Analytic Review

To Wean or Not to Wean: A Practical Patient Focused Guide to Ventilator Weaning

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Abstract

Since the inception of critical care medicine and artificial ventilation, literature and research on weaning has transformed daily patient care in intensive care units (ICU). As our knowledge of mechanical ventilation (MV) improved, so did the need to study patient-ventilator interactions and weaning predictors. Randomized trials have evaluated the use of protocol-based weaning (vs. usual care) to study the duration of MV in ICUs, different techniques to conduct spontaneous breathing trials (SBT), and strategies to eventually extubate a patient whose initial SBT failed. Despite considerable milestones in the management of multiple diseases contributing to reversible respiratory failure, in the application of early rehabilitative interventions to preserve muscle integrity, and in ventilator technology that mitigates against ventilator injury and dyssynchrony, major barriers to successful liberation from MV persist. This review provides a broad encompassing view of weaning classification, causes of weaning failure, and evidence behind weaning predictors and weaning modes.

Keywords

mechanical ventilation, weaning, spontaneous breathing trial, ventilator discontinuation

Introduction/History

Weaning is an intricate intervention that demands the attention and expertise of critical care specialists. Seventy years ago, Dr Ibsen introduced the revolutionary technique of positive-pressure ventilation during the polio epidemic in Copenhagen that saved countless lives.[1,2] In 1955, Dr Carl-Gunnar Engström introduced the first volume oriented-ventilator.[3] In 1961, Drs. Henrik Bendixin and Henning Pontoppidan founded the first respiratory intensive care unit (ICU) at Massachusetts General Hospital and conducted ventilator weaning research.[4] By 1977, Henning, Shubin and Weil were using esophageal-balloon catheters to make detailed measurements of the work of breathing.[5] In the 1970s, synchronized intermittent mandatory ventilation (SIMV) was widely used as the weaning mode of choice in most ICUs. Prior to the application of SIMV, weaning techniques comprised of disconnecting patients from the ventilator for 3–4 minutes at a stretch every thirty minutes and ascertaining their tolerance to abrupt discontinuation. In the 1980s, patient-ventilator interactions studies showed the limitations of SIMV as a weaning mode. By the mid 1990's, there was a shift in intensivists comparing various modes of weaning from MV.[1]

Definition and Classification

Weaning is defined as a gradual decrease in ventilatory support from patients whose underlying cause for respiratory failure is improving and should be thought of as a continuum.[6,7] Initially, patients require full ventilatory support to manage acute respiratory failure. Thereafter, recovering PaO_2/FiO_2 ratios, lower FiO_2 requirements and lower ventilator settings might indicate the initiation of weaning readiness assessments. Various clinical and objective readiness assessment criteria must be met.[8] A patient undergoes measurements of weaning predictors while on a spontaneous breathing trial (SBT) for a prescribed amount of time. Weaning success is defined by extubation and absence of ventilatory support 48 hours after extubation.[9] Conversely, weaning failure is defined as the inability to pass a SBT or the need for reintubation within 48 hours following extubation.[10]

Weaning can be classified as simple, difficult, or prolonged.[8,9,11] Simple weaning is associated with a higher incidence (30-60%) of success and a lower mortality (5-10%). The main objective for this group is to identify readiness to wean as soon as possible, and ensure a systematic approach to ventilator discontinuation.[8] In difficult weaning, a patient

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requires up to three SBTs or as long as seven days to wean. For the difficult-to-wean patient, a major objective is identifying and addressing reversible causes for SBT failure. Finally, prolonged weaning occurs when a patient fails more than three SBTs or requires more than 7 days to be liberated from MV. In combination, difficult and prolonged weaning groups are associated with lower incidence (15-40%) of success and higher mortality (10-30%).[7,9] In the prolonged weaning patient, preventive measures such as encouraging early spontaneous breathing, well controlled use of sedation, and early mobilization may help.[8]

Pathophysiology of Weaning Failure

In order to address reversible causes of weaning failure, a simple structured approach allows for a systematic review of the pathophysiology of weaning failure (Table 1). Discontinuation failure may depend on several factors and is often consequent to more than a single cause. Irrespective of the underlying disorder leading to the need for MV, the most common mechanism is generally an imbalance between the force generating capacity of the respiratory muscles and the load they must face once MV is discontinued.[11–13]

Table 1. Pathophysiology of Weaning Failure.

Causes of Weaning Failure	Interventions
Airway & lung dysfunction	Inhaled bronchodilators
	Inspiratory occlusion
	Calculating intrinsic PEEP
	Diagnostic Bronchoscopy during SBT
	Diuretics
	Thoracentesis
Weaning-induced cardiac dysfunction	EKG during SBT
	Echocardiography before & after SBT
	Bedside Cardiac POCUS
	Afterload reduction strategies
Cognitive dysfunction	Delirium screening tools
	Reorientation techniques
	Early Mobilization
	Reducing noise/light during sleep
	Behavioral therapy
	Anxiolytics
Endocrine & metabolic dysfunction	Electrolytes and Blood gas
	Plasma cortisol and thyroid hormone levels
Diaphragm dysfunction	Early Mobilization
	Diaphragm EMG
	Transdiaphragmatic pressure using gastric and esophageal balloon catheters
	Diaphragm muscle biopsy
Nutrition	Indirect calorimetry

EKG = electrocardiogram; PEEP = positive-end-expiratory pressure; SBT = spontaneous breathing trials; POCUS = point-of-care ultrasound; EMG = electromyography.

Airway and Lung Dysfunction

Airway and lung dysfunction can be broadly viewed through the prism of illnesses that increase airway resistance and those that reduce compliance.[10] Causes of upper airway resistance are presence of an endotracheal tube, tracheal injury such as tracheal stenosis, tracheomalacia, granulation tissue formation, and small airway diseases such as asthma and chronic obstructive pulmonary disease (COPD).[9,11,13] However, in general, it is a misconception that, after extubation, upper airway resistance decreases. In fact, the work of breathing in patients mechanically ventilated for ± 5.5 days increased after extubation, a probable consequence of upper airways edema.[14] In a study of COPD patients failing an SBT, airway resistance significantly increased (9 ± 2 cm H_2O up to 15 ± 2 cm H_2O; $p < 0.05$), whereas successfully weaning patients, airway resistance stayed the same.[15,16] Additionally, increased airway resistance is associated with the development of intrinsic positive end-expiratory pressure (PEEPi). PEEPi may develop because of increased flow resistance, expiratory flow limitation, high breathing frequency, and loss of elastic recoil of the lungs.[10] Pulmonary hyperinflation resulting from PEEPi places the diaphragm at a suboptimal position on the length-tension curve, impairing the ability to generate negative pressure. PEEPi is associated with patient-ventilator asynchrony and, in particular, with ineffective triggering (Figure 1).

Causes of reduced compliance include: pulmonary edema, pleural fluid, ascites, elevated abdominal pressures, obesity, pneumonia, interstitial lung diseases (ILD), and alveolar edema.[10] Compliance of the respiratory system (C_{rs}) is dependent on PEEP and plateau pressure (P_{plat}) and is calculated as per: $Vt/(P_{plat} - PEEP_{total})$. Normal static lung compliance is 200 mL per cm H_2O for non-intubated patients and 60 mL

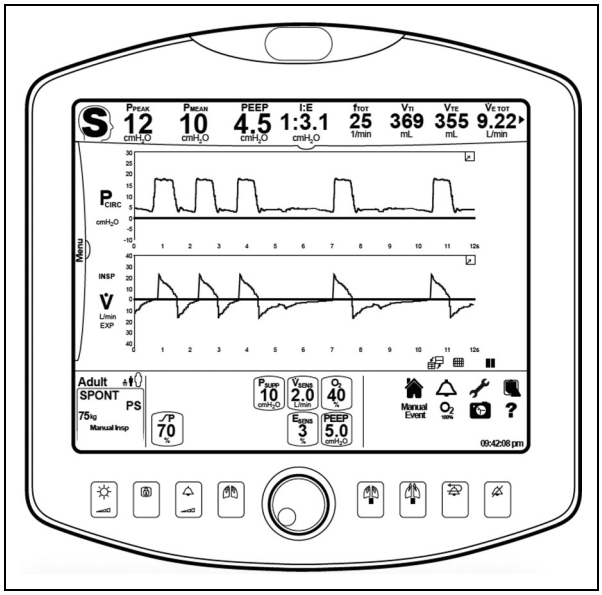

Figure 1. Ineffective triggering on a ventilator: airway pressure and flow waveforms.

per cm H_2O or lower for patients who need mechanical ventilation.

Flexible bronchoscopy is the gold standard for diagnostic assessment of potential causes of upper airway resistance such as tracheal injury, tracheostomy malposition, tracheomalacia and thick respiratory secretions.[9–11] Interventions such as non-invasive ventilation and endotracheal stents can be used to relieve resistance.[17,18] Furthermore, in patients with small airway diseases, applied PEEP should match the level of PEEPi, as estimated by the expiratory occlusion technique.[10] Bronchoconstriction can be reduced by routine use of bronchodilators.[19] Diuretics can reduce lung and chest wall edema,[20,21] while thoracentesis and paracentesis can resolve pleural fluid and ascitic fluid respectively,[11,13,22] and help improve atelectasis thereby improving compliance and facilitating weaning.[8–10]

Laryngeal edema is associated with prolonged intubation and induces post-extubation stridor, which increases the risk of reintubation. A cuff leak test can be used as a surrogate indicator of laryngeal edema and to guide critical decisions to extubate patients or to continue mechanical ventilation. A recent meta-analysis and systematic review points to the excellent specificity and moderate sensitivity of the cuff leak test to predict post-extubation airway obstruction. The most salient risk factors for post-extubation stridor include traumatic intubation, intubation for longer than six days, a large endotracheal tube, female gender, and reintubation after unplanned extubation.[23] The cuff leak test is a useful tool in the decision-making about extubation, but the low sensitivity suggests that a negative test cannot completely exclude post-extubation airway obstruction and that patients still need to be closely monitored post-extubation.[23] Furthermore, systemic steroid therapy reduces both the reintubation rate and post-extubation stridor (PES) rate.[23] The ATS/ACCP clinical practice guideline suggests performing cuff leak test in mechanically ventilated adults who meet extubation criteria and deemed high risk for PES and suggest that for adults who have failed a cuff leak test but are otherwise ready for extubation, systemic steroids should be administered at least 4 h before extubation.[11,18,23–25]

In the context of uniquely primary respiratory disorders, such as chronic obstructive pulmonary disease, cystic fibrosis, obesity hypoventilation syndrome, neuromuscular disorders and pediatric disorders prone to chronic hypercapnic respiratory failure, IMV and non-invasive ventilation have become a well-established treatment option.[17] Special considerations need to be accounted for while managing these patients during weaning attempts and well-defined algorithms have been proposed by the German Respiratory Society for treating chronic respiratory failure.[17]

Weaning-Induced Cardiac Dysfunction

Weaning-induced cardiac dysfunction was first described 30 years ago.[21] Investigators have used simple cardiac bedside maneuvers to study ventilated patients who may have underlying congestive heart failure, myocardial ischemia or coronary artery disease during the weaning phase. There are many proposed mechanisms for cardiac dysfunction and weaning-induced left ventricular (LV) dysfunction (Figure 2).[21] A marked decrease in intrathoracic pressure, activation of the adrenergic tone, hypoxemia, hypercapnia, and increased work of breathing are important consequences of unsuccessful weaning which may eventually lead to an acute increase in left ventricular end-diastolic pressure (LVEDP) and to cardiogenic pulmonary edema.[20,21,26]

Suspected weaning failure due to a cardiovascular element may prompt early use of diagnostic techniques to determine the specific etiology.[20] An electrocardiogram can reveal ischemic changes (eg, T-wave inversions or ST-segment elevations). Bedside transthoracic echocardiography (TTE) and lung ultrasonography can diagnose diastolic dysfunction. TTE can also reliably demonstrate LV relaxation (e′ wave) and the grade of LV diastolic dysfunction by calculating the E/e′ ratio. Biomarkers of volume status and cardiac function, mainly serum B-type natriuretic peptide (BNP) and/or N-terminal (NT)-proBNP, have been used as surrogate markers of cardiovascular dysfunction.[26] Patients detected with an increase in pulmonary artery occlusion pressure (PAOP) during SBTs, usually experience a substantial decline in mixed venous oxygen saturation during SBTs indicative of the contribution of cardiovascular dysfunction to the severe imbalance between oxygen delivery and increased oxygen consumption. Acute rises in plasma protein or hemoglobin concentration, both greater than 5% during a SBT, reflecting volume contraction induced by pulmonary edema formation, have correlated with PAOP increase above 18 mm Hg.[27,28]

For suspected or confirmed cases of cardiac dysfunction, effective mitigating and management strategies include diuretics, nitrates and other vasoactive medications.[20,26] Diuretics can decrease global volume overload by reducing left ventricular end diastolic volume (LVEDV). In fact, a small decrease in LVEDV will result in a marked reduction in LVEDP.

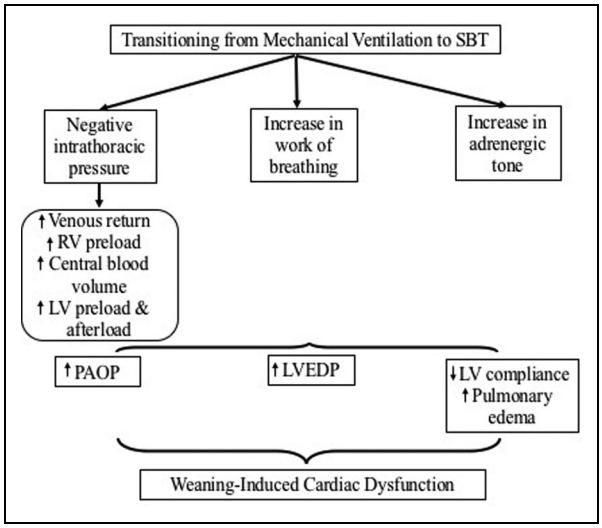

Figure 2. Hemodynamic and cardiopulmonary interactions during SBT.

Furosemide has been associated with negative fluid balance, shorter duration of mechanical ventilation, and a stronger effect in patients with LV systolic dysfunction.[27,29] Nitrates cause systemic venous dilatation leading to a reduction of central blood volume, arterial vasodilatation and thus a reduction in LV afterload, and coronary vasodilatation with improved myocardial oxygen delivery.[21,30]

The calcium sensitizer and ATP-sensitive potassium channel opener, levosimendan and phosphodiesterase-3 inhibitors such as milrinone, amrinone and enoximone have a vasodilatory effect in decreasing RV afterload and reducing RV failure, and they have shown evidence of improved LV function leading to successful weaning.[20,21,26] Phosphodiesterase-5 inhibitors, such as sildenafil, have shown efficacy in patients with COPD and pulmonary hypertension.[20] Beta-blockers such as atenolol and esmolol have been used in conjunction with angiotensin converting enzyme inhibitors and calcium channel blockers, in a subset of patients with cardiogenic pulmonary edema associated with LV diastolic dysfunction unmasked during SBT.[21] These treatment options can address weaning-induced cardiac dysfunction when established in a difficult-to-wean patient.

Cognitive Dysfunction

Delirium, depression, anxiety, and sleep disturbances make up the majority of weaning failure in ICU patients with prolonged admissions.[31,32] Importantly, treatment and patient factors lead to a dysregulation in circadian rhythms and contribute to cognitive dysfunction in difficult-to-wean patients. Frequent monitoring such as laboratory tests, radiological studies, and intra-hospital transportation for procedures can contribute to sleep fragmentation. Medications such as opioids and benzodiazepines and MV itself can also lead to disrupted sleep architecture and cognitive dysfunction. Older age, temperature dysregulation, comorbidities, and certain underlying psychiatric illnesses can also adversely affect weaning.[32]

Diaphragmatic Dysfunction

Common causes of diaphragmatic dysfunction include COPD, ICU-acquired weakness (ICUAW) such as critical illness polyneuropathy and critical illness polymyopathy, neuromuscular disorders such as myasthenia gravis, ventilator-induced diaphragmatic dysfunction, and phrenic nerve injury.[8,33,34]

To understand diaphragmatic dysfunction, measurements such as maximal inspiratory pressure (MIP), transdiaphragmatic pressure (Pdi), diaphragmatic ultrasound measurements, and diaphragm electromyography (EMG) may be useful.[11,22,34] MIP and maximal expiratory pressure (MEP) are tests of global respiratory muscle strength and can be measured using a hand-held device connected to the artificial airway.[11] A MIP above 30 cm H_2O is associated with a shorter time to successful extubation. Recording of esophageal pressure (Pes) and gastric pressure (Pga) using dedicated balloons allows calculation of transdiaphragmatic pressure ($\Delta Pdi = \Delta Pga - \Delta Pes$), a specific measure of diaphragm contractility.[13] Acquisition and interpretation of these measures requires expertise. Diaphragm ultrasonography is a practical and noninvasive tool for assessment of diaphragm excursion and thickness fraction. A diaphragmatic thickness fraction of >30–36% was associated with an increased likelihood of successful weaning after SBT.[34] Diaphragm EMG, a good indicator of neural respiratory drive to the diaphragm, may provide important data on respiratory muscle unloading, patient-ventilator interaction, and the effect of residual sedation on respiratory drive.[34]

More recently, phrenic nerve stimulation devices have alleviated phrenic nerve induced weaning failure. The Lungpacer DPT System™ is designed to electrically stimulate the phrenic nerves of a patient through a temporary, single use, indwelling multi-electrode stimulating catheter (LIVE Catheter). There is a proximal electrode targeting the left phrenic nerve and distal electrode targeting the right phrenic nerve. As shown in the RESCUE 1 safety and feasibility trial, MIP increased by 105% in those successfully weaned (mean change 19.7 ± 17.9 cm H_2O; $p = 0.03$), while mean rapid shallow breathing index (RSBI) improved by 44% (mean change -63.5 ± 64.4; $p = 0.04$).[35] In the European RESCUE 2 randomized control trial, change in MIP from baseline was significant [difference 15 ± 4 cmH2O, $p = 0.0002$]; change in RSBI from baseline was also significant [difference -30 ± 15, $p = 0.049$]; and both variables showed a stimulation dose-response relationship in temporary transvenous diaphragm neurostimulation candidates.[36]

Metabolic and Endocrine Dysfunction

Hypokalemia, hypophosphatemia and hypomagnesemia can lead to weaning failure. Adrenal insufficiency and hypothyroidism have also been associated with weaning failures. Corticosteroid use and strict glycemic control can reduce weaning failure.[10,13] Stress-dose corticosteroid supplementation before extubation of patients with adrenal insufficiency led to a significantly higher success rate for ventilator liberation and a shorter weaning duration.[37] Hypothyroidism carries a 3% rate of weaning failure and thyroid supplementation has been anecdotally linked to successful liberation from MV.[38]

Gastrointestinal and Renal Dysfunction

Intra-abdominal conditions and acute kidney injury (AKI) have shown to worsen outcomes while liberating patients from MV.[22,39] Intra-abdominal hypertension, pneumoperitoneum, hemoperitoneum, abdominal trauma, pancreatitis, end-stage liver disease, liver transplantation can lead to ARDS.[22] As the pressure-volume curve shifts to the right since the compliance decreases from the upward deflection of the diaphragm's initial position; the respiratory workload increases and there is an increase in inspiratory pressures required to ventilate.[22] Furthermore, in comparison to patients without AKI, patients with AKI are less likely to wean and are prone to difficult

liberation.[39] They are also more likely to have longer duration of MV in ICU and increased LOS in the ICU.[39] These organ-specific dysfunctions aggravate some patients' ability to be disconnected successfully from MV.

Nutrition

Malnutrition frequently occurs in ventilated patients and is associated with poor prognosis. Nutritional status can be evaluated by determining body mass index, plasma albumin concentration, and nitrogen balance. Ideally, energetic needs should be determined by indirect calorimetry to prevent under- or over-feeding.[13]

Process of Usual Weaning

The weaning period consists of a two-step strategy which involves readiness assessments and SBT. To assess readiness, clinicians must first address clinical and objective criteria as early as 48–72 hours into an ICU admission. Sedation vacation plays a major part in readiness assessments. Reversible contributors to respiratory failure (eg, electrolyte derangements, volume overload, pneumonia, and other pathophysiologic factors) should be corrected. Subsequently, objective criteria to further assess readiness should be applied (Table 2).

When these criteria are met, the patient can be assessed for parameters predicting weaning success. In 2012, McMaster University evaluated the role of eight parameters with significant likelihood ratios for predicting ventilator discontinuation success (Table 3).[6,40] Despite the statistical significance of these parameters, the generally low likelihood ratio indicate that the clinical applicability of these parameters alone to individual patients is inconsequential.[6]

In a landmark study, an RSBI of <105 was associated with a 97% probability of successful extubation while an RSBI of >105 carried a 64% probability of extubation failure.[41] However, a follow up meta-analysis showed much lower pooled sensitivity and specificity of 84% and 44%, respectively.[42] Additionally, a comparison of RSBI with clinical decision to wean showed a significantly shorter median duration for weaning time when RSBI was not used (2.0 vs. 3.0 days, $p = 0.04$).[43]

Table 2. Objective Criteria for Readiness Assessments.

1. Improved etiology for respiratory failure
2. $PaO_2/FiO_2 \geq 150$ or $SpO_2 \geq 90\%$ on $FiO_2 \leq 40\%$ and PEEP ≤ 5 cmH_2O
3. pH >7.25
4. Hemodynamic stability (no or low dose vasopressor medications)
5. Initiate inspiratory effort
6. Hemoglobin ≥ 7 mg/dL
7. Core temperature $\leq 38\,^{\circ}C$
8. Awake and alert or easily arousable.

Spontaneous Breathing Trials

Various SBT techniques have been proposed with varying types of support. A T-piece trial entails disconnecting the patient from the ventilator and providing additional oxygen (T-piece trial).[44] A pressure support ventilation (PSV) trial is performed without disconnecting the patient from the ventilator, using low levels of pressure support (PS 5-8 cm H_2O, PEEP ≤ 5 cm H_2O, $FIO_2 \leq 0.4$-0.5).[45] Automated tube compensation (ATC) is based on an indirect closed-loop working principle. It compensates for the flow-dependent pressure drop across the tracheal tube during both inspiration and expiration. ATC studies have shown to reduce work of breathing, increase respiratory comfort, and allow prediction of successful extubation.[46] ATC is not a stand-alone ventilatory mode, but rather a component of flow-proportional pressure support that can be combined with all conventional ventilatory modes.

The tolerance of a 30- to 120-minute SBT should prompt consideration for permanent ventilator liberation. If, however, a patient fails a SBT based on specific criteria (Table 4), the cause for the failed SBT must be determined. Once reversible causes for failure are corrected, SBT should be reattempted every 24 hours and matched with spontaneous awakening trials. Following failed SBT, patients should receive a stable, non-fatiguing, comfortable form of ventilatory support.[6]

Sedation, Neuromuscular Blockade, Early Mobilization, and Ventilator Weaning

The goal of adequate sedation is to minimize pain and anxiety during mechanical ventilation without disrupting the patient's ability to assume spontaneous breathing.[8] Commonly used sedatives include propofol, fentanyl, dexmedetomidine, and benzodiazepines. A daily interruption in sedation linked with a weaning trial has been shown to maximize the patient's breathing potential and reduce the time spent on MV, frequency of complications, and costs.[18,24,25,47] In 2013, the ACCM/SCCM task force endorsed sedation strategies that

Table 3. Ventilator Parameters Studied in Weaning.

Parameters	Threshold Values	Range of Positive Likelihood Ratios
Ventilator Measurements		
V_E	10–15 L/min	0.81–2.37
Negative inspiratory force	−20 to −30 cm H_2O	0.23–2.45
P_{Imax}	−15 to −30 cm H_2O	0.98–3.01
$P_{0.1}/P_{Imax}$	0.30	2.14–25.3
CROP index	13	1.05–19.74
Parameters Measured during SBT		
f/V_T	60–105 breaths/min/L	0.84–4.67

V_E = minute volume; P_{Imax} = maximum inspiratory pressure; $P_{0.1}$ = airway-occlusion pressure 0.1 s after the start of inspiratory flow; CROP index = compliance, rate, oxygenation and pressure index; RSBI (f/V_T) = rapid shallow breathing index; Adapted from Reference.[6]

Table 4. SBT Failure Criteria.

- Respiratory rate >35 breaths/min
- Increased accessory muscle activity
- SpO_2 persistently <92% (or < 88% in case of underlying chronic lung disease) on FiO_2 ≥0.4 or at least 6L/min of oxygen
- Hemodynamic instability defined as HR >140 bpm or SBP 180 mm Hg, with signs of hypoperfusion (appearance of cyanosis or mottling)
- Depressed mental status or agitation

preferentially use nonbenzodiazepine sedatives (either propofol or dexmedetomidine) over benzodiazepines (either midazolam or lorazepam) to improve clinical outcomes in mechanically ventilated adult ICU patients (Evidence Level + 2B).[48,49] The ATS/ACCP recommend the use of a protocol to minimize sedation in acutely hospitalized patients ventilated >24 hours.[18,24,25]

One of the limits to the use of neuromuscular blocking agents (NMBA) in the ICU is the occurrence of ICUAW. The incidence of ICUAW is 34–60% in patients with ARDS.[50] Female gender, multiple organ dysfunction (≥2), duration of MV, administration of corticosteroids, duration of vasopressor support, ICU length of stay (LOS), hyperglycemia, low serum albumin, and neurological failure are all independent risk factors for ICUAW.[51] Furthermore, the concomitant use of NMBA and corticosteroids and infusion of NMBA exceeding 48 hours favor the development of ICUAW.[52] However, in a recent meta-analysis of NMBA use in ARDS, cisatracurium was not associated with an increased risk of ICUAW.[53] NMBA do not increase the risk of ICUAW, when used for a short duration and without concomitant steroids.[53]

Early mobilization has been shown to decrease the incidence of ICUAW, improve functional capacity, increase number of ventilator-free days, and reduce delirium, ICU readmissions, and ICU LOS.[54] In mechanically ventilated patients >24 hours, protocolized rehabilitation directed toward early mobilization has been recommended.[18,24,25] ICU clinicians must be cognizant of several barriers to early mobilization, including those related to patients and processes of care, inadequate rehabilitation medicine and ICU staffing, and cultures within the ICU and healthcare organizations.[55]

Weaning Techniques: What's the Evidence?

In the 1990s, two types of SBT (T-piece and PSV) were performed with nearly the same frequency.[56] However, these two techniques are not equivalent in terms of patient breathing effort. Physiological studies have shown that work of breathing measured during T-piece was similar to work of breathing after extubation. In contrast, work of breathing is markedly lower during PSV trial than during T-piece. Consequently, while PSV trial may potentially hasten extubation, it may also increase the risk of reintubation by underestimating the work of breathing needed after extubation.[56]

Several seminal trials have evaluated the aforementioned techniques. In the Spanish Lung Failure trial, four weaning techniques were compared: SIMV, PSV, intermittent trials of spontaneous breathing, and once-daily trial of spontaneous breathing with a T-piece. After adjustment for baseline characteristics in a Cox proportional-hazards model, the rate of successful weaning with a once-daily trial of spontaneous breathing was 2.83 times higher than with SIMV ($p < 0.006$) and 2.05 times higher than that with PSV ($p < 0.04$). The length of time from the initiation of weaning to successful extubation was shorter in the intermittent and once-daily trials group in comparison to the SIMV/PSV group.[56] However, in the same year, Brochard showed diametrically opposite results.[44] A lower number of weaning failures was found with PSV than with T-piece and SIMV (8% PSV; 43% T-piece; 42% SIMV; $p = 0.05$). With PSV, the probability of remaining on MV was lower ($p < 0.03$), and both weaning duration and ICU LOS were shorter ($p < 0.05$ and $p < 0.001$, respectively).[44] These seminal trials paved the way for our current societal recommendations, for acutely hospitalized patients ventilated >24 h, the initial SBT should be conducted with inspiratory pressure augmentation (5-8 cm H2O) rather than without (T-piece or CPAP).[18,24,25] However, they do not inform how to ventilate patients between unsuccessful SBTs.[18]

In a trial to determine whether an initial SBT using PSV could increase successful extubation rates among patients at high risk of extubation failure by comparing PSV or T-piece as weaning techniques, the authors concluded that PSV may hasten extubation without an increased risk of reintubation.[57] Furthermore, in patients who are high risk of extubation failure after being ventilated for >24 hours and who have successfully completed their initial SBT, extubation to preventive non-invasive ventilation (NIV) is recommended.[18,24,25]

In an attempt to increase a patient's chances of remaining extubated and successfully weaned from MV, it was postulated that resting respiratory muscles after a SBT would prevent extubation failures. However, reconnection to MV after a successful SBT compared with direct extubation did not result in a statistically significant reduction (12.9% vs. 18.2%, 95% CI [-2.49 to 13.12]; $p = 0.18$) in the risk of reintubation in MV patients.[58]

Moreover, a recent multi-center trial investigated ventilator weaning and discontinuation practices for critically ill patients in 142 ICUs over a three-year period.[59] Of the 1868 patients enrolled in the study, 68.7% survived and were extubated from MV after a SBT. During the SBT, 49.1% used low-level PSV, 25.4% used a T-piece trial, and 10.8% used CPAP. The remaining patients (31.3%) were extubated directly without a breathing trial.[60] In the US, SBT is used widely compared to other countries. Outcomes showed that patients who received SBT fared worse than those who underwent direct extubation (10.3% vs. 4.7%), longer invasive MV duration (4.1 vs. 2.9 days), and longer ICU LOS (8.1 vs. 6.7 days).[60] The regional variability seen is likely due to differences in screening tool utilization, ventilator management, and early mobilization.[59]

Standardized Weaning Protocols

The initial use of weaning protocols came into existence after three randomized controlled trials totaling approximately 1000 patients.[61–63] In 1996, a study of medical and cardiac critical care units demonstrated a decreased duration of mechanical ventilation, lower costs, and fewer reintubations in the group adhering to a weaning protocol.[61] The same findings were corroborated in 1997.[62] In 2000, protocolized weaning was associated with a trend for reduced rate of ventilator-associated pneumonia in a subset of trauma patients in surgical intensive care units.[63] In a systematic review and meta-analysis, protocolized weaning in comparison to usual care showed beneficial effects in medical, surgical, and mixed ICU.[8] However, in mostly closed ICU with generous staffing of physicians, respiratory therapists and nurses, and with structured multidisciplinary system-based rounds, clinical equipoise exists on the value and role of protocol-directed weaning.[64]

Conclusion

The ICU team must evaluate readiness to wean as early as possible and mitigate risk factors for weaning failure. For patients who fail weaning trials, a detailed structured approach is critical in trying to identify potential causes and mechanisms. If these causes are reversible, corrective measures must be promptly undertaken to enable patients to overcome their clinical condition and achieve adequate cardiopulmonary tolerability to SBT. Standardized weaning protocol are attractive and compelling for most ICUs. In the era of patient-customized care, it is important to choose a patient-appropriate mode to wean. Finally, as intensivists, when we address the question: to wean or not to wean, let us allow our patients to be our best guides.

Abbreviations

ICU	intensive care unit
SIMV	synchronized intermittent mandatory ventilation
SBT	spontaneous breathing trial
SV	spontaneous ventilation
PSV	pressure support ventilation
MV	mechanical ventilation

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Ethical Approval

Not applicable, because this article does not contain any studies with human or animal subjects.

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