Extubation failure: magnitude of the problem, impact on outcomes, and prevention
Robert C. Rothaar, MD, and Scott K. Epstein, MD, FCCP

Extubation failure, defined as the need for reinstitution of ventilatory support within 24 to 72 hours of planned endotracheal tube removal, occurs in 2 to 25% of extubated patients. The pathophysiologic causes of extubation failure include an imbalance between respiratory muscle capacity and work of breathing, upper airway obstruction, excess respiratory secretions, inadequate cough, encephalopathy, and cardiac dysfunction. Compared with patients who tolerate extubation, those who require reintubation have a higher incidence of hospital mortality, increased length of ICU and hospital stay, prolonged duration of mechanical ventilation, higher hospital costs, and an increased need for tracheostomy. Given the lack of proven treatments for extubation failure, clinicians must be aware of the factors that predict extubation outcome to improve clinical decision making. Risk factors for extubation failure include being a medical, multidisciplinary, or pediatric patient; age greater than 70 years; a longer duration of mechanical ventilation; continuous intravenous sedation; and anemia. Tests designed to assess for upper airway obstruction, secretion volume, and the effectiveness of cough can help to improve prediction of extubation failure. Rapid reinstitution of ventilatory support in patients who fail extubation may improve outcome.

Keywords
extubation failure, mechanical ventilation, outcome, noninvasive ventilation, respiratory secretions, upper airway obstruction, predictors

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Complications of invasive mechanical ventilation, such as ventilator-associated pneumonia, tracheal injury, ventilator-associated lung injury, and death, increase with the duration of ventilator dependence [1,2]. Recognition of the time-dependent nature of these complications has led clinicians and investigators to concentrate their efforts on liberating patients from mechanical ventilation as expeditiously as possible. Liberation refers to the rapid or gradual transfer of the work of breathing (WOB) from the machine to the patient (weaning) [3,4]. In contrast, removal of the endotracheal tube (extubation) has, until recently, received little emphasis; rather, it has been viewed as a routine and automatic step at the end of the weaning process. However, extubation is of great importance because failed extubation is associated with increased duration of mechanical ventilation, increased length of ICU stay, greater cost of care, and higher mortality rates [5–7,8•].

Causes of extubation failure
Extubation failure is usually defined as the need for reinstitution of ventilatory support within 24 to 72 hours of planned extubation. This is in contrast to liberation failure, which is the inability to tolerate spontaneous breathing without the support of a ventilator. Despite this, the imbalance between respiratory muscle capacity and load that typically characterizes weaning failure may contribute to extubation failure [9–11]. Weaning failure, which was not present (or not appreciated) before extubation can manifest as extubation failure, especially if the duration of the spontaneous breathing trial (SBT) is too short or when partial support modes of SBT provide too much assistance. As many as 50% of patients with extubation failure may have evidence of hypoxemia or hypercapnia or may show signs of increased WOB [12]. Evidence suggests that the traditional monitoring of a SBT using respiratory rate, oxygen saturation, blood pressure, heart rate, and blood gases is not sufficiently sensitive to detect early signs of load–capacity imbalance [6,13].

A number of other causes of extubation failure have been identified (Table 1), many of which reflect the integrity of the patient’s upper airway. Risk factors for glottic or subglottic narrowing include excessive cuff pressure, traumatic intubation, prolonged duration of intubation, tracheal infection, and female gender. In fact, recent studies suggest that postextubation WOB may equal or actually exceed that seen with T-piece breathing [14].
Table 1. Causes of extubation failure

1. Upper airway obstruction [103,104]
   a. Granulation tissue, inflammation, ulceration, edema
2. Excess respiratory secretions [91••,92,94,95]
3. Inability to protect airway [15,105–109]
4. Cardiac failure or ischemia [110–116]
5. Encephalopathy [50•]
6. Respiratory failure (respiratory muscle load and capacity imbalance) [9,10,81]
7. Other
   a. Gastrointestinal bleeding [37], sepsis [17,37,52], seizures [69], need for surgery [20]

Swallowing dysfunction, with increased risk of aspiration, is common in extubated patients: the incidence exceeds 50% among patients intubated for 48 hours or more [15]. When coupled with ineffective cough, resulting from glottic incompetence, respiratory muscle weakness, or sedative/narcotic administration, efficient clearance of respiratory secretions may fail.

Magnitude of the problem
The prevalence of extubation failure ranges from 2 to 25% depending on the population studied and the time frame (24–72 h) included for analysis [5,6,12,13,16,17]. Medical, pediatric, and multidisciplinary ICU patients have the highest rates of reintubation, whereas, in the absence of comorbid conditions, only 5% of cardiothoracic, general surgical, and trauma patients ultimately require reintubation [7,18–20]. In addition, other factors have been associated with increased risk of extubation failure (Table 2). Recently, ICU physician staffing and nurse-to-patient ratios have been shown to influence reintubation rates in patients with esophageal resection and abdominal aortic surgery [21–25]. In a study of patients undergoing esophageal resection, a night nurse-to-patient ratio of less than 1:2 was associated with an increased risk of reintubation (OR, 2.6; 95% CI, 1.4–4.5) [22]. Similar results were found in patients undergoing abdominal aortic surgery: ICU nurse-to-patient ratios of less than 1:2 were associated with over twice the risk of reintubation (OR, 2.09; 95% CI, 1.47–3.03) [21]. In a study of 2987 patients undergoing abdominal aortic surgery, reintubation was associated with a 20% increase in total hospital costs (95% CI, 10–31%) or an excess annual expense of US $143,650 for hospitals in the upper quartile of extubation failure rates [8••].

Table 2. Factors associated with increased risk of extubation failure

1. Advanced age (>70 y) [5–7,19,61,76]
2. Duration of ventilation before extubation [7,59,76,117]
3. Anemia (hemoglobin <10 g/dL, hematocrit <30%) [91••,118]
4. Severity of illness at the time of extubation [5,6]
5. Semirecumbent positioning after extubation [42]
6. Use of continuous intravenous sedation [119]
7. Need for transportation outside of the ICU [120]
8. Unplanned extubations [121–127]

In determining a patient’s readiness for extubation, the duration of SBT, as well as the mode of ventilation used, could influence reintubation rates. Most investigators use 1- to 2-hour spontaneous (T-piece) breathing trials, whereas others use pressure support or intermittent mandatory ventilation weaning trials lasting 2 [6,26] to 24 hours [17,27–29]. Prospective data are now available both for T-piece and pressure support modes, demonstrating that patients randomized to an initial trial of either 30 minutes’ or 120 minutes’ duration experience no difference in reintubation rates [13,30]. Randomized, controlled clinical trials comparing various combinations of T-piece ventilation, pressure support ventilation, intermittent mandatory ventilation, continuous positive airway pressure, and automatic tube compensation demonstrate no difference in extubation failure rates [6,26,27,31,32].

Impact on outcomes
The outcome for patients who tolerate extubation for a minimum of 24 to 72 hours is generally favorable, with hospital mortality rates below 10 to 15% [5–7,13,16,19,33,34]. In contrast, univariate analyses have shown that the mortality rate associated with extubation failure ranges from 2.5 to 10 times that experienced by successfully extubated patients [5,6,13,16,17,30,34]. Most, but not all, studies using multivariate analysis, adjusting for severity of illness and comorbid conditions, indicate an independent association between extubation failure and mortality [5,6]. In a recent retrospective chart review, Glanemann et al. [35•] used Kaplan-Meier estimates to assess overall patient survival for 5 years after hospital discharge in patients receiving orthotopic liver transplantation with and without an episode of extubation failure. This investigation showed that the mortality difference persisted throughout the 5-year study period. Extubation failure has also been reported to be associated with an increased duration of mechanical ventilation, longer ICU and hospital stays, an increased need for post–acute care hospitalization, and a higher rate of tracheostomy [6,7,36]. In one study of medical ICU patients, reintubation resulted in 12 additional days of mechanical ventilation, 21 additional days in the ICU, and 30 additional days in the hospital [36]. Of those reintubated patients surviving to discharge, two thirds required transfer for post–acute care hospitalization and underwent tracheostomy. The cause of extubation failure is also a determinant of outcome: mortality rates are lowest when reintubation must be performed as a result of upper airway obstruction, aspiration, or excess pulmonary secretions [6,13,20,37].

A number of hypotheses have been generated to explain the association between extubation failure and increased mortality rate. Extubation failure may serve as a surrogate maker for increased severity of illness. Alternatively, the increased mortality rate may be a result of direct
complications of reintubation, clinical deterioration between extubation and reintubation, or the adverse effects of prolonged total duration of mechanical ventilation.

The act of reintubation is clearly associated with numerous life-threatening complications that could translate into increased hospital mortality rates [20,38–40]. Despite this, three studies found no difference in mortality when comparing cohorts with and without complications after reinsertion of the endotracheal tube [6,13,37]. Some studies, such as a recent case-control investigation (n = 20), have suggested an increased incidence of nosocomial pneumonia in patients undergoing reintubation [41–44]. Nosocomial pneumonia is associated with increased hospital mortality rates, but, in a prospective study, de Lassence et al. [45] did not find an increased rate when comparing successfully extubated patients with those requiring reintubation after planned extubation (n = 56).

Delayed reintubation may allow the clinical condition of patients with extubation failure to deteriorate before adequate ventilatory support is reinstated. Indeed, patients requiring reintubation have significantly higher postextubation Simplified Acute Physiology II and Logistic Organ Dysfunction scores compared with scores obtained before extubation [45]. This may explain why delayed time to reintubation is associated with an increased likelihood of death in patients with extubation failure [5,18,26,34,46]. In addition, two studies showed that patients who are reintubated after self-extubation (an event that occurs within 1 hour in 75% of cases) do not have an increased hospital mortality rate [36,45]. In an investigation of reintubated medical patients, increased time to reintubation was an independent predictor of mortality, even after controlling for the origin of extubation failure [37]. Torres et al. [42] noted a lower incidence of pneumonia in patients immediately reintubated compared with patients in whom reintubation was delayed [45]. These observations are significant because they suggest that early reestablishment of mechanical support could prevent deterioration and lead to improved outcomes.

Prevention

Based on the medical literature to date, there are few (if any) interventions that are clearly proven to prevent extubation failure. Therefore, the key to prevention is improved decision making regarding the timing of extubation. The capacity of ICU practitioners, using clinical gestalt alone, to predict weaning or SBT outcome is limited, and their ability to predict extubation outcome has not been assessed [47,48]. Recent investigations have examined purely protocol-directed extubation strategies in an attempt to standardize decision making and improve outcomes, but so far none have been shown to be superior to standard medical care in improving extubation failure rates [49,50–54]. Practicing clinicians must be aware of the factors that predict success and failure to make sound, evidence-based judgments regarding extubation.

The decision to extubate cannot be based solely on routine screening criteria for weaning (eg, adequate oxygenation, hemodynamic stability) because nearly 40% of the patients who meet these criteria require reintubation [55]. Additional information is gained by successful completion of a SBT because 80 to 95% of patients who pass a trial will also tolerate extubation [6,13,17,27,56]. Despite this, routine observation during the SBT, including standard assessments of oxygen saturation, blood pressure, heart rate, and respiratory frequency, may not be sensitive enough to identify patients at increased risk for extubation failure [6,13]. For example, in patients with chronic obstructive pulmonary disease failing extubation, electromyographic evidence of diaphragmatic fatigue was observed, despite the absence of classical signs of intolerance during a 60-minute preextubation SBT [57].

**Prediction of extubation outcome using weaning parameters**

Multiple weaning parameters have been investigated as possible predictors of extubation outcome (Table 3) [34,56,58–64]. In an evidence-based review, Meade et al. [65] concluded that these indices have only limited utility in predicting weaning outcome. Not surprisingly, these parameters are even less accurate predictors of extubation outcome [12,65]. The most accurate and well-studied test is the frequency–tidal volume ratio, but even this parameter rarely leads to moderate or large changes in the probability of success or failure. The capacity of sustained maximal inspiratory pressure (the product of peak inspiratory pressure and maximum sustained inspiratory time) to predict extubation outcome was investigated in 27 general ICU patients [66]. The sustained maximal inspiratory pressure was found to be significantly lower in those who failed extubation, and a threshold value of 57.5 pressure time units perfectly separated the two groups. A limitation of this technique

<table>
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<th>Table 3. Weaning parameters used to predict extubation outcome</th>
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<tr>
<td>1. Negative inspiratory force</td>
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<td>2. Vital capacity</td>
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<td>3. Minute ventilation</td>
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<tr>
<td>4. Respiratory frequency</td>
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<td>5. Tidal volume</td>
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<td>6. Respiratory frequency–tidal volume ratio</td>
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<td>7. Maximal inspiratory pressure, sustained maximal inspiratory pressure</td>
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<td>8. work of breathing</td>
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<td>9. Dead space</td>
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<td>10. Airway occlusion pressure (P&lt;sub&gt;0.1&lt;/sub&gt; or P&lt;sub&gt;100&lt;/sub&gt;)</td>
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<td>11. Gastric intramural pH</td>
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is that it requires patients to be able to follow commands. The effect of measuring parameters at the end of a successful SBT has been recently investigated in pediatric patients and was shown not to increase their predictive value [67].

Work of breathing may be determined by using an esophageal balloon system and by calculating the area under either the pressure–volume curve or pressure–time curve. Levy et al. [68] found that an elevated WOB (>0.8 J/L) was not associated with extubation failure among patients tolerating a SBT, but only one of 24 patients required reintubation. Nevertheless, research has suggested a rationale for using WOB in the decision to extubate patients who do not tolerate a SBT. For example, 90% of tachypneic trauma patients (during a room air continuous positive airway pressure trial) tolerated extubation when either the total WOB was less than 1.1 J/L or the physiologic WOB (total WOB – imposed WOB) was less than or equal to 0.8 J/L [69,70].

Two recent investigations have suggested a possible role for gas exchange measurements in predicting extubation outcome. In one study, a higher gastric–arterial carbon dioxide gradient, determined by gas tonometry, was found in patients who failed extubation [71]. In a pediatric study, extubation failure was associated with an elevated volume of dead space (volume of dead space/tidal volume > 0.65); similar findings have been reported in adults with extubation failure [34].

Airway occlusion pressure measured at 100 milliseconds (P_{100} or P_{0.1}) has been used to assess respiratory drive and to predict extubation outcome [52,72–75]. When corrected for maximal inspiratory pressure, airway occlusion pressure provides a numerical expression of the balance between load and capacity. Several investigators have noted higher airway occlusion pressure values among patients who fail extubation, and the capacity of some ventilators to provide measurement of P_{100} encourages future investigation [57,61,76,77]. Using an innovative approach, Hilbert et al. [78] demonstrated that P_{100} measured immediately after extubation (via face mask in pressure support ventilation mode), could predict which patients with chronic obstructive pulmonary disease subsequently developed postextubation respiratory failure.

Comprehensive analysis of the breathing pattern during SBT may predict extubation failure. A prospective trial of 52 patients undergoing SBT revealed that an irregular breathing pattern was associated with an increased risk of extubation failure when analyzed using the coefficient of variation and Kolmogorov entropy [79•]. Similar findings were noted in a cohort of cardiothoracic surgical patients weaned from mechanical ventilation [80].

Prediction of extubation outcome using parameters that measure the capacity for airway patency

Unlike the decision to proceed with SBT through an endotracheal tube, the decision to extubate is influenced by upper airway patency and the capacity to protect the airway. Upper airway obstruction may increase the WOB after endotracheal tube removal, but assessment of airway patency before tube removal is challenging. The absence of an audible air leak after deflation of the endotracheal tube balloon (qualitative cuff leak test) has been associated with an increased risk of postextubation stridor, but the subjective nature of the test is a limiting factor [81–83]. An objective assessment involves the indirect measurement of the volume of gas escaping around the tube during balloon deflation (quantitative cuff leak test). For example, using the difference between inspiratory and expiratory volume after cuff deflation in assist–control ventilation, a cuff leak of less than 110 mL predicted the development of postextubation stridor [84]. When expressed as a percentage of inspiratory volume, an expiratory gas leak around the endotracheal tube of less than 12 to 16% was predictive of extubation failure, although the positive predictive value can be low (25%) [85]. This is in keeping with other studies that have shown a high rate of false-positive test results [86,87]. When deciding how to manage the patient with a positive cuff leak test result, it must be remembered that effective treatment in adults has not been clearly established. Notably, fewer than 50% of patients with postextubation stridor require reintubation, and those that do have reasonably favorable outcomes [6,13,20,37,88,89]. The results of a meta-analysis of randomized, controlled trials in children showed that routine preextubation corticosteroid administration reduced postextubation stridor but did not clearly reduce reintubation rates [90]. A pooled analysis of three adult studies failed to show a reduction in reintubation, but the low extubation failure rate makes the analysis problematic. To our knowledge, trials focusing on high-risk patients have not been performed.

Prediction of extubation outcome using parameters that measure the capacity for airway protection

The capacity of a patient to protect his or her airway is an integrated function of cough strength, pharyngeal muscle competency, secretion volume, and mental status. The risk of extubation failure is increased with ineffective cough, a propensity for aspiration, abundant secretions, and depressed mental status [50•,61,91••,92]. Effective cough requires adequate expiratory muscle function, as assessed by peak cough flow rates [93] and maximal expiratory pressure [17]. Bach and Saporto [93] studied patients with primarily neuromuscular causes for acute respiratory failure and found that unsuccessful extubation or tracheotomy decannulation was likely with
peak cough flow rates less than 160 L/min. Among patients with a neurologic cause for respiratory failure, maximal expiratory pressure was predictive of extubation outcome [17]. The presence of a strong catheter-stimulated or spontaneous cough [61,92], especially one capable of propelling secretions onto a white index card placed a short distance from the open endotracheal tube, may also predict extubation success [91••].

There are several approaches to determining the volume of respiratory secretions. A sawtooth pattern on the flow-volume curve provides a qualitative indication of the presence of airway secretions [94,95]. When volume is assessed quantitatively, the presence of moderate to abundant secretions increases the risk of extubation failure compared with the presence of no or small amounts of secretions [91••]. One strategy for quantifying secretions is to determine the frequency of airway suctioning. The relative risk of extubation failure increases for patients requiring endotracheal suctioning more frequently than every 2 hours [91••,92].

Brain dysfunction can contribute to extubation failure by impairing the capacity to protect the airway, as well as by causing hypoventilation. Depressed mental status (Glasgow Coma Scale score ≤ 8) has been shown to be a variable predictor of extubation outcome, with two studies in brain-injured patients arriving at conflicting conclusions [50•,92]. Some of the predictive value of certain parameters described previously (eg, sustained maximal inspiratory pressure and the white card test) may be a result of the fact that they require patients to follow instructions, thereby incorporating some degree of mental status evaluation. In summary, the best predictor of extubation success at present is the successful completion of a SBT coupled with an adequate cough, absence of excessive respiratory secretions (eg, airway requires suctioning less frequently than every 2 hours), and a patent upper airway.

Treatment of extubation failure

Treatment of extubation failure can be divided into specific therapies (eg, epinephrine for laryngospasm, diuretics and nitrates for cardiac ischemia and heart failure, helium–oxygen for stridor [96]) and nonspecific therapies (eg, reestablishment of ventilatory support). Therapies may be prophylactic or may be initiated in response to a developing medical condition. None of these have been clearly shown to reduce reintubation rates in a general ICU population. Clinicians may rely overly on medical strategies when treating extubation failure in an attempt to avoid reintubation, an invasive procedure. However, data showing higher mortality rates with delayed reintubation suggest that physicians should not hesitate to reintubate patients who fail to improve with specific treatments.

Studies have had conflicting results regarding the efficacy of noninvasive positive pressure ventilation (NIPPV) when applied to all extubated patients [97,98]. Jiang et al. [97] found that bilevel positive pressure ventilation tended to be less effective than oxygen alone when applied to all extubated patients. This study was notable for the advanced age of the patients (mean age, 73 y) and the inclusion of patients with unplanned extubation. In another study of routine use after extubation, NIPPV was effective in 18 of 20 patients in “preventing” reintubation; however the nearly 40% reintubation rate in the control group raises significant questions about patient selection [98]. Using a different strategy, Carlucci et al. [99] randomized 52 patients at high risk for extubation failure and demonstrated that NIPPV administered for at least 6 hours per day lowered the reintubation rate from 25% to 6% and reduced the ICU mortality rate and hospital length of stay.

Noninvasive positive pressure ventilation has also been investigated as a treatment for more established respiratory distress in the postextubation period. Retrospective and prospective observational studies [100] and one case-control investigation [101] suggest that NIPPV may be effective in 65 to 90% of patients experiencing extubation failure. In the only published randomized, controlled trial, Keenan et al. [102••] found that the initiation of NIPPV once an extubated patient developed overt respiratory distress (respiratory rate > 30 breaths/min or >50% increase from baseline, use of accessory muscles of respiration or abdominal paradox) had no positive effect on outcomes such as need for reintubation, mortality, duration of mechanical ventilation, and length of ICU stay. Therefore, for noninvasive ventilatory support to be beneficial in patients with extubation failure, very early initiation may be necessary.

Conclusions

Extubation failure occurs commonly among mechanically ventilated patients and is associated with adverse outcomes. Recent scientific literature shows that prediction of extubation outcome is best achieved by assessing a patient’s tolerance of a SBT and by careful evaluation of upper airway patency and the adequacy of airway-protective mechanisms. Rapid re-institution of ventilatory support appears to improve outcome for patients with evidence of extubation failure. The role of noninvasive ventilation in extubation failure remains to be elucidated.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

• Of special interest

•• Of outstanding interest

1 Fagon JY, Chastre J, Domart Y, et al.: Nosocomial pneumonia in patients receiving continuous mechanical ventilation. Prospective analysis of 52 epi-


In this study, the investigators retrospectively reviewed 2987 patients’ status after abdominal aortic surgery to investigate interhospital variability in complication rates, including the need for reintubation. Hospital-to-hospital variation in reintubation rate was high (7% in hospitals in the lowest quartile vs 18% in hospitals in the highest quartile), and average cost per extubation failure was estimated to be US $9510 (in 1996).


The medical records of 546 adult liver transplant recipients were reviewed to analyze the incidence and indications for reintubation. The incidence of reintubation was 14.2% and was associated with a significantly higher mortality rate at 1, 2, 3, and 5 years. Indications for reintubation included pulmonary complications (44.6%), cerebral complications (19.1%), and surgical complications (14.9%).


A retrospective, case-control study of 20 surgical patients who required reintubation within 72 hours of planned extubation is reported. Analysis revealed no difference in mortality rate between patients and control subjects; however, patients had a longer ICU stay and a higher incidence of nosocomial pneumonia and tracheostomy. Multivariate analysis identified only volume control ventilation on the morning of extubation as an independent predictor of reintubation.


In this study, the investigators analyzed 105 patients from a prospectively collected database who experienced at least one episode of unplanned extubation (acciden-
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50 Namen AM, Ely EW, Tatter SB, et al.: Predictors of successful extubation in neonatal patients, Am J Respir Crit Care Med 2001, 163:658–664. One hundred neonatal surgeon were randomized to a respiratory therapist-driven weaning protocol, including daily screens and SBTs, or standard therapy. No difference in duration of mechanical ventilation or outcome was discovered. Multivariate analysis showed that Glasgow Coma Scale score and partial pressure of oxygen/fraction of inspired oxygen were associated with extubation success.


50 Fifty-two intubated patients deemed ready for extubation underwent continuous positive airway pressure trials with computerized respiratory profile monitoring and continuous measurement of respiratory parameters. The coefficients of variation of the spontaneous tidal volume, spontaneous peak inspiratory flow, Kmolgorov entropy, and the duration of the spontaneous breathing pattern were all significantly lower (P<0.08) in the successfully extubated group (n=39).


Respiratory system

who had completed a SBT and were ready to be extubated. Age, severity of illness, duration of mechanical ventilation, oxygenation, rapid shallow breathing index, and vital signs during SBT did not differ among those successfully extubated versus those who failed extubation. Weak cough, negative white card test result, anemia, and abundant respiratory secretions were associated with an increased likelihood of extubation failure.


Eighty-one ICU patients who developed respiratory distress within 48 hours of extubation were randomized to receive noninvasive positive pressure ventilation versus standard medical therapy. The investigators found no difference between groups in rates of reintubation, hospital mortality, duration of mechanical ventilation, or length of ICU or hospital stay.


