellouche et al.[75] In this second study, patients randomized in the computerized system had shorter median times to first successful spontaneous breathing trial (1.0 vs. 4.0 days; $p < 0.0001$), extubation (3.0 vs. 4.0 days; $p = 0.02$), and successful extubation (4.0 vs. 5.0 days; $p = 0.01$).

In Australia, Rose et al[77] undertook an RCT using the same ventilator employed by Lellouche et al[75] and Burns et al,[76] and reported that the median time to successful extubation was approximately 40 hours in both groups of patients. At least two factors are likely to have contributed to the different outcome. First, 68% of enrollees in the study of Lellouche et al[75] and 72% of enrollees in the study of Burns et al[76] were medical patients, whereas 78% of enrollees in the study of Rose et al[77] were surgical patients, which are typically less challenging to wean. In this regard, it is worth noting that computerized weaning in a bench model performed poorly in the presence of Cheyne–Stokes respiration,[74] a pattern of breathing, that is, likely more common among medical than among surgical patients. Second, the nurse-to-patient ratio in the study of Rose et al[77] was 1:1.

A fourth RCT of computerized weaning versus usual care was undertaken in Brazil by Taniguchi et al.[73] These Brazilian researchers employed a computerized system that was slightly different from the SmartCare used by the European,[75] Australians,[77] and Canadian[76] investigators. Taniguchi et al[73] found no difference in weaning duration with the two approaches. Similar to the study of Rose et al,[77] enrollees in the study of Taniguchi et al[73] consisted solely of postoperative patients. That surgical patients may not benefit from computerized weaning is further supported by the results of Schädler et al[78] who reported that in 300 surgical patients there was no difference between weaning using the computerized approach and weaning based on a standardized written instructions (►**Fig. 15**, right panel).

Management of the Problem Patient

Weaning attempts that are repeatedly unsuccessful usually signify either incomplete resolution of the illness that

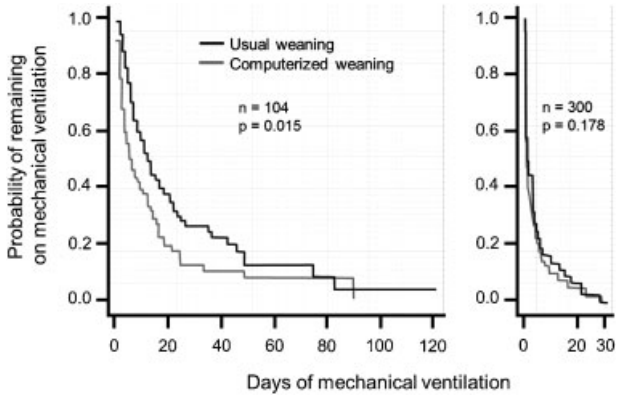


Fig. 15 Computerized approaches to weaning. *Left panel*: Kaplan–Meier analysis of weaning time until successful extubation or death in 70 patients randomized to usual weaning (solid line) and 74 patients randomized to computerized weaning (grey line). The probability of remaining on mechanical ventilation in this study in which medical patients accounted for more than two-thirds of randomized subjects was significantly reduced with the computer-driven weaning (log-rank test, $p = 0.015$). (Redrawn from Lellouche et al.[75]) *Right panel*: Kaplan–Meier curves for overall ventilation time in 150 patients randomized to usual weaning (solid line) and 150 patients randomized to computerized weaning (grey line). The probability of remaining on mechanical ventilation in this study that enrolled only surgical patients was not reduced by computer-driven weaning (log-rank test, $p = 0.178$). (Redrawn from Schädler et al.[78])

precipitated MV or the development of new problems. A team approach, including efficient communication and coordination among intensivists, nurses, and respiratory therapists, is important. A thorough diagnostic work-up with correction of all reversible pathology is mandatory. Important aspects in the care of these patients include the optimization of ventilator settings and optimization of cardiovascular function. In addition, selected patients may benefit from respiratory muscle training, physical and occupational therapy, and psychological interventions.

Optimization of Ventilator Settings

Careful adjustment of the ventilator settings is necessary to minimize respiratory work. It is important to spot the presence of PEEPi, as this will interfere with ventilator triggering.[79] A careful interpretation of flow, volume, and airway pressure waveform at the bedside is necessary to identify patient–ventilator asynchronies.[2] As there is a strong association between asynchronies and duration of MV,[80] intensivists should actively adjust ventilatory settings in patients who experience asynchronies.[2,81] Alternatively, they may consider the use of novel modes of MV such as neurally adjusted ventilatory assist.[82,83] Of note, whether reducing the number of asynchronies decreases the duration of MV in the problem patient remains to be determined.

Optimization of Cardiovascular Function

Cardiovascular dysfunction can be an important cause of weaning failure both in patients with known or previously unrecognized heart disease.[58] Accordingly, intensivists should have a low threshold to suspect and treat cardiovascular dysfunction, including volume overload. Bedside transthoracic echocardiography, if properly executed during the weaning trial, can provide important information regarding left ventricular systolic and diastolic dysfunction and ischemia-induced systolic dysfunction.[17,58]

Ideally, volume overload should be treated before carrying out a weaning trial as volume overload has been associated with worse weaning outcome.[84] In a RCT of 304 patients allocated to either a BNP-driven or physician-driven strategy of fluid management during ventilator weaning using a computer-driven weaning system, Mekontso Dessap et al[85] reported a shorter time to successful extubation in the intervention group as compared with the control group: median (interquartile range [IQR]) of 42 (21, 108) hours versus 59 (23, 140) hours, respectively ($p = 0.034$). These effects were especially pronounced in patients with left ventricular systolic dysfunction.

Respiratory Muscle Training

The growing recognition that many weaning-failure patients have severe respiratory muscle weakness has been the springboard of a recent RCT designed to determine whether inspiratory muscle-strength training would improve the weaning outcome of patients who had received MV for approximately 1 to 2 months.[86] Strength training was achieved with the use of a commercial threshold inspiratory muscle training device equipped with an adjustable spring-loaded valve (►**Fig. 16**). Five days a week, patients in the intervention group were required to perform four sets of 6 to 10 threshold-loaded inspirations; between each set, patients were returned to the ventilator for 2 minutes. During these sessions, the spring-loaded valve in the threshold device was adjusted to the highest pressure setting that the patient could consistently open during each inspiration. In contrast, patients in the sham arm inspired through an inspiratory muscle training device that contained a large hole, with the

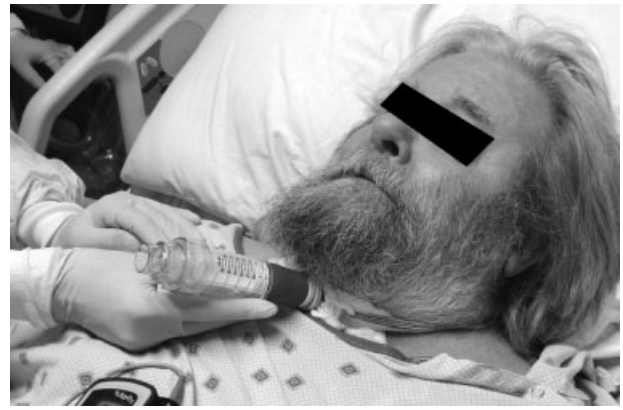


Fig. 16 Inspiratory threshold device used for inspiratory muscle training. This device contains an adjustable, spring-loaded, mushroom valve. To inhale through the device, the patient must generate an inspiratory pressure, that is, sufficient to compress the spring of the mushroom valve. To keep the valve open throughout inhalation, the inspiratory pressure must be maintained above the threshold pressure. The patient exhales through the training device via a low-resistance, one-way, silicone rubber diaphragm (see text for details).

result that little pressure was required to generate airflow. Upon completion of the study, 71% patients in the strength-training arm were weaned as compared with 47% patients in the sham arm ($p = 0.039$). Moreover, over the course of the trial, patients in the strength-training arm exhibited an increase in $P_I$max from 44 ± 18 to 54 ± 18 cm H_2O ($p < 0.0001$); corresponding values of $P_I$max in the sham arm were 44 ± 18 and 45 ± 20 cm H_2O.

The results of this study suggest that the use of a simple device (a threshold loader) can markedly increase the weanability of patients requiring long-term MV. The challenges now are to reproduce these findings, determine whether further adjustments to the training regimen might achieve an even greater level of success, and investigate whether the use of a threshold loading device may increase the weanability of patients in the acute care setting.

Physical and Occupational Therapy to Aid Weaning

In 1974, Petty hypothesized that ambulation in MV patients could be a useful strategy to improve strength and coordination during weaning.[87] This hypothesis was tested 35 later by Schweickert et al.[88] At two university hospitals, the investigators enrolled patients who had received less than 72 hours of MV and who had exhibited functional independence 2 weeks before admission. From an initial screening of 1,161 patients, 104 were enrolled. Of these, 49 were randomized to early exercise and mobilization (physical and occupational therapy), starting on the day of enrollment, and 55 to usual care that did not include routine physical therapy. Each day, infusions of sedative agents were interrupted in both groups.

The primary end point, the number of patients returning to independent functional status at hospital discharge, was reached by 29 (59%) patients in the intervention group and 19 (35%) in the control group ($p = 0.02$). Duration of MV was also shorter in the intervention group, 3.4 days (IQR: 2.3–7.3) versus 6.1 days (IQR: 4.0–9.6; $p = 0.02$).

The study of Schweickert et al[88] while encouraging leaves several important questions answered. Can physical and occupational therapy shorten duration of MV in the type of patients excluded from that study such as patients with significant baseline-dependent functional status or who have been ventilated for more than 72 hours? Can alternative strategies, such as transcutaneous neuromuscular electrical stimulation[89–91] alone or in combination with anabolic agents,[92] be of benefit in selected patients who are not candidates or who do not tolerate physical and occupational therapy? Finally, is it more cost-effective to combine a limited number of physical and occupational therapy sessions with transcutaneous neuromuscular electrical stimulation than it is to perform an intensive program of physical and occupational therapy alone[88]?

Psychological Interventions

The negative impact of psychological factors on weaning underscores the need for active screening for delirium, depression, anxiety, and PTSD.[21,22,24] Aggressive treatment of depression may increase the likelihood of weaning.[93,94] Biofeedback therapy, weaning in specialized centers, and improving the patients' environment, communication, and mobility have been used to decrease psychological problems in ventilated patients.[22] Whether novel adjuncts such as music therapy may benefit anxious patients who repeatedly fail weaning remains to be determined.[95]

Role of Sedation in Weaning

Pharmacologic agents that produce sedation are almost invariably used in patients receiving MV with the goals of decreasing anxiety and agitation, enhancing patient–ventilator synchronization, and facilitating patient care.[1] More than 10 years ago, Kress et al[96] undertook an RCT in 128 adult patients receiving MV in a medical ICU and concluded that the daily interruption of sedation resulted in a shorter duration of MV and a shorter ICU stay. Girard et al[97] extended these findings by combining daily interruption of sedation with spontaneous breathing trials. The paired intervention resulted in more days breathing without ventilator assistance, and earlier discharge from both the ICU and hospital. In an accompanying editorial, Brochard[98] pointed out several problems with the design of the study—the absence of a requirement to stop sedatives in the control group before a spontaneous breathing trial, the timing of weaning onset, and markedly increased rate of failed weaning trials in the control arm—that render the interpretation of this study highly problematic.

Recently, Mehta et al[99] reported that among 430 mechanically ventilated adults, the addition of daily sedation interruption to protocolized sedation designed to maintain a comfortable yet arousable state equivalent did not shorten duration of MV or ICU stay. In a third study, Shehabi et al[19] noted that a daily interruption of sedation increased the overall need for benzodiazepines and the workload of the nurses. Strøm et al[100] went even further and, in a single-blinded study of 140 mechanically ventilated patients, sought to determine if complete withholding of sedation would be superior to daily interruption of sedation. No sedation was associated with significantly more days without ventilator assistance (mean: 4.2 days; 95% confidence interval, 0.3–8.1 days), and earlier discharge from both the ICU and hospital. Agitated delirium was more frequent in the intervention group than in the control group (20 vs. 7%; $p = 0.04$). Two years later, a neuropsychologist interviewed 13 patients from each group and concluded that there were no differences in terms of quality of life, depression, and anxiety.[101] The investigators concluded that "a protocol of no sedation applied to critically ill patients undergoing MV does not increase the risk of long-term psychological sequelae."[101] Two interdepended observations, however, limit the strength of this conclusion. First, only a minority of patients enrolled on the original study[19] were available for the follow-up neuropsychologist's interview.[101] Second, it is likely that the incidence of psychological problems would have been higher among patients who declined the interview than among those who agree to it.[102] (See also article "Sedation and analgesia in MV" by T. Strøm of this issue.)

Weaning Outcome and Short-Term and Long-Term Prognoses

The panelists of a recent International Consensus Conference on weaning from MV[103] proposed that weaning be

categorized into three groups according to the difficulty and duration of the weaning process. According to the proposed classification, patients with "simple weaning" are those extubated at the first attempt of spontaneous breathing. Patients with "difficult weaning" are extubated within 7 days from the first trial of spontaneous breathing. Patients with "prolonged weaning" are those who fail at least three weaning attempts or who require more than 7 days of weaning.

To this date, four groups of investigators have assessed the usefulness of this classification in determining the outcome of patients who require MV. The investigators are concordant in reporting greater mortality,[104–107] longer duration of MV,[105,106] and longer duration of ICU stay[104–107] with prolonged weaning. The last two findings are not surprising considering how the weaning categories are defined. Any other result would be counterintuitive.[108] In one (retrospective) study,[104] investigators assessed long-term outcome according to the new classification and found no association between weaning group and 1-year mortality.

Extubation

When a patient tolerates a weaning trial without distress, a clinician may feel reasonably confident that the patient will be able to sustain spontaneous ventilation and extubates the patient. In the hours following extubation, the patients are carefully monitored for ability to protect the upper airway and sustain ventilation (►**Fig. 17**). Most patients will display progressive improvement and will eventually be discharged from the ICU. However, between 10 and 20%[109] of patients experience respiratory distress in the postextubation period. Many of them will require reinsertion of the endotracheal tube and MV.[49] In contrast to the relatively short time required to recognize that a patient is failing a weaning trial, the time course for the development of postextubation distress extends over a longer time span. In a study by Epstein and Ciubotaru,[110] for example, 33% of reintubations occurred within the first 12 hours after extubation, and 42% occurred after 24 hours.

The mortality rate among patients who require reintubation is more than six times as high as the mortality rate among patients who tolerate extubation.[61] The reason for the higher mortality rate is unknown. It might be related to the development of new problems after extubation or to complications associated with reinsertion of a new tube or that the need for reintubation reflects greater severity of the underlying illness.[111] Recent data, however, suggest that reintubation following a planned extubation may affect survival independently of the underlying illness severity.[112,113]

Causes of Postextubation Distress

The listed indications for reintubation vary considerably from study to study. Of these, postextubation upper airway obstruction has attracted the most attention.

Postextubation Upper Airway Obstruction

Upper airway obstruction is one of the most urgent and potentially lethal medical emergencies. Complete upper airway obstruction lasting for as little as 4 to 6 minutes can cause irreversible brain damage. The upper airway, which encompasses the passage between the nares and carina, can be obstructed by functional or anatomic causes. Among the functional causes are vocal cord paralysis, paradoxical vocal cord motion, and laryngospasm. Anatomic causes include trauma (including arytenoid dislocation), burn, granulomas, infections, foreign bodies, tumors, tracheomalacia, compression by a hematoma in close proximity to the airway and supraglottic, and retroarytenoidal and subglottic edema.[3] Edema can develop as early as 6 hours after intubation.[114] Life-threatening functional and anatomic obstruction can occur postoperatively in patients with redundant pharyngeal soft tissue (sleep apnea) and loss of muscle tone related to the postanesthesia state.[115]

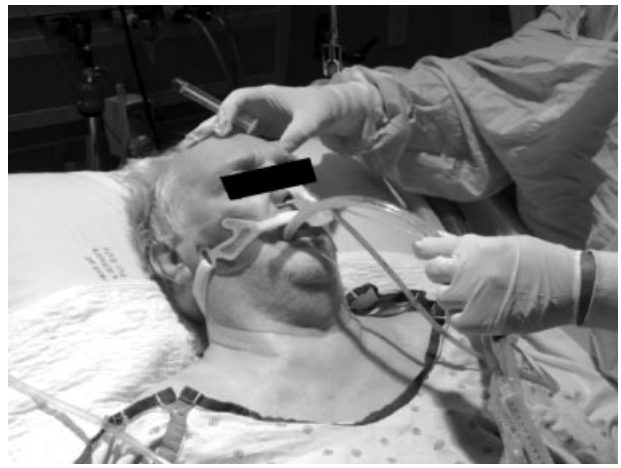


Fig. 17 Extubation. In terms of medical decision analysis, extubation is a confirmatory test of the weaning trial. That is, extubation is used to diagnose/screen for readiness to maintain spontaneous respiration. Extubation is typically performed under controlled conditions. Enteral feeding is temporally withheld for about 4 hours. Following extubation, the patient is given supplemental oxygen. The development of severe respiratory distress after extubation, if sufficient to require reintubation, is associated with a high mortality rate.

Upper airway obstruction causes stridor only if the patient is capable of generating sufficient airflow; if airflow is insufficient, obstruction may cause hypercapnia, hypoxemia, or paradoxical breathing, but not stridor. Of note, arterial blood gases are not particularly helpful in making a diagnosis of postextubation upper airway obstruction because they are not specific to airway patency,[116] and because they may show little change until a patient is in extremis.[116]

The amount of air leaking around the outside of an endotracheal tube on deflating the balloon cuff has been used by several investigators to predict upper airway obstruction after extubation (►**Fig. 18**).[117–125] For several reasons, however, it is difficult to provide general recommendations on how to perform, and how to interpret a cuff-leak test.[3] First, the method for performing the test has not been standardized. Second, the outcome criterion is not always clearly stated: rate of reintubation for any reason, occurrence of stridor of any severity, or occurrence of stridor that requires reintubation. Third, in some studies, it is not clear

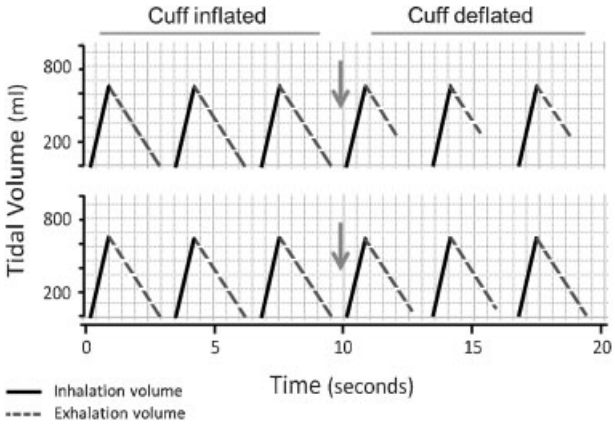


Fig. 18 Cuff-leak test. Schematic representation of tidal volume recorded by the ventilators' inspiratory pneumotach (solid line) and by the ventilators' expiratory pneumotach (dash line) during inhalation and exhalation in two patients before and after deflation of the cuff on the endotracheal tube (*arrow*). *Upper panel*: The patient develops a large leak after cuff deflation (positive test result), as signified by the expired tidal volume being markedly smaller than the inspired tidal volume. *Lower panel*: The patient develops a small leak after cuff deflation (negative test result), as signified by the expired tidal volume being only approximately 40 to 75 mL or 6 to 12% less than the inspired tidal volume.

whether the investigators carefully excluded reasons for reintubation other than stridor. If a patient is reintubated because of left ventricular failure, it is not logical to expect the cuff-leak test to predict such an event. Finally, in adult patients, small or absent cuff leaks do not necessarily translate in the development of stridor or the need for reintubation (and vice versa).[118,121,123]

In view of all the above observations, some investigators reason that—in adult patients—failing a cuff-leak test should not be used as an indication for either delaying extubation or initiating other specific therapy but, possibly, as an indicator of increasing vigilance at the time of extubation.[111] Factors which may contribute to small or absent cuff leaks in patients not developing post-extubation distress include secretions located around the endotracheal tube, head and neck position, presence or absence of sedation, and large endotracheal tube relative to the size of the patient's larynx.[123,126] When upper airway obstruction due to laryngeal edema is of concern, intensivists may opt to administer systemic corticosteroids before extubation.[127]

Other Causes of Postextubation Distress

Conditions other than upper airway obstruction that cause postextubation distress include respiratory failure, congestive heart failure, aspiration or excessive secretions, encephalopathy, onset of new sepsis, and other conditions.[61,110,128]

Tracheostomy and Long-Term Acute Care Hospitals

Patients who receive MV and cannot be extubated often undergo tracheostomy. A tracheostomy is considered more comfortable and thus it may allow lowering the doses of sedatives and narcotics. The optimal timing of tracheostomy remains uncertain. Some data suggest that, compared with "late" tracheostomy (> 10 days after intubation), "early" tracheostomy (≤ 10 days after intubation) may shorten duration of MV and ICU length of stay.[129,130] In a current meta-analysis, however, investigators concluded that "*at present there is no specific information about any subgroup or individual characteristics potentially associated with better outcomes with either early or late tracheostomy.*"[131] Tracheostomized patients requiring prolonged MV (> 21 days) are commonly weaned in long-term acute care hospitals (LTACHs). In these centers, weaning is started as soon as possible, as approximately 20% of patients succeed weaning at their first trial of unsupported respiration. The best time window for successful weaning seems to be within the initial 3 weeks from transfer to an LTAC.[58,132,133]

In a recent study of more than 300 tracheostomized patients cared for in an LTACH, investigators compared the effect of unassisted breathing through a tracheostomy collar versus pressure support on weaning duration.[134] In that study, weaning by unassisted breathing through a tracheostomy resulted in shorter median weaning time (15 days with tracheostomy collar vs. 19 days with pressure support). Weaning mode had no effect on survival at 6 months (51% with tracheostomy collar vs. 56% with pressure support) and 12 months (60% with tracheostomy collar vs. 66% with pressure support).[134] When liberation from MV ultimately becomes improbable (more than 1 month of a structured, multidisciplinary weaning approach), home ventilation has to be considered.[132,133]

Conclusion

In conclusion, to reduce the possibility of delayed weaning or premature extubation, intensivists should contemplate a three-step diagnostic strategy: first, measurement of weaning predictors, then a trial of unassisted breathing (T-tube trial) and, finally, a trial of extubation. The key point is for physicians to consider the possibility that a patient *just might* be able to tolerate weaning. Such diagnostic triggering is facilitated through use of a screening test, and is the rationale for measurement of weaning-predictor tests. A positive result on a screening test (weaning predictor test) is followed by a confirmatory test (weaning trial), to increase the possibility that a patient will successfully tolerate extubation. It is important not to postpone the use of a screening test by waiting for a more complex diagnostic test, such as a T-tube trial. In contrast to our greater knowledge on prediction of weaning outcome, our knowledge on prediction of extubation outcome is still rudimentary.

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