The Decision to Extubate in the Intensive Care Unit

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The day of extubation is a critical time during an intensive care unit (ICU) stay. Extubation is usually decided after a weaning readiness test involving spontaneous breathing on a T-piece or low levels of ventilatory assist. Extubation failure occurs in 10 to 20% of patients and is associated with extremely poor outcomes, including high mortality rates of 25 to 50%. There is some evidence that extubation failure can directly worsen patient outcomes independently of underlying illness severity. Understanding the pathophysiology of weaning tests is essential given their central role in extubation decisions, yet few studies have investigated this point. Because extubation failure is relatively uncommon, randomized controlled trials on weaning are underpowered to address this issue. Moreover, most studies evaluated patients at low risk for extubation failure, whose reintubation rates were about 10 to 15%, whereas several studies identified high-risk patients with extubation failure rates exceeding 25 or 30%. Strategies for identifying patients at high risk for extubation failure are essential to improve the management of weaning and extubation. Two preventive measures may prove beneficial, although their exact role needs confirmation: one is noninvasive ventilation after extubation in high-risk or hypercapnic patients, and the other is steroid administration several hours before extubation. These measures might help to prevent postextubation respiratory distress in selected patient subgroups.

Keywords: laryngeal injury; weaning; noninvasive ventilation; organ dysfunction; endotracheal tube

The day of extubation is a critical time during the intensive care unit (ICU) stay in all patients surviving an episode of mechanical ventilation. Although extubation is generally uneventful after anesthesia, it is followed by a new episode of respiratory failure in a substantial number of ICU patients. Very different clinical approaches have been used to manage extubation. Not all patients are equal regarding the risk of reintubation, and the pathophysiology of extubation failure is incompletely understood. Consequently, our knowledge about the best approaches for preventing and managing extubation failure remains limited.

DEFINING EXTUBATION FAILURE

Extubation failure is usually defined as a need for reintubation within hours or days after planned extubation. The time interval used in the definition varies from 48 hours (1–3) to 72 hours (4–7) or 1 week (8, 9). The increased use of noninvasive ventilation (NIV) in the postextubation period has further limited the validity of this definition. A consensus conference on weaning defined success as the absence of ventilatory support during the first 48 hours after extubation (10). Reintubation, NIV initiation, or death within 48 hours after extubation were taken to indicate extubation failure, and these criteria were recently used in a prospective study on weaning (11). Death may occur in patients who are extubated with a prior do-not-reintubate decision. NIV can be initiated to treat postextubation respiratory distress or prophylactically before the onset of respiratory distress. In the first situation, reintubation might have been required in the absence of NIV or shortly after the time of NIV initiation, although there is no strong evidence that NIV prevents reintubation in this setting. Nevertheless, because NIV may delay reintubation, the time interval needed to assess extubation failure when NIV is used should probably be longer than 48 hours and perhaps should be 72 hours or 1 week. The use of prophylactic NIV cannot be classified as failure of extubation. Also, some studies focused chiefly on the occurrence of respiratory distress (12). Reintubation can merely indicate poor clinical judgment, whereas resuming mechanical ventilation is probably a less subjective criterion than the occurrence of respiratory distress. A consensus regarding the definition of extubation failure is needed to determine the acceptable reintubation rate and to understand the risks associated with reintubation.

INCIDENCE AND IMPACT OF EXTUBATION FAILURE

Even among patients who meet all weaning criteria and successfully perform a weaning readiness test, 10 to 20% experience extubation failure (1–7, 13, 14) (Table 1). Failure of planned extubation occurs in 5 to 10% of all intubated ICU patients, a relatively low rate that hinders research into this event. Indeed, planned extubation occurs in only 50 to 60% of ICU patients (4, 6, 13) because about 30% of patients die while intubated (4, 6), tracheostomy may be performed without a prior extubation attempt, about 5 to 15% of extubations are unplanned events (accidental or self-extubation), and some patients at the end of life undergo terminal extubation. Nevertheless, failure of planned extubation is associated with prolonged mechanical ventilation and extremely high mortality rates of 25 to 50% (1–4, 6, 14) (Table 1). A central question for clinicians is whether extubation failure is simply a marker of poor prognosis or contributes to a poor prognosis. Although the high mortality rate after failed extubation may be ascribable to greater illness severity at the time of extubation, there is some evidence that extubation failure, reintubation, and/or prolongation of mechanical ventilation adversely affect survival independently of the underlying illness severity (6, 14). In the largest case-series study of planned extubation, after adjustment for known outcome variables, reintubation was independently associated with ICU mortality (14). In a prospective observational study, Thille and colleagues determined the daily sequential organ

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TABLE 1. RATES OF PLANNED EXTUBATION FAILURE AND MORTALITY

Study (Reference)	Number of Extubations	Rate of Extubation Failure [% (*n*)]	ICU Mortality in Reintubated Patients [% (*n*)]	ICU Mortality in Nonreintubated Patients (%)
Esteban *et al.*, 1997 (1)	397	19 (74)	27 (20)	3
Esteban *et al.*, 1999 (2)	453	13 (61)	33 (20)	5
Epstein *et al.*, 1997 (4)	287	14 (40)	43 (17)	12
Vallverdu *et al.*, 1998 (3)	148	15.5 (23)	35 (8)	5.6
Thille *et al.*, 2011 (6)	168	15 (26)	50 (13)	5
Frutos-Vivar *et al.*, 2011 (14)	1,152	16 (180)	28 (50)	7
Funk *et al.*, 2009 (38)	257	10 (26)	Not available	Not available
Tonnelier *et al.*, 2011 (39)	115	10 (12)	Not available	Not available
Sellares *et al.*, 2011 (34)	181	20 (36)	Not available	Not available
Peñuelas *et al.*, 2011 (40)	2,714	10 (278)	26 (72)	5

failure assessment (SOFA) scores during the postextubation period (6). The SOFA score improved on the day of extubation compared with the preceding days irrespective of extubation outcome (Figure 1). The SOFA score worsened rapidly in the failure group but continued to improve in the group with successful extubation. This result constitutes indirect evidence that extubation failure and/or reintubation *per se* can diminish the chances of survival. Reintubation was significantly associated with ventilator-associated pneumonia in several studies (6, 15), and a reasonable assumption is therefore that reintubation may lead to clinical deterioration in fragile patients. The time of reintubation may also influence the outcome. Epstein and colleagues reported higher mortality rates after late compared with early reintubation (5). In a multicenter trial of NIV to treat postextubation respiratory failure, mortality was higher in the NIV group (16), and the only finding that seemed capable of explaining this mortality difference was that time to reintubation was about 2 hours in the standard-treatment group versus more than 12 hours in the NIV group. Unlike reintubation for other reasons, reintubation for transient upper airway obstruction does not seem to be associated with increased mortality (5). This finding suggests that extubation failure, rather than reintubation *per se*, is the reason for the higher mortality rate.

CAUSES OF EXTUBATION FAILURE

The reason for extubation failure often escapes identification. Reintubation is usually performed because of an apparently new episode of respiratory distress, which may be related to primary respiratory failure, congestive heart failure, aspiration, ineffective cough with airway secretion build-up, or upper airway obstruction. Other reasons for reintubation include the onset of new sepsis, surgical complications, acute coronary syndrome, and neurological impairment. This multiplicity of causative factors contributes to explain the clinical difficulties raised by extubation and the persistent uncertainties about the pathophysiology of extubation failure. Given the many causes for extubation failure, data centered only on respiratory physiology may fail to constitute a reliable guide for extubation decisions.

Respiratory distress can occur without lung function impairment (e.g., when upper airway obstruction is unmasked by endotracheal tube removal). Upper airway obstruction is a direct consequence of endotracheal intubation and occurs in about 5 to 15% of patients (17–21), being more common in women (17, 21) and when the height/tube-diameter ratio is low (21). Other predictors have been reported, such as reason for admission (19, 21), duration of mechanical ventilation (17, 21), and traumatic or difficult intubation (19). In studies focusing on the overall causes for extubation failure, upper airway obstruction was the reason for reintubation in 10 to 20% of cases (1, 5, 35). In studies focusing specifically on the incidence of postextubation stridor, 20 to 80% of patients who required reintubation were diagnosed with upper airway obstruction (30–33). A large multicenter study evaluating the preventive efficacy of steroids on postextubation stridor found that reintubation was directly ascribable to upper airway obstruction in 38% of cases (21). These contradictory results suggest observation bias in studies looking specifically for upper airway obstruction or frequent failure to diagnose upper airway obstruction in other studies. A good marker for severe upper airway obstruction is the absence of air leakage when the endotracheal tube cuff is deflated. The amount of leakage can be quantified using a cuff-leak test to measure the difference between the insufflated volume and the expired volume in assist-control volume mode after balloon deflation (18, 19). A low cuff-leak volume (<110 or 130 ml) around the endotracheal tube before extubation may indicate a high risk of upper airway obstruction (18, 19). Although the absence of air leakage is a good predictor of upper airway obstruction, the presence of a detectable leak does not rule out upper airway edema (22). The cuff-leak test is extremely useful because methylprednisolone therapy at least 12 hours before extubation might reduce the incidence of stridor (20, 21) and the rate of reintubation (21) due to upper airway obstruction. The risk/benefit ratio of steroids in patients with negative cuff-leak test results seems to favor steroid administration. The main drawback of routine steroid therapy may be that steroids seem to be effective only when given several hours before extubation and not when used only 1 hour before extubation (21, 25, 33). Routine steroid administration several hours before all planned

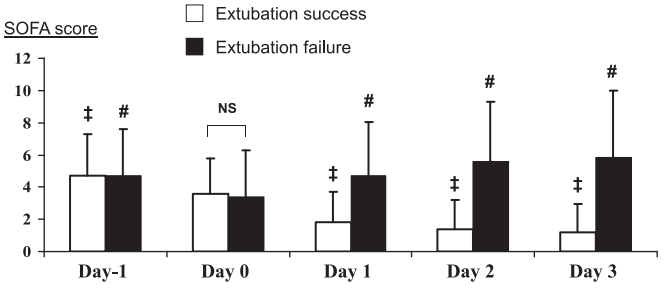

Figure 1. Changes in acute disease severity indicated by the Sequential Organ Failure Assessment score (SOFA) from the day before planned extubation to Day 3 after extubation. SOFA scores at extubation were not significantly different between patients who were successfully extubated (*open bars*) and patients who failed extubation (*solid bars*). The patients in both groups had improved SOFA scores within 24 hours before extubation. After extubation, the SOFA scores worsened substantially in the patients who failed extubation and improved in the successfully extubated patients. Figure adapted by permission from Thille and colleagues (6). $^{\ddagger}P < 0.05$ compared with the day of extubation in the failed-extubation group. $^{\#}P < 0.05$ compared with the day of extubation in the successfully extubated group.

extubations might result in delaying extubation until evidence of systemic steroid activity is obtained. In addition, some patients scheduled for extubation are not extubated and would therefore receive steroids unnecessarily. A reasonable approach may be a routine cuff-leak test before extubation followed by steroid administration when this test is negative. Laryngeal edema is not the only injury responsible for postextubation upper airway obstruction and/or stridor. In a prospective study of 136 patients ventilated for longer than 24 hours, routine examination of the larynx after extubation showed laryngeal injuries in three-quarters of the patients, with an even higher proportion after prolonged intubation (23). Patients failing extubation and requiring reintubation more often had granulations and vocal cord dysmotility compared with the other patients. These findings suggest that laryngeal injuries may often go unrecognized and may participate in postextubation respiratory distress by increasing the work of breathing and/or promoting aspiration via glottis dysfunction.

RISK FACTORS FOR EXTUBATION FAILURE AND HIGH-RISK POPULATIONS

Factors reported to be associated with extubation failure are listed in Table 2. In several studies, neurological disorders (3) or impaired neurological status (24, 25) were independently associated with extubation failure. It has also been suggested, however, that some comatose neurosurgical patients with Glasgow Coma Scale scores $\leqslant 8$ can be successfully extubated without delay and without an increased risk of reintubation provided the airway secretions are minimal. Thus, delaying extubation may be unwarranted when an impaired neurological status is the only reason for considering prolonging the intubation (26). Cough strength (30–32) and amount of secretions (29, 31) seem to be good predictors of extubation failure, especially in patients with impaired neurological status, but this is a field where further objective measurements and research are needed.

The usual severity scores measured at ICU admission are poor predictors of extubation failure (7, 24, 27, 28) even when measured at the time of extubation (6, 25). The primary reason for intubation may help to predict the extubation outcome, but the available results are conflicting (4, 7). By contrast, several studies showed higher extubation failure rates in older patients (6, 7). Thille and colleagues identified a subset of patients at high risk for extubation failure. These were medical patients older than 65 years with underlying chronic cardiac or respiratory diseases, and their reintubation rate was 34% compared with only 9% in the other patients (6). In another study, a positive fluid balance on the day before extubation was associated with an increased risk of extubation failure (7). Along the same line, high baseline levels of B-type natriuretic peptides (BNP) or a BNP increase during a spontaneous breathing trial (SBT) have been shown to predict failure of a weaning readiness test (29), postextubation respiratory distress (30), or extubation failure (31). In a recent multicenter study, diuretic therapy guided by BNP values shortened the duration of weaning, suggesting that inducing a negative fluid balance may hasten extubation (32). Lung failure may also be the reason for extubation failure. A recent innovative study found that loss of lung aeration as assessed by lung ultrasound during the SBT, suggesting lung derecruitment, predicted postextubation distress better than did BNP or echocardiography (33). A minimal oxygenation threshold is among the key criteria used to select patients for extubation, and readiness testing is usually not performed in severely hypoxemic patients. This point may explain the low predictive value of preextubation blood gas values for the outcome of extubation. One study showed that Pa_{O_2}/FI_{O_2} below 200 mm Hg was associated with an increased risk of extubation failure in neurosurgical patients (24), but most studies found no differences in terms of oxygenation between patients who succeeded and those who failed extubation (4, 6, 7, 25, 27). Patients who fail extubation have higher values of the rapid shallow breathing index (f/V_T) before extubation than those who succeed extubation (7, 24, 25, 28), although considerable overlap exists between these two groups. Unlike hypoxemia, hypercapnia *per se* may predict weaning outcomes (25, 34). One study found that hypercapnia during the SBT, defined as $Pa_{CO_2} \geqslant 44$ mm Hg, was independently associated with extubation failure (25). Another study including selected patients with a high prevalence of chronic respiratory disorders showed that $Pa_{CO_2} \geqslant 54$ mm Hg during the SBT independently predicted prolonged weaning and mortality (34). Prophylactic NIV was particularly effective in patients with hypercapnia (35). Therefore, hypercapnia before extubation may constitute not only a valuable warning signal for an increased risk of prolonged weaning but also a good criterion for starting prophylactic NIV (34).

An international consensus panel on weaning suggested that ventilated patients be categorized into three groups according to the difficulty of their weaning process (10): "simple weaning" refers to patients who succeed the first weaning test and are extubated without difficulty, "difficult weaning" refers to patients who fail the first weaning test and require up to three tests or 7 days to achieve successful weaning, and "prolonged weaning" refers to patients who require more than 7 days of weaning after the first test. According to earlier studies (3, 36, 37), approximately 70% of mechanically ventilated patients fall into the simple weaning group. Four recent studies evaluated the proportion of patients in each group using a strategy of daily screening (34, 38–40) (Figure 2). The failure rate of the first test in these studies was 40 to 50%. Prolonged weaning was independently associated with increased mortality (34, 38–40) and with a significantly higher risk of reintubation in one study (39) and with a trend

TABLE 2. POTENTIAL RISK FACTORS FOR EXTUBATION FAILURE

Study (Reference)	Number of Episodes of Extubation Failure	Risk Factors for Extubation Failure
Thille *et al.*, 2011 (6)	26	Age $>$ 65 yr or underlying chronic cardiorespiratory disease
Epstein *et al.*, 1997 (4)	40	Age, APACHE II at time of weaning, and acute respiratory failure of cardiac origin
Frutos-Vivar *et al.*, 2006 (7)	121	Pneumonia as the reason for intubation, high rapid shallow breathing index (f/V_T), and positive fluid balance
Vallverdu *et al.*, 1998 (3)	23	Neurological patients
Namen *et al.*, 2001 (24)	44	Rapid shallow breathing index (f/V_T) $>$ 105, $Pa_{O_2}/FI_{O_2} <$ 200 mm Hg, Glasgow Coma Scale score $<$ 8
Mokhlesi *et al.*, 2007 (25)	16	Abundant endotracheal secretions, Glasgow Coma Scale score $\leqslant$ 10, $P_{CO_2} \geqslant$ 44 mm Hg during spontaneous breathing trial
Smina *et al.*, 2003 (28)	13	Peak expiratory flow $\leqslant$ 60 L/min and rapid shallow breathing index $\geqslant$ 100
Khamiees *et al.*, 2001 (27)	18	Moderate or abundant endotracheal secretions, cough absent or weak, hemoglobin $\leqslant$ 10 g/dl
Chien *et al.*, 2008 (31)	19	Increase in B-type natriuretic peptide during a spontaneous breathing trial
Teixeira *et al.*, 2010 (82)	31	$>$4.5% reduction in central venous saturation 30 min after spontaneous breathing trial initiation

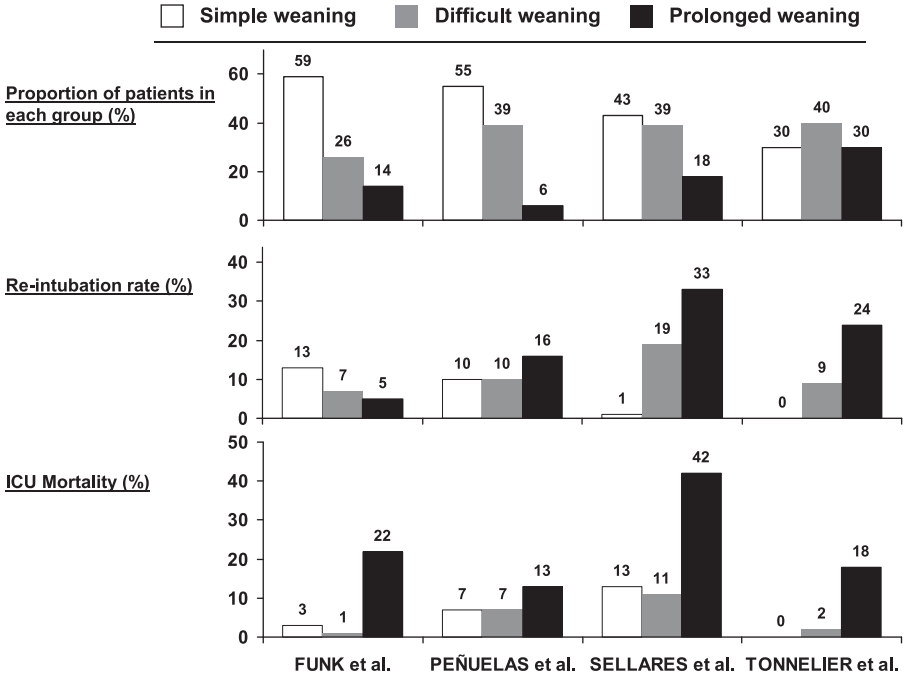

Figure 2. The proportion of patients (*top*), rate of reintubation (*middle*), and rate of in-ICU mortality (*bottom*) according to weaning difficulties. The results are adapted from the four studies evaluating three groups of ventilated patients defined based on difficulty and duration of weaning (34, 38–40) according to the international conference consensus on weaning (10): "simple weaning" (*white histograms*) refers to patients who are extubated without difficulty after the first weaning test, "difficult weaning" (*gray histograms*) refers to patients who fail the first weaning test and require up to three spontaneous breathing tests or 7 days to achieve successful weaning, and "prolonged weaning" (*black histograms*) refers to patients who require more than 7 days of weaning after the first weaning test. Using this definition, prolonged weaning was associated with significantly higher mortality rates in all four studies compared with simple and difficult weaning. However, in none of these four studies did the reintubation rate differ among the three groups.

toward a higher risk of reintubation in two studies (34, 40). Thus, the classification scheme is of only moderate usefulness for predicting extubation failure.

It has been suggested that the patient's confidence about being able to breathe without the ventilator may be a good predictor of extubation success, with the opposite being much less accurate (11). In one study, patients considered by healthcare providers to be at high risk for extubation failure often failed extubation, but many patients who failed were not considered to be at risk (41).

UNCERTAINTIES ABOUT EXTUBATION FAILURE

Extubation failure may be caused by other factors than the above-mentioned predictors, such as delirium, sleep deprivation, adrenal insufficiency, or ICU-acquired weakness. Delirium is frequent in the ICU and predicts mortality (42). Acute brain dysfunction may promote extubation failure through consciousness alterations, agitation, sedation induced by medications given for agitation, aspiration, and refusal of treatments including NIV. Sleep is an essential physiological activity allowing physical, psychological, and mental recovery. No studies have evaluated the impact of sleep quality on weaning success, although in another context poor sleep quality was associated with an increased risk of NIV failure in hypercapnic patients (43). In a randomized study, stress-dose hydrocortisone supplementation shortened the time to extubation and increased the rate of successful extubation among patients with adrenal insufficiency (44). However, adrenal insufficiency is difficult to detect with the usual tests, and the steroids may have been effective because of their stimulating effects. The promising results of this study have not been confirmed. ICU-acquired paresis may occur in about 25% of patients after prolonged mechanical ventilation (45) and may affect peripheral and respiratory muscles (46). It has been shown that ICU-acquired polyneuromyopathy causing peripheral muscle weakness is independently associated with prolonged mechanical ventilation duration, higher ICU and hospital mortality rates (47), weaning difficulties (46, 48, 49), and a high risk of extubation failure (49). However, few studies have assessed the potential contribution of the inspiratory/expiratory muscles to weaning or extubation difficulties in patients with ICU-acquired polyneuromyopathy (46, 49). A recent study showed that diaphragmatic dysfunction assessed by ultrasonography was associated with longer weaning times and higher reintubation rates (50). Diaphragmatic dysfunction at the time of extubation may correlate clinically with hypoventilation and inefficient cough, subsequently increasing the risk of weaning failure (51).

WEANING READINESS TESTS

Physiological Results

The ideal weaning readiness test would exhibit perfect accuracy in predicting the tolerance of unassisted spontaneous breathing after extubation by mimicking the postextubation physiological conditions. Thus, all patients passing the ideal weaning test would be able to maintain adequate ventilation after extubation. We will discuss the predictive accuracy of current weaning tests based on physiological and clinical data. A standard test for extubation readiness is the SBT performed using the T-piece by disconnecting the patient from the ventilator and providing additional oxygen. Another weaning test is performed without disconnecting the patient from the ventilator by using a low level of pressure support (PS) with or without positive end-expiratory pressure (PEEP) while continuously monitoring the respiratory rate and tidal volume on the ventilator display. Cabello and colleagues compared the SBT on a T-piece and the low-PS test (7 cm H_2O) with or without PEEP in patients with heart failure and difficult weaning (52). Patient effort was lower during the low-PS test than during the T-piece test and decreased further when PEEP was added to PS (Figure 3). These findings are consistent with previous evidence that PS and PEEP can reduce patient effort by about 30 to 40% (60). An important point in the study by Cabello and colleagues is that most patients succeeded the PS test, although all patients failed the T-piece test (52). PS was initially introduced to reduce the work imposed by the ventilator circuit/valve and endotracheal tube (53), which since then has decreased considerably in parallel with technological improvements (54). Moreover, the postextubation period is characterized by relatively high upper airway resistance, so that the work of breathing after extubation is virtually unchanged (55) or increased (56). A

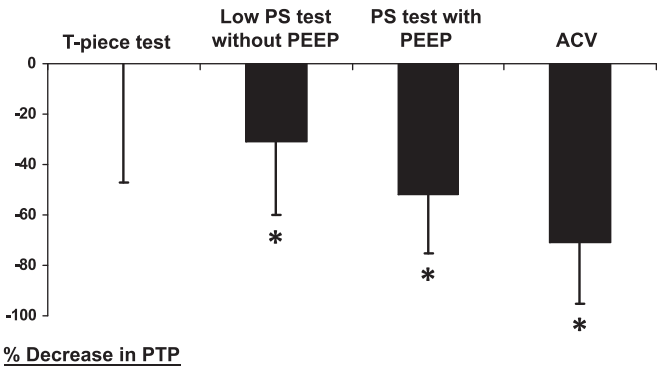

Figure 3. Reduction in patient effort expressed as a percentage (measured using the esophageal pressure time product [PTP] in cm H_2O/s/min) between spontaneous breathing on a T-piece as the reference (*left*), low pressure support (low PS, 7 cm H_2O) with or without positive end-expiratory pressure (PEEP) (*middle*), and reconnection to the ventilator in assist-control ventilation (ACV, *right*). Patient effort was significantly lower with the low-PS trial that with the T-piece trial (*$P < 0.05$): the decreases were $-31 \pm 29\%$ with no PEEP and $-52 \pm 23\%$ with PEEP. Figure drawn from data in Reference 52.

common misconception is that breathing through an endotracheal tube necessarily increases the work of breathing, as occurs in healthy volunteers breathing through a resistive tube (57). Straus and colleagues showed that the work of breathing was similar before and immediately after extubation in 14 successfully extubated patients breathing on a T-piece (55). The high upper airway resistance measured after extubation was due mainly to the glottis, which was the narrowest part of the airway, whereas supraglottic resistance was within the normal range (55). The high glottic resistance may be due to transient upper airway edema or to laryngeal lesions, as recently reported in many patients in the postextubation period (23). Therefore, a T-piece test accurately replicates the work of breathing required from the patient after extubation and probably constitutes a reliable assessment of the ability of an intubated patient to maintain sufficient ventilation without assistance. By contrast, adding even low PS levels may lead to underestimation of the extubation failure risk in some patients (58). However, the resistance of the endotracheal tube may be increased after several days of mechanical ventilation (59) and may exceed that of the upper airways. This is a theoretical concern that may deserve further research.

An increase in capillary pulmonary pressure can also occur during the transition from mechanical to spontaneous ventilation and may vary according to the type of weaning readiness test (Figure 4) (52). In 1988, Lemaire and colleagues reported the development of pulmonary edema and subsequent respiratory distress shortly after the beginning of spontaneous breathing, leading to unsuccessful weaning (60). Switching from mechanical to spontaneous ventilation can decrease left ventricular performance and unmask latent left ventricular dysfunction (60) by increasing preload and afterload (61). Cardiac dysfunction is a frequent cause for weaning test failure (52, 62) and should be diagnosed by all available means because it can respond to diuretics and/or vasodilators and sometimes to coronary angioplasty in case of cardiac ischemia (63). Echocardiography can differentiate systolic and diastolic left ventricular dysfunction and can detect elevation of the pulmonary occlusion artery pressure during the weaning test (64). It has been shown that high baseline BNP or a BNP increase at SBT completion can predict weaning failure of cardiac origin (65, 66). BNP measurement may be helpful as a first-line test before an echocardiographic assessment for systolic or diastolic cardiac dysfunction.

Clinical Results

The ideal weaning readiness test would predict the tolerance of unassisted breathing. However, the sensitivity and specificity of weaning tests for predicting successful extubation are difficult to assess. The extubation failure rate (i.e., the rate of false-positive test results for predicting a successful extubation:patients tolerating the test but needing reintubation) is about 15%, which makes the specificity of the test for predicting successful extubation 85%. By contrast, the proportion of patients able to tolerate extubation despite failing the weaning test (i.e., false-negative test results, used to determine sensitivity) is difficult to evaluate because, for obvious ethical reasons, patients who fail a weaning test are usually not extubated. Several types of studies have provided indirect and imperfect estimates of the false-negative rate. *1*) Among patients who self-extubate at a time when they do not meet weaning criteria, only 40 to 60% require reintubation. However, no information on weaning test results just before self-extubation is available. *2*) In a relatively small study, 68% of the patients who failed a T-piece test passed a low-PS test and were then successfully extubated, suggesting a high false-negative rate with the T-piece test (67). *3*) A recent trial studied extubation outcomes in patients who failed a SBT (9). Among them, 42% did not require rescue NIV to treat postextubation respiratory failure and only 37% were reintubated, indicating limited sensitivity of the weaning test. *4*) In clinical practice, the determination of T-piece test failure is partly subjective, with many clinicians being somewhat biased toward overestimating ventilator dependency (68).

In a large, multicenter, randomized controlled trial, Esteban and colleagues compared the T-piece and low-PS tests (1). In accordance with physiological data, the proportion of patients who failed the first weaning test was higher with the T-piece than with low PS. The proportion of successfully extubated patients after 48 hours was not significantly different between the two groups. A smaller study showed that some patients were able to pass a low-PS test immediately after failing a T-piece test and were then extubated with no increase in the risk of extubation failure (67). Thus, the T-piece test may slightly delay the identification of weaning readiness, or the low-PS test may carry a higher risk of reintubation. Physiological data support the latter explanation, as indicated by Tobin in a comment on

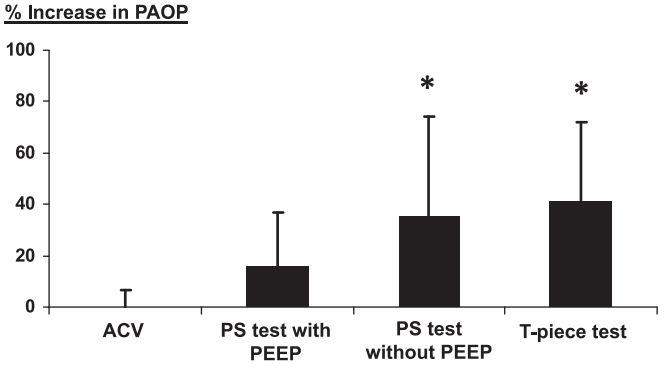

Figure 4. Increase in pulmonary wedge pressure expressed as a percentage (measured using the pulmonary artery occlusion pressure [PAOP] in mm Hg) between assist-controlled ventilation (ACV) as the reference (*left*), low pressure-support (low-PS, 7 cm H_2O) with or without positive end-expiratory pressure (PEEP) (*middle*), and a T-piece (*right*). PAOP was significantly higher during the T-piece and low-PS without PEEP trials than during the low-PS with PEEP trial (*$P < 0.05$): the increases were $16 \pm 21\%$ during the low-PS with PEEP trial, $35 \pm 39\%$ during the low-PS without PEEP trial, and $41\% \pm 31$ during the T-piece trial compared with ACV. Figure drawn from data in Reference 52.

the myth of "minimal ventilator settings" (58). Nevertheless, there is no clinical evidence of a higher reintubation risk with the low-PS test, and extubation failure rates have been lower than 20 or 15% in studies of this method. The number of patients requiring reintubation remained relatively low even in large, randomized controlled trials, which may have been underpowered for this endpoint. The largest studies of weaning readiness tests included about 500 extubation episodes but only about 30 reintubated patients in each group. Randomized controlled trials evaluated unselected patients and, therefore, a majority of patients at low risk for extubation failure. The individual risk of reintubation may become unacceptably high only in high-risk populations. In two randomized controlled trials, reintubation rates were similar using a T-piece test or a low-PS test lasting 30 minutes or 2 hours (69). Again, these studies focused chiefly on simple weaning, whereas an observational study showed that many difficult-to-wean patients failed the weaning test only between 30 and 120 minutes (3). Clinical trials are probably underpowered to demonstrate the safety of a procedure in high-risk patients, and their results should be extrapolated with caution.

A large international survey on mechanical ventilation found that reintubation was significantly associated with the use of CPAP compared with T-piece or low-PS tests (14). This result, coupled to physiological data, suggests that weaning tests might be done without PEEP to better detect latent cardiac dysfunction and/or lung failure. Indeed, a low PEEP level in itself provides ventilatory and cardiac support, as shown by the demonstrated benefits of CPAP (70), and may result in underestimation of the extubation failure risk in some patients. A first-line weaning test before extubation can probably be performed on the ventilator using a low-PS test without PEEP, but in many high-risk patients a prolonged T-piece test is probably more reliable for making extubation decisions.

In summary, the results of the T-piece and low-PS tests may depend on the skill of the clinician taking the decision and on the prevalence of extubation failure in a given population. T-piece test results may be too conservative if the clinicians are very cautious and/or if the prevalence of extubation failure is low (e.g., in postoperative patients). On the other hand, the low-PS test may underestimate the risk of extubation failure, especially if the clinician is overoptimistic or if the prevalence of extubation failure is high (e.g., in patients under prolonged mechanical ventilation or having ICU-acquired polyneuromyopathy). Keeping PEEP during the test may increase the rate of extubation failure due to lung or heart failure.

SELECTING THE OPTIMAL STRATEGY IN PATIENTS AT HIGH RISK FOR EXTUBATION FAILURE

An international consensus panel on weaning insisted on the need to perform the first weaning test as soon as the patient meets the following criteria (10): resolution of the initial reason for intubation, cardiovascular stability with minimal or no need for vasopressors, no continuous sedation, and adequate oxygenation defined as $Pa_{O_2}/FI_{O_2} \geq 150$ mm Hg with PEEP up to 8 cm H_2O. Early identification of patients who can breathe spontaneously results in better outcomes. Daily screening followed by a weaning test and then by extubation if the test is successful can shorten the intubation time without increasing the risk of reintubation (71, 72). In most patients, a short test (30-min low-PS or T-piece test) is likely to be sufficient. However, there is a subgroup of easy-to-wean patients whose observed reintubation rate is less than 10% and another subgroup of high-risk patients who require reintubation in 20 to 30% of cases. The more challenging 2-hour T-piece test might be particularly useful for decreasing the false-negative rate in high-risk patients such as elderly patients with chronic obstructive pulmonary disease, heart failure, or neuromuscular disorders (4, 6). In patients at high risk for extubation failure and/or clinically considered borderline at weaning test completion, it may be reasonable to evaluate whether the patient might better tolerate spontaneous breathing after 24 hours due to a more negative fluid balance or a significant neurological improvement with stronger cough or decreased airway secretions. Thus, in some cases, most notably in high-risk fragile patients, it may be worth waiting another 24 hours before reassessing the patient for extubation.

Therapeutic NIV used in patients with postextubation respiratory distress must be distinguished from prophylactic NIV used to prevent respiratory distress. Prophylactic NIV is the routine use of NIV immediately after extubation in the absence of evidence of respiratory failure. Studies suggest that prophylactic NIV may help to prevent postextubation acute respiratory failure (35, 73, 74). Prophylactic NIV is beneficial only in patients at high risk for reintubation. In a recent study including more than 400 unselected ICU patients extubated after a successful 2-hour SBT, reintubation rates were similar in patients treated with prophylactic NIV or oxygen therapy (75). Again, the extubation failure rate in this randomized controlled trial was low (13.2 and 14.9%) in an unselected population (75). By contrast, Nava and colleagues found that NIV in high-risk patients decreased the need for reintubation (73). They used various criteria to define high-risk patients, such as previous weaning test failure, more than one comorbidity, $P_{CO_2} > 45$ mm Hg after extubation, chronic heart failure, weak cough, or upper airway obstruction with stridor (73). A study by Ferrer and colleagues (74) defined patients at high risk for extubation failure using the criteria identified by Epstein and colleagues (4): age older than 65 years, high severity score, or heart failure as the reason for intubation. Early NIV avoided respiratory failure after extubation and decreased ICU mortality without significantly decreasing the reintubation rate (74). A subgroup analysis suggested that NIV was chiefly beneficial in hypercapnic patients with chronic respiratory disorders (74). In a prospective randomized controlled trial in 106 patients performed by the same group, NIV was effective in patients who had hypercapnia at SBT completion and reduced Day-90 mortality (35). In contrast with prophylactic NIV, therapeutic NIV has no proven benefit in the overall population of patients with postextubation acute respiratory failure (76) and can even increase the risk of death by delaying reintubation (16). Therapeutic NIV may decrease the risk of reintubation after major elective abdominal surgery (77) or lung resection (78).

Finally, few studies have reported the use of NIV as a weaning method to hasten extubation in difficult-to-wean patients with chronic obstructive pulmonary disease who failed a weaning test (9, 79–81). A recent multicenter study compared conventional weaning versus extubation followed by NIV or standard oxygen therapy in patients who failed a 2-hour T-piece test (9). NIV reduced the risk of postextubation respiratory failure, but the weaning success and reintubation rates were similar regardless of the weaning method. The overall time on mechanical ventilation taking NIV into account was longer in the NIV group (9). Consequently, NIV cannot be recommended as a weaning method in clinical practice.

One important research objective regarding the indication for prophylactic NIV is to better identify the high-risk population of patients most likely to benefit from this intervention. The existing data suggest that routine prophylactic NIV might be indicated immediately after extubation in hypercapnic patients. Further studies should evaluate whether NIV can also benefit patients older than 65 years with underlying chronic cardiorespiratory disease, a population identified as being at high risk for extubation failure (6).

CONCLUSIONS

In the ICU, the decision to extubate a patient is an important one. Clinical trials have established that hastening the weaning process is the best way to minimize the duration of mechanical ventilation. Extubation failure, which occurs in up to 20% of cases, has often been considered the price to pay for this approach. Several lines of evidence, however, suggest that extubation failure and reintubation can worsen outcomes and, consequently, that the rules used to make extubation decisions need to be improved, especially regarding the identification of patients at high risk for extubation failure. Future research should focus on identifying as yet unrecognized factors associated with extubation failure, which might include delirium, poor sleep quality, limb muscle and diaphragmatic weakness, and systolic or diastolic left ventricular dysfunction. Prophylactic NIV during the postextubation period may be helpful, but studies are needed to identify the patients most likely to benefit from this intervention. Randomized controlled trials should have sufficient power to evaluate reintubation rates, as opposed to weaning rates, to better detect differences among weaning procedures.

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