Weaning from mechanical ventilation in chronic obstructive pulmonary disease: Keys to success

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Abstract

Invasive mechanical ventilation (IMV) for management of chronic obstructive pulmonary disease (COPD) associated respiratory failure is increasing in Intensive Care Units. However, IMV is not without its own complications. Hence, aim of managing such patients is to get them off the ventilator as early as possible. This bridging process from IMV to extubation is called weaning in which mechanical ventilation is gradually withdrawn and the patient resumes spontaneous breathing. Many objective parameters have been defined for weaning success. Many of these patients are difficult-to-wean because of various pathophysiologic mechanisms that are of particular relevance to patients of COPD. The following review focuses on these mechanisms and how to troubleshoot patients who are difficult-to-wean.

Key words: Chronic obstructive pulmonary disease, ventilation, weaning

INTRODUCTION

Prolonged mechanical ventilation (MV) leads to high resource utilization and poor outcomes. Increasing use of MV for the management of chronic obstructive pulmonary disease (COPD) associated respiratory failure has in turn increased the burden of patients with difficult weaning in Intensive Care Units (ICUs) worldwide. Weaning from MV is a process where MV is gradually withdrawn and the patient resumes spontaneous breathing,[1] thereby meaning liberation or freedom from ventilator. Difficult-to-wean patients are defined as those who require more than 7 days of weaning after first spontaneous breathing trial (SBT).[2] Data collected from studies in various ICUs have estimated that approximately 20–30% of mechanically ventilated patients fulfill this criteria.[3] In patients with COPD on MV, almost 50% meet this criteria,[4] highlighting the importance of delayed weaning in this subgroup of patients, as longer MV duration leads to increased complications and in-hospital mortality. Mortality is around 2.6% in successfully weaned patients whereas it is significantly higher at 27% in those requiring re-intubation.[5] Invasive ventilation leads to considerable reduction in respiratory muscle strength and increase in the incidence of ventilator-associated pneumonia. If the weaning procedure is started early, it can often lead to cardiorespiratory failure. On the other hand, if it is started too late, it can be unsuccessful because of respiratory muscle weakness caused by deconditioning and disrupted breathing regulation,[6] so optimal time of decision to wean is of utmost importance in modern ICUs.

Liberating a COPD patient from ventilator is a continuous process as with any other disease condition which starts with recognition of patient being ready to be weaned from ventilator by letting the patient breathe on T-piece and,
if successful, proceeding to SBT followed by extubation, if it is tolerated well (simple weaning), else letting the patient on ventilator till next such trial till being successful. Before the next trial, patient needs to be evaluated for the possible causes of weaning failure and its correction in an individual patient (difficult weaning −33%). Repeated failures of SBT >3 times or longer than 7 days on ventilator make patients more dependent on ventilator (prolonged weaning −20%). Such patients are more challenging and need interventions to prevent such patients from becoming permanent weaning failures where either transfer to dedicated weaning centers or home ventilation are the options left for them [Figure 1].

Patients after successful extubation may require re-intubation due to “extubation failure,” which carries high mortality and morbidity and needs to prevented using accurate predicting indices prior to extubation using various clinical and laboratory parameters, while patient is being put on SBT and bridging with noninvasive ventilation (NIV) in high risk for failures.

FIRST KEY TO SUCCESS: RECOGNITION OF READINESS TO WEAN

COPD patients are put on MV on account of giving rest and are invariably needed for 48–72 h. Readiness to wean is the first step to recognize as soon as possible for every patient on ventilator. This is assessed by the following criteria:

• Acceptable oxygenation – PaO\textsubscript{2}/FiO\textsubscript{2} >200 on positive end expiratory pressure (PEEP) <4 cm H\textsubscript{2}O
• Hemodynamic stability – no vasopressors infusions
• Adequate neurological response – awake or arousable
• Cough and secretions – good cough on endotracheal tube suction with manageable secretions
• Respiratory response – rapid shallow breathing index (RSBI) <100 after 2 min of SBT.

RSBI has a sensitivity of 87 ± 14% with a specificity of 52 ± 26% and is by far most widely used index for readiness to wean predicting high chances of passing SBT trial. However, it is to be followed by SBT trial in all patients who are ready to wean, which has been shown to occur in 60% only.

SECOND KEY TO SUCCESS: CLOSELY MONITORED AND PROTOCOLIZED SPONTANEOUS BREATHING TRIAL

The SBT simulates the conditions after extubation and should therefore, be performed without PEEP and pressure support. Once patient is considered ready to wean, patient is given SBT for 2 h and proposed criteria for failure during 2 h on T-piece are listed in Table 1. However, some of these criteria singly may not be an indication to abandon and label it a “SBT failure” as readiness to wean does not predict the success of SBT trial [Figure 2].

THIRD KEY TO SUCCESS: EVALUATE THE CAUSE OF SPONTANEOUS BREATHING TRIAL FAILURE, RECTIFY, AND REPEAT SPONTANEOUS BREATHING TRIAL NEXT DAY

Failure of first SBT trial makes patient difficult-to-wean and its cause in an individual patient needs to be evaluated.

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**Figure 1:** Scheme of weaning and interventions recommended
Common causes of weaning difficulty are enumerated in Table 2. Multiple pathophysiologic mechanisms may exist in COPD patients in and each has to be evaluated and managed individually for next SBT trial.

FOURTH KEY TO SUCCESS: SUSPECT, DIAGNOSE, AND TREAT SPECIAL CONDITIONS PERTAINING TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH WEANING FAILURE

Approximately, 60% COPD patients fail the first SBT trial with 40% experiencing difficulties in weaning.[7] Six common conditions peculiar to COPD patient’s failing to wean, needs special attention are given below.

Tracheal obstruction
According to a study by Rumbak et al., tracheal injury leads to weaning failure in patients on invasive mechanical ventilation (IMV) for more than 4 weeks.[8] Tracheal injury includes tracheal stenosis, tracheomalacia, and granulation tissue formation. Secretions in the endotracheal tube also increase resistance. Paradoxical increase in upper airway resistance postextubation due to edema of upper airways needs to be suspected when patient develops laryngospasm immediately after extubation.[9] Flexible fiberoptic bronchoscopy of computerized tomography scans with three-dimensional reconstruction images are used to diagnose tracheal stenosis or tracheomalacia.

Increased airway resistance
Airway resistance has been found to be significantly greater in patients who failed weaning trial as compared to successful trial in same patients. Expiratory flow limitation along with high respiratory drive can lead to respiratory muscle fatigue, which is a contributing factor for prolonged ventilation. Cornerstone in the management of ventilated COPD patients is to reduce bronchoconstriction using bronchodilators and anti-inflammatory drugs. Guidelines have been published for optimizing delivery of inhaled medications in ventilated patients.[10]

Inspiratory muscle fatigue
Dynamic hyperinflation in COPD patients leads to flattening of diaphragm. Its contraction requires more work of breathing being at flat part of length-tension relationship. Levine et al.[11] found significant diaphragmatic muscle atrophy in patients mechanically ventilated for 18–96 h. Isolated measurement of Maximal Inspiratory Pressure does not take into account inspiratory muscle endurance; hence, its role as a weaning predictor is controversial.[12] Absence of hypercapnia in a weaning-failure patient virtually excludes inspiratory muscle fatigue. Rehabilitation and muscle retraining with inspiratory muscle training has an important role in successful weaning in patients unable to wean. Antioxidant supplementation with N acetylcysteine may attenuate low-frequency human diaphragm fatigue and has been shown to reduce ventilator-dependent days.[13]

Acute cardiac dysfunction
Acute cardiac dysfunction can contribute in weaning failure. Airway obstruction and dynamic hyperinflation in mechanically ventilated COPD patients can increase preload by increasing venous return. Patients with occult cardiac dysfunction cannot tolerate this additional load and can lead to the development of cardiogenic pulmonary edema during weaning of difficult-to-wean COPD patients.[14] Weaning also results in increase in afterload, which is more prominent in patients with...
systemic hypertension and in a study by Routsi et al., they showed beneficial effect of vasodilatory therapy using nitroglycerine in difficult-to-Wean COPD patients with hypertension.[14]

Nonthyroidal illness syndrome
Nonthyroidal illness syndrome (NTIS) is a variable condition of abnormal thyroid hormone concentrations that can rise in the serum following any acute or chronic illness that is not due to an intrinsic abnormality in thyroid function.[18] The prevalence of NTIS is about 60–70% in patients admitted to the ICU.[16] The proposed pathogenesis is imbalance between the activities of Types I and II deiodinase, decreased sensitivity of the hypothalamus and pituitary gland to thyroid hormones, and reduced T4 protein binding and cellular uptake.[17] NTIS has been seen in MV in ICU patients.[19] COPD is associated with hypoxemia, which can cause abnormal thyroid hormones. Yasar et al. proposed NTIS to be an independent predictor of prolonged weaning in intubated COPD patients.[19] Whether thyroid hormones substitution is helpful in weaning is unknown.

Critical illness neuromyopathy
Critical illness neuromyopathy (CINM) includes critical illness neuropathy and critical illness myopathy, which often co-exist, but usually myopathy predominates. It is common in the mechanically ventilated (25–60% patients ventilated for >7 days) patients. Multiple pathogenic factors are involved in its causation including axonopathy, mitochondrial dysfunction, microvascular ischemia, sodium channelopathy, catabolism, and immobility. CINM is associated with sepsis, systemic inflammation, poor glycemic control, steroids, neuromuscular blocking agents, immobility, and malnutrition.[20] CINM presents as flaccid quadriparesis with hypo or areflexia and confirmed by nerve conduction and electromyography studies.[21] Optimal therapy for this condition is unknown. Treatment is usually supportive therapy with intensive glycemic control, minimizing the use of corticosteroids and neuromuscular blockade, early mobilization, neuromuscular stimulation, electrolyte replacement, and optimizing nutrition. Nearly, 70% of survivors recover completely over 4–5 months.[22] Low body mass index and wasting in COPD patients predisposes to CINM and prevention and treatment need early extubation with the use of NIV. Physiotherapy with early mobilization of critically ill patients is a relatively new management strategy advocated to address and to reduce the disability associated with ICU-acquired weakness.[23] This therapeutic approach has been reported in clinical studies and is recommended by the European Respiratory Society.[24]

Nutritional abnormalities
Weaning from artificial nutritional intake with the subsequent possibility to eat is an essential rehabilitative outcome in tracheostomized difficult-to-wean COPD patients. In these COPD patients, meals may induce an increase in respiratory rate, end-tidal carbon dioxide, and dyspnea. Inspiratory pressure support ventilation (PSV) during meals may prevent worsening of dyspnea.[25] Percutaneous endoscopic gastrostomy (PEG) as a measure of enteral feeding has gained wide acceptance, and it is currently the preferred method for providing enteral nutrition in long-term settings with the aim to prevent the most serious complications. Short-term studies have demonstrated the advantages of PEG as compared with the nasogastric tube feeding in patients with dysphagia due to chronic neurological diseases. PEG insertion is a quick procedure that is generally well tolerated by patients, and a relatively low complication rate in the outcome has been described.[26] Obese individuals with COPD may have associated obstructive sleep apnea. These patients may be more difficult to wean and require early use of NIV post-extubation.

FIFTH KEY TO SUCCESS: RECOGNIZE AND CORRECT PATIENT–VENTILATOR ASYNCHRONY DURING WEANING
Intrinsic (PEEPi) is a common problem in patients with COPD leading to asynchrony and needs to recognized and treated as is associated with weaning failure. PEEPi has been reportedly higher in COPD patients with weaning failure as compared to those being successfully weaned.[27] Multiple mechanisms are responsible for the development of PEEPi in mechanically ventilated COPD patients, for example, insufficient expiratory time for complete emptying of lungs due to increased airflow resistance with expiratory airflow limitation and high breathing frequency and promotes patient–ventilator asynchrony. This leads to ineffective breaths being triggered, a significant factor for difficult weaning. A study by de Wit et al. demonstrated significantly longer duration of MV in patients with more than 10% ineffective trigger breaths.[28]

SIXTH KEY TO SUCCESS: CHOOSE NONINVASIVE VENTILATION TO FACILITATE WEANING
Gradual weaning methods
- Synchronized intermittent mechanical ventilation (SIMV)
- PSV
- SIMV + PSV
- Extubation + NIV.
A study by Matic et al. tried to compare T-tube weaning with PSV in mechanically ventilated COPD patients in whom extubation failed after a 2-h SBT.\[29\] They found PSV to be more suitable than T-tube for difficult-to-wean patients with COPD based on shorter time needed for weaning from MV, total MV duration, and median time spent in ICU.

A prospective randomized controlled study, which included fifty COPD patients with Type II respiratory failure requiring initial invasive MV found statistically significant difference between groups weaned by noninvasive positive pressure ventilation (NIPPV) and those weaned by conventional PSV.\[30\] Randomization of patient groups was done after failing a T-piece trial. Statistically significant difference was found between the two groups in terms of duration of MV, weaning duration, length of ICU stay, occurrence of nosocomial pneumonia, and outcome, each favoring NIPPV. Authors concluded that NIPPV is a promising weaning modality for mechanically ventilated patients and be tried in resource-limited settings in developing countries.

Use of NIV has been shown to be more safe with lesser complications. It preserves the cough reflex and reduces the risk for ventilator-associated pneumonia.\[31\] With NIV, oral intake and speech can be maintained along with no requirement of sedation. In a recent Cochrane systematic review on NIV as a weaning strategy for MV in adults with respiratory failure, which included 16 trials, suggested that noninvasive weaning reduces mortality and pneumonia without increasing the risk of weaning failure or re-intubation [Figure 3].\[32\]

In subgroup analysis, the authors found significantly reduced mortality in noninvasive weaning in patients with COPD compared involving mixed populations. This recent meta-analysis again confirmed the importance of NIV in weaning of COPD patients. NIV application immediately postextubation of COPD patients can reduce SBT time to 30 min or 1 h and can lead to successful extubation even after failure of SBT trial.

**SEVENTH KEY TO SUCCESS: RECOGNITION AND PREVENTION OF EXTUBATION FAILURES**

Extubation failure is defined by the need of re-intubation within the 48 or 72 h of extubation and is associated with significant deterioration in patients’ clinical condition. This occurs in 10–20% of patients and needs to be avoided as carries up to 50% mortality and is highest for late re-intubations partly due to different severity of disease and of underlying comorbidities at the time of extubation, but also contributed by clinical deterioration directly generated by extubation failure and respiratory distress of re-intubation, and later by the issues of prolongation of MV. As organ failures have been shown to worsen after re-intubation with increase in mortality, it is prudent to prevent it as far as possible by refining decisions to extubate and postextubation management. Hence, to make extubation in COPD a success, there is a need to optimize preextubation strategies as well as postextubation interventions so as to prevent re-intubation.

**Management prior to extubation**

Preventing extubation failure needs to optimize patient prior to extubation so as to address the causes of extubation failure which are similar to the causes of weaning failure mentioned earlier with fluid balance and cardiac dysfunction being of more significance in COPD. Left ventricular heart failure and/or fluid overload is the recognized cause for extubation failure as and biomarkers such as BNP or NT-proBNP may play a role in optimizing fluid therapy prior to extubation.\[33\] Patient’s own confidence predicts success in 90% versus 45% in patients not confident about their own extubation.

**Management after extubation**

Hypercapnia is more than a good predictor of extubation failure in COPD during SBT and is a marker for the need of prophylactic NIV after extubation.\[35\] Prophylactic NIV after extubation may prevent acute respiratory failure (ARF) and has been shown to reduce mortality in selected high risk population of patients, for example, COPD.\[35-37\] At-risk patients include at least one weaning trial failure, PCO2 >45 mmHg during the T-piece trial, and chronic heart failure.\[38\] Using these various criteria, the use of NIV resulted in a reduction of risk of ICU mortality.\[36\] Preventive NIV should probably be systematically applied immediately after extubation of hypercapnic patients. The excellent clinical tolerance of this technique could facilitate its systematic application.

![Figure 3: Effect of noninvasive weaning on weaning failures](http://www.jacpjournal.org/)

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<th>Subgroup and study</th>
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<th>Control No. of events patients</th>
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<td>Total 307 298 0.63 (0.42 to 0.98)</td>
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**Figure 3:** Effect of noninvasive weaning on weaning failures.
EIGHTH KEY TO SUCCESS: REMEMBER WHEN NOT TO USE NONINVASIVE VENTILATION

When patient has established weaning failure, there is no clear role of using NIV with curative intent to treat extubation failure. Although its feasibility has been suggested by Meduri et al.,[38] subsequently, a multicenter study involving 221 patients (20% postoperative ARF) was later stopped on the basis of intermediate analysis which showed significantly increased ICU mortality in NIV group (25 vs. 14%).[39] Current results should prompt clinicians to be cautious in using “curative NIV” routinely in the management of postextubation ARF in medical ICU patients, not to delay re-intubation. There is no study that addressed the issue of use of NIV in patients who get self extubated.[40]

NINTH KEY TO SUCCESS: JUDICIOUS USE OF TRACHEOSTOMY

The use of tracheostomy is increasing in patients requiring prolonged MV,[41] although the advantage of this strategy on outcome is still debatable. In some studies, tracheostomy did not favorably influence ICU survival,[42] whereas it has been reported that tracheostomy performed in ICU for long-term MV patients was associated with lower ICU and in-hospital mortality rates.[43] Efforts should be made to identify patients who might clearly benefit from this technique to avoid unnecessary and unwanted prolonged MV. A recent survey on 719 patients from 22 Italian respiratory ICUs shows that tracheostomy was maintained in a substantial proportion of patients without any need for home MV.[44] Consequently, the decision to perform tracheostomy is more of an experience driven, rather than an evidence-based decision and should be made with caution.

TENTH KEY TO SUCCESS: AVOID INVASIVE MECHANICAL VENTILATION

The most important decision at the time of intubation in a patient of COPD with respiratory failure is to intubate or use NIV. Unless clearly contraindicated, such patients should be tried on NIV first and to intubate only if it fails. Unconsciousness, hemodynamic instability, severe acidosis (pH<7.20) and hypercapnia (>80 mmHg) are contraindications for use of NIV. Severe encephalopathy is also considered a contraindication to NPPV due to the concern that a depressed sensorium would predispose the patient to aspiration. In a prospective case-control multicenter study of patients with acute exacerbation COPD and moderate to severe hypercapnic encephalopathy, the use of NIV versus IMV was associated with similar short- and long-term survivals with fewer nosocomial infections and shorter durations of ventilation and hospitalization. In a single-center study in patients of COPD with respiratory failure and do not intubate (DNI) orders showed 45% survival, which was much less than the group with full resuscitation orders, but encouraging to use NIV in such situations.[45]

CONCLUSION

Successful liberation of COPD patients from MV needs all patients with COPD be assessed on a daily basis for their readiness to wean, followed by SBT, which may be abbreviated to be followed by extubation and use of NIV to facilitate weaning and preventing extubation failure. Optimization of ventilatory strategy, bronchial hygiene, relief of bronchospasm, and reversal of underlying disease form cornerstones to successful weaning. Special emphasis of physiotherapy, nutrition and systemic illness, and comorbidities associated with COPD needs proactive management. Given the data supporting the use of NIPPV postextubation in COPD patients, its use for this indication should be increased, especially in resource-limited settings and extending to situations such as DNI. However, meticulous monitoring and technically skilled staff make an integral component of good dedicated NIV unit to cater to patients with COPD and difficult weaning and should be established in each tertiary care unit to achieve best outcomes in such patients.

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Conflicts of interest
There are no conflicts of interest.

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