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REVIEW

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Decision to extubate

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Abstract The need for reintubation within 24–72 h of planned extubation is a common event, occurring in 2–25% of extubated patients. Risk factors for extubation failure include being a medical, multidisciplinary or paediatric patient; age >70 years; a longer duration of mechanical ventilation; use of continuous intravenous sedation; and anaemia (haemoglobin <10 g/dl or haematocrit <30%) at the time of extubation. The pathophysiology of extubation failure can be distinct from that seen with weaning failure and includes upper airway obstruction, inadequate cough, excess respiratory secretions, encephalopathy, and cardiac dysfunction. Extubation failure prolongs the duration of mechanical ventilation, increases the length of ICU and hospital stay, increases the need for tracheostomy, and is associated with a higher hospital mortality. Great emphasis has been placed on accurately predicting extubation outcome because extubation delay is also associated with increased length of stay and mortality. Tests designed to assess for upper airway obstruction, secretion volume, and the effectiveness of cough seem most promising for improving the decision to extubate. Mortality increases with delays in reintubation for patients failing extubation. Timely identification of patients at elevated risk of extubation failure followed by rapid re-establishment of ventilatory support can improve outcome.

Keywords Extubation failure · Mechanical ventilation · Outcome · Non-invasive ventilation · Respiratory secretions · Upper airway obstruction · Predictors

Introduction

Invasive mechanical ventilation can effectively support the patient with acute respiratory failure. Recognition of the time-dependent nature of complications associated with invasive ventilatory support led investigators to concentrate efforts on removing the patient from mechanical ventilation as expeditiously as possible [1, 2]. The first phase of this process, termed weaning or liberation, has received much attention [3, 4]. Investigators have focused on determining patient readiness for weaning, methods for conducting spontaneous breathing trials, the optimal strategy of progressive withdrawal of support, and elucidating the causes for weaning failure [5, 6, 7, 8]. Once ventilatory support is deemed no longer necessary, the clinician must then decide whether or not the patient can tolerate removal of the endotracheal tube (extubation). This "decision to extubate" is of considerable consequence as both delayed extubation and failed extubation are associated with increased duration of mechanical ventilation and increased mortality. Developing predictive tools and optimizing extubation decisions require knowledge of the risk factors for, and causes of, extubation failure.

Risk factors for extubation failure

The prevalence of extubation failure (usually defined as the need for reintubation) occurring within 24–72 h of planned extubation ranges from 2–25%, with medical, paediatric, and multidisciplinary ICU patients at highest risk [9, 10, 11, 12, 13, 14]. In general, only 5% of cardiothoracic, general surgical, and trauma patients ultimately require reintubation [15, 16, 17, 18]; though the rate rises substantially when co-morbid conditions (e.g., COPD) are present [19]. The importance of cause of respiratory failure has varied between studies, though some investigators find neurologically impaired patients to be at greatest risk, with reintubation rates as high as 36% [14, 20, 21]. Other factors are associated with a higher prevalence of extubation failure include older age (>70 years) [9, 11, 16, 18, 22, 23], duration of ventilation prior to extubation [18, 23, 24, 25], anaemia (Hb <10 g/dl or haematocrit <30%) [26, 27], severity of illness at the time of extubation [9, 11], semi-recumbent positioning after extubation [28], use of continuous intravenous sedation [29], and the need for transport out of the ICU [30]. ICU physician staffing and nurse-to-patient ratios also influenced reintubation rates in patients with oesophageal resection or abdominal aortic surgery [31, 32, 33].

Planned extubation typically follows completion of a successful spontaneous breathing trial (SBT), the mode and duration of which could influence extubation outcome. For example, partial support modes (e.g., CPAP, pressure support) may over-assist the patient leading to extubation in a patient not yet ready to fully sustain unassisted breathing. In addition, when work imposed by the endotracheal tube or ventilatory circuit is substantial, the pressure support ventilation (PSV) level required to offset the additional load ranges widely and may be difficult to predict [34]. However, studies directly comparing T-piece to CPAP [35] or T-piece to PSV (7–10 cmH_2O) [11, 13] found no difference in 48-h reintubation rates. In addition, randomized controlled trials of different modes of progressive withdrawal (e.g., T-piece, pressure support, SIMV) observed no significant differences in rates of extubation failure [5, 7]. Protocol-directed weaning appears not to influence extubation failure; five studies showed no difference compared to controls [36, 37, 38, 39, 40], one study noted a trend toward a higher reintubation rate [41], while another study observed a lower prevalence of extubation failure among patients managed with a protocol [6].

The duration of the pre-extubation SBT is potentially important as too brief a trial can result in premature removal of the endotracheal tube and the need for subsequent reintubation [42]. On the other hand, if the work imposed by the ventilator circuit and endotracheal tube is high, too long a trial may result in failure to tolerate the SBT (e.g., iatrogenic weaning failure) [43]. In one randomized, prospective investigation, Esteban et al. found no difference in extubation failure when comparing patients undergoing 30- vs 120-min T-piece trials [12]. In another study, none of 30 patients capable of tolerating a 6-h T-piece trial required reintubation [44].

Causes of extubation failure

The distinction between weaning or liberation failure (inability to tolerate spontaneous breathing without ventilatory support) and extubation failure (inability to tolerate removal of the translaryngeal tube) has been increasingly recognized. Nevertheless, the respiratory muscle capacity and load imbalance that frequently characterizes weaning failure may also lead to extubation failure [8, 44, 45]. For example, up to 50% of patients with extubation failure have evidence of hypercapnia or hypoxaemia, or demonstrate signs of an increased work of breathing [10]. This can occur when the SBT duration is too short or when partial support provides over-assistance. Alternatively, the traditional monitoring of a SBT (e.g., respiratory rate, oxygen saturation, blood pressure, heart rate, and blood gases) may be too insensitive to detect early signs of load-capacity imbalance [11, 12]. In one study of patients with COPD who failed extubation, electromyographic evidence of diaphragmatic fatigue was observed despite the absence of classical signs of intolerance during a 60-min trial of spontaneous breathing [46]. El-Khatib et al. investigated the breathing pattern during CPAP by measuring the breath-to-breath variability in peak flow rate and tidal volume using the coefficient of variation and by computing the Kolmogorov entropy [47]. Patients who failed extubation demonstrated a more chaotic and irregular breathing pattern than patients who tolerated extubation. These studies demonstrate that an imbalance between respiratory load and capacity may not always be detected using standard assessment techniques during a 2-h trial of spontaneous breathing. Under these conditions, weaning failure may manifest as extubation failure.

A similar phenomenon may exist with cardiac disease; investigators have demonstrated an association between cardiac dysfunction and weaning failure. Cardiac ischaemia, manifested as electrocardiographic changes or thallium scanning defects [48, 49, 50, 51], can occur during T-piece trials, as can left ventricular dysfunction without ischaemia [52]. Among surgical patients recovering from anaesthesia, extubation can be associated with ischaemia [53], possibly related to increased catecholamine levels [54]. In a study of COPD patients with cardiac disease, Lemaire et al. observed a dramatic increase in transmural pulmonary artery occlusion pressure when patients were removed from ventilatory support and placed on a T-piece (i.e., negative intrathoracic pressure) [55]. Indeed, cardiac-related extubation failure appears more likely to occur when a partial support mode

is used to determine readiness for extubation [10]. Positive pressure unloads the heart and may result in improved left ventricular systolic function compared to extubated breathing. When a T-piece is used the unfavorable loading effects of negative intrathoracic pressure occur *prior* to extubation: these haemodynamic effects only become manifest *after* extubation in those breathing on partial support modes.

Extubation failure, as distinct from weaning failure, can occur secondary to upper airway obstruction or to an inability to manage respiratory secretions, factors that are recognized only after the endotracheal tube has been removed. Glottic or subglottic narrowing may result from laryngotracheal trauma and can take the form of inflammation, granuloma formation, ulceration, or oedema [56, 57]. The risk for such injury increases with the duration of intubation, overly large or excessively mobile endotracheal tubes, excess cuff pressure, tracheal infection, and female gender [58, 59, 60]. Indeed, several recent studies have found that the work of breathing after extubation may equal or exceed that observed with a T-piece [61, 62, 63, 64].

Efficient clearance of respiratory secretions depends on a number of factors including adequate laryngeal function, expiratory muscle function, and effective cough. Laryngeal dysfunction can result from the presence of the nasogastric tube, depressed mental status, or the adverse effects of sedative/hypnotic and narcotic agents. These medications can further negatively impact upper airway protective mechanisms by leading to a depressed mental status. Swallowing dysfunction and increased risk for aspiration is common in extubated patients. Approximately one-third of patients ventilated for 18 h or more manifest defective airway protective mechanisms [65]. The incidence of swallowing dysfunction increases with more prolonged duration of ventilation and may take a week or more to resolve [66, 67, 68, 69, 70]. In one study, using fibreoptic endoscopic airway assessment within 48 h of extubation, swallowing dysfunction was present in 56% of patients ventilated for a minimum of 48 h [68].

Ineffective cough can result from glottic incompetence, expiratory muscle dysfunction [14, 71], inspiratory muscle weakness [72], tracheomalacia, and narcotic administration. Increased airway secretions can occur secondary to endotracheal tube irritation, non-infectious airway inflammation, lower or upper respiratory tract infection, or aspirated secretions originating from the naso- or oropharynx. Secretions from these latter sources can accumulate between the glottis and the balloon of the endotracheal tube and be difficult to adequately suction.

Outcome

The outcome for patients who tolerate extubation for a minimum of 24–72 h is generally favorable, with hospital mortality rates below 10–15% [9, 11, 12, 13, 16, 18, 73, 74]. In contrast, ICU and hospital mortality is markedly higher among patients who require reintubation within 24–72 h after extubation. The highest rates (up to 50%) have been reported in general surgical, medical, multidisciplinary, and paediatric ICUs, [9, 11, 12, 13, 14, 15, 25, 28, 73, 74, 75] while lower rates are observed in trauma and cardiothoracic patients (~10%) [15, 16, 18]. Extubation failure also prolongs the duration of mechanical ventilation, length of ICU and hospital stay, need for post-acute care hospitalization, and the need for tracheostomy [9, 11, 18]. In one study of medical ICU patients, reintubation resulted in 12 additional days on mechanical ventilation, 21 additional days in the ICU, and 30 additional days in hospital [9]. Of survivors, two-thirds required transfer for post-acute care hospitalization and the need for tracheostomy increased compared to patients not experiencing reintubation (18% vs 4%).

A number of hypotheses have been generated to explain the association of extubation failure and increased mortality. These include an increased severity of illness, direct complications of reintubation, and clinical deterioration between extubation and reintubation. Poor outcome could also result from the adverse effects of prolonged mechanical ventilation. An increased duration of mechanical ventilation has been associated with excess mortality, but the relationship is controversial, and studies specifically controlling for extubation failure are not available [76]. Alternatively, extubation failure may not cause excess mortality, rather it may serve as a marker for a worse outcome.

Although reintubated patients have a greater severity of illness, chronic co-morbid conditions, and are older than those successfully extubated, extubation failure is an independent predictor of hospital mortality in studies of medical or multidisciplinary ICU patients [9, 11]. Extubation failure was associated with an increased duration of mechanical ventilation, ICU and hospital stay, but not mortality in one multivariate analysis of cardiac surgical patients [18]. On the other hand, reintubation was an independent predictor of mortality in a cohort of patients ventilated for at least 48 h after coronary artery bypass surgery [77]. With multivariate analysis, reintubation is also associated with increased mortality in patients after abdominal aortic surgery [33].

The act of reintubation (often an emergency procedure) is associated with numerous life-threatening complications that could translate into excess hospital mortality [17, 78, 79, 80]. Reintubation increases the risk for nosocomial pneumonia, an entity which contributes to excess hospital mortality [28, 81, 82]. Although mortality may be directly attributable to the act of reintubation in some patients, three studies found no significant difference in mortality when comparing patient cohorts with and without complications after reinsertion of the endotracheal tube [11, 12, 83].

Table 1 Relationship between hospital mortality and time between extubation and reintubation

Author, year	Setting	Time from extubation to reintubation (h)	Mortality (%)
Tahvanainen et al. 1983 [74]	Respiratory ICU	0–12	17
		13–24	33
Demling et al. 1988 [15]	Surgical ICU	0–12	10
		13–24	25
		>24	45
Epstein et al. 1998 [9]	Medical ICU	0–12	24
		13–24	39
		25–48	50
		49–72	69
Esteban et al. 1999 [7]	Multidisciplinary ICU	0–12	28
		13–24	54
		25–48	48
Tanios et al. 2000 [85]	Medical ICU	0–24	11
		25–48	50

An intriguing hypothesis is that delayed reintubation may allow patients with extubation failure to deteriorate before adequate ventilatory support is ensured, and thereby contribute to decreased survival. Farias et al. noted a lower ICU and hospital mortality for infants who failed a SBT compared to those who passed the SBT but failed extubation [13]. The concept is important because it implies that early re-establishment of mechanical support could prevent deterioration and lead to improved outcome. For example, Torres and coworkers noted a lower incidence of pneumonia in patients immediately reintubated compared to patients with delayed reintubation [28]. Similarly, patients reintubated after unplanned (self) extubation (an event that occurs within 1 h in 75% of cases) do not experience excess hospital mortality [84]. A number of studies have found that delayed time to reintubation is associated with increased mortality in patients with extubation failure (Table 1). In one study of reintubated medical patients, an increased time to reintubation was an independent predictor of mortality even after controlling for the aetiology of extubation failure [83]. The latter observation is important because mortality for patients reintubated because of upper airway obstruction or excess respiratory secretions is lower than that for patients with other aetiologies of extubation failure [11, 12, 17, 83]. In a prospective follow-up study, these authors found that a reduced median time to reintubation (from 21 h in historic controls to 6 h) was associated with a lower hospital mortality (from 43% in historic controls to 20%) [85]. Furthermore, Carlucci et al. recently found that early use of non-invasive ventilation in patients at increased risk for extubation failure resulted in lower reintubation rates and a lower ICU mortality [86].

Given the poor outcome associated with extubation failure, what is the optimal extubation failure rate? The answer is complex as Coplin and coworkers demonstrated that brain-injured patients with delayed extubation were at increased risk of pneumonia, experienced longer ICU stays, and had higher hospital mortality compared to patients with timely extubation [87]. Using a decision analytic model to address these competing risks of reintubation and extubation delay, Cardinal et al. could identify no fixed acceptable rate of extubation failure [88]. The decision to extubate, after tolerating a spontaneous breathing trial, was most strongly influenced by the rate of improvement in the patient's condition, i.e., a daily increase in the probability of successful extubation. For example, continued mechanical ventilation for another 1–2 days was preferable when a patient with a probability of extubation failure greater than 5% was rapidly improving. In other words, the benefit of an increasing likelihood of extubation success outweighed the risk of an additional 48 h of invasive ventilation. This might occur in a patient with abundant purulent secretions who had just been initiated on antibiotics. On the other hand, even with a high probability of extubation failure, removal of the endotracheal tube was recommended for patients who had little or no chance of further improvement.

Prediction of extubation outcome

The complexity of the decision to extubate, simultaneously weighing the substantial risks associated with both extubation delay and extubation failure, provides a strong rationale for developing accurate predictors of extubation outcome (Table 2). In addition, patients predicted to be at very low risk of reintubation would require a shorter period of ICU observation post-extubation. With an elevated (though not prohibitive) risk of reintubation, a longer period of ICU monitoring would be indicated to rapidly detect post-extubation respiratory failure, and enable expeditious re-establishment of ventilatory support. Indeed, recent preliminary data suggest that this cohort may benefit from early institution of non-invasive ventilation [86].

The capacity of ICU practitioners to predict weaning or spontaneous breathing trial outcome is limited [89, 90]. To date, the ability of clinicians to predict extubation outcome has not been assessed. The decision to extubate cannot be based solely on routine screening criteria for weaning (e.g., adequate oxygenation, haemodynamic stability), as nearly 40% of these patients require reintubation [42]. Additional information is gained by successful completion of an SBT as 80–95% of patients passing the trial will also tolerate extubation [5, 11, 12,14, 91]. Routine observation during the SBT, including standard assessments of oxygen saturation, blood pressure, heart rate, and respiratory frequency, do not ap-

Table 2 Parameters used to predict extubation outcome

Weaning parameters
1. Vital capacity
2. Minute ventilation
3. Negative inspiratory force
4. Maximal inspiratory pressure
5. Respiratory frequency, tidal volume, frequency-tidal volume ratio
Parameters requiring specialized technology
1. Airway occlusion pressure
2. Work of breathing
3. Dead space
4. Gastric tonometry (pHi, $PgCO_2$, $PgCO_2$-$PaCO_2$)
5. Diaphragmatic electromyography
6. Breathing pattern (coefficient of variation, entropy)
Parameters that assess airway patency and protection
1. Maximal expiratory pressure
2. Peak expiratory flow rate
3. Cough strength
4. Secretion volume
5. White card test
6. Suctioning frequency
7. Cuff leak test (qualitative, quantitative)
8. Neurological function (Glasgow Coma Scale)

pear to identify patients at increased risk of extubation failure [11, 12].

Weaning parameters

In seeking to improve the prediction of extubation outcome, and taking into consideration the pathophysiological basis for weaning failure, investigators have studied a large group of weaning parameters such as negative inspiratory force, vital capacity, minute ventilation, respiratory rate, tidal volume, and the frequency-tidal volume ratio. A recent evidence-based medicine review of weaning parameters concluded that these predictors had only limited utility in predicting weaning outcome [92]. Not surprisingly, because of the distinct pathophysiological basis for extubation failure, these parameters (when measured prior to a SBT) were also poor predictors of extubation outcome in adults [10, 92]. Indeed, a positive test (e.g., a frequency-tidal volume ratio <105 breaths·l·min) adds little to decision-making as the successful completion of a SBT itself indicates a probability of extubation success exceeding 80%. The probability of extubation success after a successful SBT also remains high (negative predictive values <0.50) despite the presence of a negative test (e.g., a frequency-tidal volume ratio >105 breaths·l·min) [10]. In some paediatric series, weaning parameters have appeared more promising but their predictive value for extubation outcome still remains uncertain [91, 93, 94, 95, 96]. The effect of measuring parameters at the *end* of a successful SBT on prediction of extubation outcome has not been adequately investigated.

Parameters requiring specialized technology

Several studies have noted higher values for airway occlusion pressure ($P_{0.1}$) or P_{100} (a measure of respiratory drive), especially when normalized for the maximal inspiratory pressure (MIP), among patients who fail extubation [22, 23, 46]. In a prospective study, Capdevila et al. measured $P_{0.1}$/MIP after 20 min of T-piece breathing and found that patients with extubation failure had substantially higher values; using a threshold value of 0.09 the positive and negative predictive values were 1.00 and 0.92, respectively [22]. Although Hilbert et al. found no differences in pre-extubation $P_{0.1}$, these investigators found higher values 90 min *after* extubation (measured during full-face mask pressure support) in COPD patients who ultimately required reintubation [97]. The capacity of some ventilators to provide online measurement of $P_{0.1}$ encourages future investigation [98].

Two recent investigations have suggested a possible role for gas exchange measurements in predicting extubation outcome. In one study, a higher gastric-arterial CO_2 gradient determined using gas tonometry was found in patients who failed extubation [99]. In a paediatric study, an elevated dead space (V_D/V_T >0.65) was associated with an increased need for reintubation [100]; similar findings were reported in an older study of adults with extubation failure [74].

Work of breathing (WOB) may be determined using an oesophageal balloon system and calculating the area under either the pressure-volume or the pressure-time curve. Levy et al. found that an elevated work of breathing (>0.8 J/l) was not associated with extubation failure among patients tolerating a trial of spontaneous breathing [101]. The study design was limited because only one of 24 patients required reintubation and the influence of imposed WOB was not taken into account. This latter factor may provide a rationale for using WOB in the decision to extubate patients *not* tolerating SBTs. As an example, 90% of tachypnoeic trauma patients (during a room-air CPAP trial) tolerated extubation when either the total WOB was ≤1.1 J/l or the physiological WOB (total WOB minus imposed WOB) was ≤0.8 J/l [102, 103].

More sophisticated analysis of the breathing pattern during a spontaneous breathing trial may yield important information about the likelihood of extubation success. As an example, electromyographic evidence of diaphragmatic fatigue was present in a small cohort of COPD patients who tolerated a T-piece trial but required reintubation [46]. Similarly, extubation failure patients demonstrated an irregular breathing pattern when pre-extubation spontaneous breathing was analyzed using the coef-

ficient of variation and the Kolmogorov entropy [47]. Similar findings were noted in a cohort of cardiothoracic surgical patients weaning from mechanical ventilation [104].

Parameters that assess upper airway patency and the capacity for airway protection

Unlike the decision to allow a patient to breathe spontaneously through an artificial airway, the decision to extubate is influenced by assessment of upper airway patency and the capacity to protect that airway. Upper airway obstruction increases the resistive work of breathing after endotracheal tube removal, often resulting in extubation failure. Assessment of airway patency prior to tube removal is challenging. 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 post-extubation stridor [105, 106, 107], but the subjective nature of the test is a limiting factor. Another approach is indirect measurement of the volume of gas escaping around the tube during balloon deflation. Miller and Cole determined this quantitative cuff leak in medical patients by calculating the average difference (during six consecutive breaths) between inspiratory and expiratory volume (after balloon deflation) while the patient breathed on assist control ventilation [108]. When the cuff leak volume was less than 110 ml, the risk for post-extubation stridor was significantly elevated, though only half the patients required reintubation. Using a similar technique in trauma patients, a cuff leak less than 10% of the delivered tidal volume identified an increased risk for post-extubation stridor and subsequent need for reintubation [109]. In contrast to these two investigations, none of 20 postoperative cardiothoracic surgery patients with a positive cuff leak test (<110 ml) developed stridor [110]. These false positive test results can result from secretions adhering to the outside of the tube, or from a spuriously elevated exhaled tidal volume due to a higher than expected inspiratory tidal volume. The latter may occur when the patient augments machine-delivered tidal volumes with spontaneous gas inspired around the tube when the balloon is deflated. In deciding how to manage the patient with a positive cuff leak test it must be remembered that effective treatment in adults has not been clearly defined, fewer than 50% of patients with post-extubation stridor require reintubation, and those that do have reasonably favorable outcomes [11, 12, 17, 58, 59, 83]. Nevertheless, when extubating the patient with a positive cuff leak test, it is recommended to have an expert in airway management immediately available.

The decision to extubate is heavily influenced by the capacity of the patient to protect their airway; an integrated function of cough strength, pharyngeal muscle competency, secretion volume, and mental status. Extubation failure is likely to occur when cough is ineffective, a propensity for aspiration is present, secretions are abundant, and encephalopathy is present [20, 22, 26, 87].

Expiratory muscle function is crucial for effective cough; investigators have examined the former by assessing either peak cough flow rates [71] or maximal expiratory pressure (MEP) [14]. In 49 patients with primarily neuromuscular causes for acute respiratory failure, unsuccessful extubation or decannulation was likely if peak cough flow rates (unassisted or assisted with an abdominal thrust) were less than 160 l/min [71]. Vallverdu et al. [14] observed that MEP, determined using a unidirectional valve and a 25- to 30-s expiratory port occlusion, was predictive of extubation outcome among patients with a neurological cause for acute respiratory failure. The presence of a strong catheter-stimulated or spontaneous cough [22, 87], especially one capable of propelling secretions onto a white index card placed a short distance from the open endotracheal tube, was predictive of extubation success [26].

There are several approaches to assessing the burden of respiratory secretions. A “sawtooth” pattern on the flow-volume curve indicates the presence of airway secretions though it gives no insight into the volume [111, 112]. When volume is assessed, the presence of moderate or abundant secretions increases the relative risk of reintubation compared to patients with no or small amounts of secretions [26]. One strategy for quantifying secretion volume 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 h [26, 87].

Brain dysfunction can contribute to extubation failure by causing hypoventilation or by decreasing the patient’s capacity to protect the airway. A study of neurosurgical patients found that a Glasgow Coma Scale (GCS) score less than 8 was associated with an increased likelihood of extubation failure [20]. In contrast, a study of brain-injured patients found no relationship between extubation failure and GCS; indeed, 39 of 49 patients with GCS≤8 and ten of 11 patients with a GCS≤4 tolerated extubation [87]. Explanations for the divergent findings of these studies include differences in patient populations, the weaning techniques used, and uncertainty as to how the GCS was used in the decision to extubate. Neither study used a strict time frame for defining extubation failure (e.g., reintubation within 48–72 h of extubation). In the Namen study, 50% of unsuccessful extubations occurred in patients who were not reintubated; rather these patients had their care limited based on a designation of “do not resuscitate” [20].

Because of the complexity of airway assessment, investigators have applied a composite scoring approach. Coplin and coworkers developed a six-part, semi-quanti-

Table 3 Selected studies examining non-invasive ventilation (NIV) for treatment of extubation failure. (*NIPSV* non-invasive pressure support ventilation, *RCT* randomized controlled trial, *COPD* chronic obstructive pulmonary disease)

Author, year	Study design	NIV	Success in preventing reintubation
Chiang and Lee 1995 [118]	Prospective, observational	Bi-level	11/19 (58%)
Meduri et al. 1996 [119]	Retrospective, observational	NIPSV	26/39 (65%)
Munshi et al. 1999 [120]	Prospective, observational	Mask or nasal, CPAP or bi-level	52/72 (72%)
Kindgen-Milles et al. 2000 [122]	Prospective, observational	CPAP	18/20 (90%)
Hilbert et al. 1996 [123]	Case (historic) control, COPD with hypercapnic failure post-extubation	NIPSV vs standard care	24/30 (80%) 10/30 (33%)
Jiang et al. 1999 [128]	RCT, all extubated patients	Nasal bi-level vs Oxygen	34/47(72%) 39/46 (85%)
Keenan et al. 2000 [129]	RCT, respiratory failure post-extubation	Bi-level vs standard care	10/36 (28%) 12/39 (31%)
Rosinha et al. 2000 [130]	RCT, all planned extubations	Nasal bi-level vs Oxygen	19/20 (95%) 11/18 (61%)
Carlucci et al. 2001 [86]	RCT, extubated patients at high risk for extubation failure	NIPSV vs Standard care	22/24 (92%) 21/28 (75%)

tative Airway Care Score (ACS) consisting of an assessment of spontaneous cough, gag, sputum character, sputum viscosity, sputum quality, and suctioning frequency [87]. Although the ACS measured on the day of extubation was not predictive, two components (suction frequency and spontaneous cough) measured earlier in the patient's course did predict extubation outcome in a cohort of brain-injured patients. Importantly, Khamiees et al. [26] found the combination of weak cough *and* moderate to abundant secretion volume was highly predictive of extubation failure in a group of medical patients.

In summary, the best predictors of extubation success are successful completion of a spontaneous breathing trial coupled with an adequate cough, absence of excessive respiratory secretions (e.g., airway requires suctioning less frequently than every 2 h), and a patent upper airway.

Treatment of extubation failure

A major factor in the decision to extubate is consideration of the effectiveness of treatment for extubation failure. When effective therapy for extubation failure does not exist, direct extubation may not be feasible. For example, in a patient unable to protect the airway, and not expected to improve in the near future, the best approach is likely to be tracheotomy. Unfortunately, there are no randomized, controlled trials delineating the appropriate indications or timing for tracheotomy. Randomized, controlled trials of early versus late tracheotomy (performed predominantly in trauma patients) have been methodologically flawed and are inconclusive in their results [113]. Conversely, when highly effective therapy for extubation failure is readily available, clinicians may be more aggressive in deciding to extubate. Treatment for extubation failure can be divided into specific therapy (aimed at the proximate cause for failure, e.g., racemic epinephrine for laryngospasm; diuretics and nitroglycerin for cardiac ischemia and heart failure) and non-specific therapy (e.g., re-establishment of ventilatory support). The invasive nature of reintubation may lead clinicians to overly rely upon medical strategies when treating extubation failure. Yet, data showing higher mortality with longer time to reintubation suggests that clinicians should rapidly assess the response to specific therapy and not hesitate in reintubating patients failing to improve.

With the above considerations in mind, a strategy of using non-invasive ventilation (usually delivered via a full-face mask) in patients failing extubation has received increasing attention (Table 3). An advantage of this technique is the potential for early application at the first sign of respiratory distress or deterioration. Several studies, including two randomized controlled investigations in primarily COPD patients, indicate that NIV can be used to facilitate weaning from mechanical ventilation [114, 115, 116]. A number of uncontrolled series suggested that NIV could prevent the need for reintubation in approximately two-thirds of patients experiencing extubation failure [117, 118, 119, 120, 121, 122]. In the largest observational report, Meduri et al. observed that NIV was effective in 26 of 39 patients (17 with COPD) with hypercapnic respiratory failure after extubation [119]. A case control investigation of 30 COPD patients with post-extubation hypercapnic failure, found that non-invasive pressure support reduced the need for reintubation when compared to carefully matched historic con-

trols [123]. A combination of non-invasive ventilation (NIV) and Heliox may be effective primary therapy for acute exacerbations of COPD [124, 125]. A study in patients without COPD demonstrated that post-extubation administration of Heliox decreases inspiratory effort and improves patient comfort when compared to a standard nitrogen-oxygen mixture [126]. Whether Heliox or Heliox-NIV can prevent extubation failure remains to be determined.

A meta-analysis found that post-extubation nasal CPAP was effective in preventing extubation failure in pre-term infants [127]. Four randomized controlled trials of NIV to prevent or treat extubation failure in adults have been reported, three in only preliminary form [86, 128, 129, 130]. In the one published investigation, bi-level positive pressure ventilation tended to be less effective than oxygen alone when applied to *all* extubated patients [128]. This study was notable for the advanced age of the patients (mean 73 years) and the inclusion of patients with unplanned extubation. In another study of routine NIV use after extubation, non-invasive ventilation was effective in 18 of 20 patients in "preventing" reintubation; however, the nearly 40% reintubation rate in the control patients raises significant questions about patient selection [130]. On the other hand, Keenan et al. found that NIV did not prevent the need for reintubation when used in a cohort of patients with more established extubation failure (overall rate of reintubation 70%) [129]. Using a different strategy, Carlucci and coworkers randomized 52 patients at high risk for extubation failure and demonstrated that NIV (administered for at least 6 h/day) lowered the reintubation rate (from 25% to 6%), ICU mortality (from 18% to 0%), and hospital length of stay (from 33 days to 21 days) [86].

Conclusion

In summary, extubation failure is a common event among patients intubated for acute respiratory failure, with important effects on duration of mechanical ventilation, length of ICU and hospital stay, need for tracheostomy, and hospital mortality. Delayed extubation is also associated with poor outcome, emphasizing the importance of accurate prediction of extubation outcome. Parameters designed to detect upper airway patency, burden of respiratory secretions, and efficacy of airway clearance mechanisms show promise as valuable predictors of extubation outcome. Delay in re-establishing effective ventilatory support in patients with post-extubation respiratory failure is associated with an increased mortality. Improved outcome may therefore result from rapid identification of patients at increased risk, followed by timely re-institution of ventilatory support when extubation failure occurs.

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