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How Medical Conditions Affect the Weaning of Mechanical Ventilation

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Abstract

Weaning from mechanical ventilation is a common process in critically ill patients and its failure is related to worsening outcomes. A better understanding of the subject is necessary to change these unfavorable results. This chapter will review the approach to weaning from mechanical ventilation in special groups of critically ill patients. The chapter will also review the causes of failure to wean from MV along with strategies for improving evaluation and approach of the patient with difficult and prolonged weaning from mechanical ventilation. Therefore, the presence of this topic in a book on mechanical ventilation is fundamental and relevant.

Keywords: critical illness, intensive care unit, respiratory failure, mechanical ventilation, mechanical ventilator weaning

1. Introduction

Mechanical ventilation (MV) is a lifesaving intervention in critically ill patients. MV is commonly used for postoperative respiratory failure, trauma, pneumonia, sepsis, heart failure (HF), chronic obstructive pulmonary disease (COPD) and acute respiratory distress syndrome (ARDS) [1, 2]. After the condition that caused the use of MV improves, the process of removing invasive ventilatory support begins, which is called weaning from MV [3, 4]. The MV weaning process is crucial and frequent in the critically ill patient's recovery. Almost 50% of the total duration of MV is dedicated to weaning patients [3]. However, some patients may fail to wean from MV despite all criteria in a planned extubation. This extubation failure is reported in around 10–20% of critically ill patients and, consequently, this weaning failure group has a high mortality when compared to patients who successfully weaned from MV [5–9].

The MV weaning and failure process have been studied since the 70s and 80s [10–13]. Milic-Emili questioned that the MV weaning performed in this period was more based on art than science because there were few scientific studies on the topic [14]. Studies in subsequent decades evaluated the best ventilatory mode to perform weaning from MV as well as predictors of weaning from MV [15–19]. After advances in the study of MV weaning, guidelines were formulated establishing

better criteria for evaluating the weaning process [20, 21]. Despite this, there are still different ways to practice MV weaning among intensive care units (ICU) in different countries, suggesting the need for more studies on the topic [4].

This chapter aims to review the weaning from MV in special subgroups. How to evaluate and to manage MV weaning will be discussed.

2. Weaning from mechanical ventilation in special groups

The cause of weaning failure may be related to individual or associated dysfunctions (respiratory, muscular, cardiac, neurological, endocrine, metabolic and iatrogenic). However, understanding the pathophysiology of MV weaning failure can be complex in some cases and it is not always fully understood, making its treatment difficult (**Figure 1**). When a patient does not pass a weaning trial, structural evaluation could help to identify factors that played a role in that specific patient. Moreover, it is important to know and to understand peculiarities of some critical patient subgroups in order to achieve more successful weaning. The **Table 1** summarizes the main characteristics, assessment and management of the main groups of patients in the process of weaning from mechanical ventilation admitted to an ICU.

2.1 Chronic obstructive pulmonary disease

In COPD patients, the weaning process is more difficult, prolonged and has higher failure rates than general populations. The higher failure rates in COPD patients can be attributed, at least in part, to the underlying pathophysiology of the disease. In COPD patients with acute respiratory failure, dynamic hyperinflation and the generation of intrinsic PEEP are the main factors that causes increased intrathoracic pressure, which lead to increased work of breathing, MV-induced injury, asynchrony, dyspnea, hemodynamic worsening, in addition to MV dependence and weaning failure [22]. In this population, the use of prophylactic non-invasive ventilation (NIV) after extubation is also recommended, considering this group of patients is at high risk of failure. The use can be extended to immediate extubation for NIV of COPD patients who have failed T-tube spontaneous

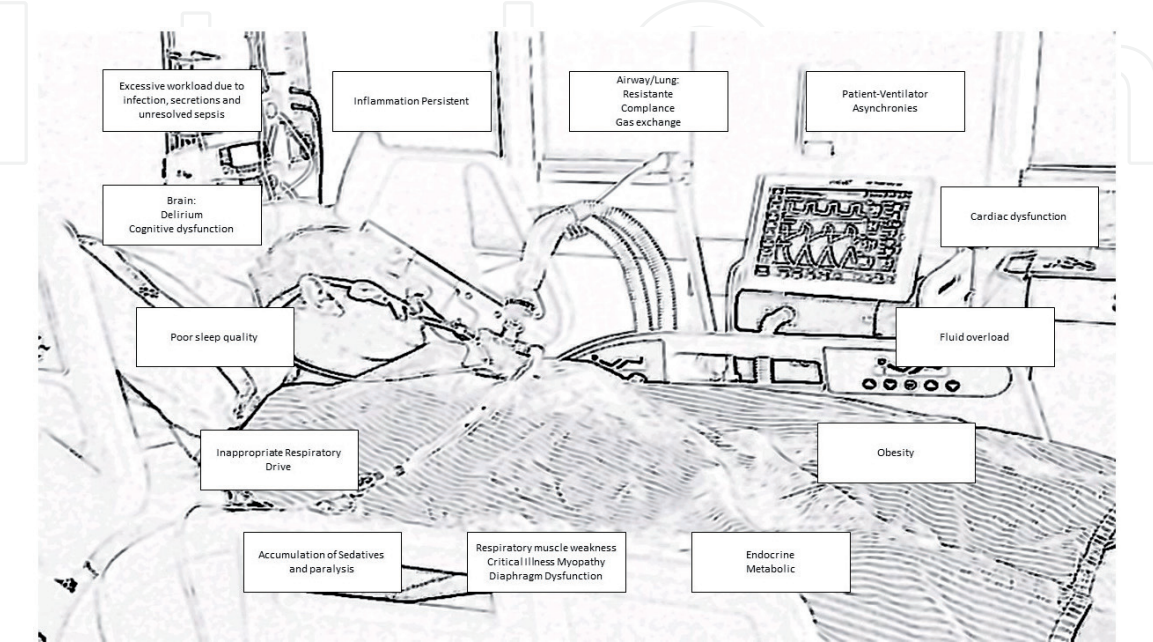


Figure 1.
Aspects of mechanical ventilation weaning failure.

Group	Characteristics	Assessment and Management
COPD	Higher weaning failure and MV dependence Dynamic hyperinflation and intrinsic PEEP	Extubation for NIV
Heart Failure	Increased left ventricular preload which afterload with reduction of the left ventricular ejection fraction	Electrocardiogram and an echocardiography Collecting a pro-brain N-terminal natriuretic peptide/central venous blood gas SvO2 Medications can also be used to optimize ventricular function – inotropic Volume overload should be adjusted - diuretics Extubation for NIV to maintain a PEEP
Neurological Dysfunction	Reduction in the level of consciousness did not impede successful extubation Ability to handle secretions and airway protection are relevant	Daily screening to assess MV weaning CAM-ICU Performing non-pharmacological and pharmacological measures for delirium
Neuromuscular Diseases	Neuromuscular alterations are relatively common Primary neuromuscular disturbance ICU-acquired muscle weakness Diaphragmatic muscle weakness can also impair weaning	Avoiding exposure to medications and hyperglycemia Motor rehabilitation
ARDS	The dangerous of excessive spontaneous ventilation with higher respiratory demands and loss of the protective-ventilation strategy Increased lung volumes, higher respiratory drive, breath stacking, pendelluft and patient-ventilator asynchrony	Evaluation of MV weaning does not differ from others patients Caution in the higher respiratory patients demands and its ventilatory repercussions
Obesity	The large weight on the rib cage can causes alveolar collapse	Higher PEEP during the pre-extubation period to prevent alveolar collapse Use of NIV
Prolonged Weaning	~10% of critically ill intubated patients High mortality Chronic critical illness	Multidisciplinary rehabilitation Swallowing dysfunction Tracheostomy Discussion of treatment goals
Others Care	Conditions for Weaning Progress: <ul style="list-style-type: none">• Adequate neurological status• Ability to cough and to manage respiratory secretions• Improvement of oxygenation• Hemodynamic stability	Use of protocols for weaning MV Daily screening for weaning with predictors Use of NIV in ICU patients at high risk for reintubation HFNC reduces the ventilatory work by supplying the demand and reversing the hypoxemic through of a high airflow therapy Cuff Leak Test: high risk of post-extubation stridor (traumatic intubation, prolonged intubation, large endotracheal tube, high cuff pressures, women and reintubation after unplanned extubation) Systemic corticosteroids recommended to patients with fail the cuff leak test Weaning Failure Causes: respiratory, muscular, cardiac, neurological, endocrine, metabolic and iatrogenic

Legend: MV, mechanical ventilation; NIV, non-invasive ventilation; CAM, confusion assessment method; HFNC, High-flow nasal cannula; COPD, chronic obstructive pulmonary disease; PEEP, positive end-expiratory pressure; ARDS, acute respiratory distress syndrome.

Table 1.
Weaning from mechanical ventilation in special groups.

breathing trial (SBT), with evidence of reduced length of stay in the ICU, nosocomial pneumonia and 60-day mortality, when compared to those weaned through invasive pressure support ventilation. These findings were corroborated by a recent meta-analysis [22, 23].

2.2 Heart failure

SBT causes spontaneous respiratory movements, which generate negative pressures and consequently hemodynamic repercussions. Negative intrathoracic pressures cause increased left ventricular (LV) preload which increases LV afterload and, ultimately, reduces left ventricular ejection fraction. This reduction in ejection fraction during an SBT can precipitate or worsen heart failure. Thus, if there are volume overload or systolic or diastolic left ventricular dysfunction, SBT can cause cardiorespiratory decompensation with pulmonary edema, reduced oxygen transport and insufficient cardiac output [24]. Furthermore, SBT can cause or worsen myocardial ischemia as a result of reduced left ventricular compliance, pulmonary edema and/or increased respiratory effort. To assess a possible cardiac dysfunction as a cause of weaning failure, it is suggested to perform an electrocardiogram and an echocardiography, in addition to collecting a pro-brain N-terminal natriuretic peptide and a central venous blood gas measuring SvO₂.

An accurate diagnosis of the mechanism of cardiac dysfunction is needed to better guide therapy. In difficult-to-wean patients, additional medications can also be used to optimize ventricular function [24, 25].

Volume overload should be adjusted before performing a SBT because it has been associated with worse weaning outcomes [24]. It can be treated with diuretics or hemodialysis and after that, direct extubation for NIV can be used in order to maintain a positive end-expiratory pressure. When there is evidence of heart pump failure, reduction in afterload and/or use of inotropic agents (such as dobutamine or milrinone) may be considered. Furthermore, the improvement in pulmonary mechanics itself will improve cardiac performance by reducing the afterload of the left ventricle [24].

2.3 Neurological dysfunction

The decision to extubate comatose neurocritical patients is complicated. Previous studies have shown that the reduction in the level of consciousness is a good predictor of extubation failure [26]. Coplin et al. have challenged common sense showing that patients with a Glasgow Coma Scale (GCS) 8 did not impede successful extubation [27]. Moreover, the delayed extubation in this population was related to more ventilator-associated pneumonia (VAP) and longer intensive care unit and hospital stays [28, 29]. Also, according to the study by Coplin et al., the professional should avoid prolonged intubation when the level of consciousness is the only reason to maintain MV. Navalesi et al. demonstrated that a daily screening to assess MV weaning is recommended for patients with neurological diseases to reduce the duration of MV [30]. Strategies that include protective ventilation, early enteral nutrition, standardization of antibiotic therapy for nosocomial pneumonia, and systematic testing to assess readiness for extubation showed an association with a reduction in MV time in brain injured patients [31].

There are still other concerns about the neurological status of patients able to wean from MV. A study has shown that the change in cognitive function had been associated with a four times greater risk of unsuccessful extubation [32]. The ability to handle secretions and airway protection is also a relevant issue. In addition, the causes of acute brain dysfunction in difficult-to-wean patients should be

considered, such as delirium, which is very common. The CAM-ICU can be a good tool to assess delirium in intubated ICU patients and performing non-pharmacological and pharmacological measures can help in symptomatic management. Improving hospital environments, for example, with poor noise and ICU-beds near to windows, besides frequent reassurance, touch, verbal orientation and family members presence can improve delirium symptoms [33]. Furthermore, it is important treating potential causal factors such as pain, constipation, infection and withdrawal of precipitating medications such as benzodiazepines and others [25]. In case of hyperactive delirium unresponsive to non-pharmacological measures, antipsychotics can be used for symptomatic management. Although there are no clinically significant differences between the classes of antipsychotics, haloperidol is one of the most used and studied.

2.4 Neuromuscular diseases

Weaning from MV requires adequate neuromuscular activity to overcome the impedance of the respiratory system and maintain adequate alveolar ventilation to eliminate carbon dioxide and ensure a metabolic balance. For this to happen, a generation of the stimulus by the central nervous system, adequate transmission via spinal respiratory motor neurons, respiratory muscles and neuromuscular junctions are necessary. Modifications anywhere of this complex system can contribute to MV weaning failure. Peripheral neurological alterations can also be the cause of weaning failure. Neuromuscular alterations are relatively common, being reported in up to 62% of patients in some studies [34]. Primary neuromuscular disturbance, such as Guillain-Barré syndrome, myasthenia gravis and motor neuron diseases, are usually diagnosed prior to intubation. Occasionally new diagnoses will occur as the difficulty of weaning from MV develops and is investigated.

In the ICU, the most common is secondary neuromuscular diseases, especially muscle weakness acquired in the ICU. It is a pure axonal disease, affecting mainly the peripheral nerves and muscles, symmetrical and bilateral and predominantly proximal. Prevalence between 50 and 100% is estimated in studies and is associated with disease severity, multiorgan dysfunction, exposure to corticosteroids, hyperglycemia and prolonged ICU stay [35–38]. Diaphragmatic muscle weakness can also impair weaning and its assessment can be challenging at the bedside, as the tests are either invasive and/or depend on the patient's ability to understand and to cooperate. There are studies that demonstrate an association between ICU-acquired muscle weakness and longer weaning duration or failure [34, 39–41]. Diaphragmatic muscle weakness can also impair weaning and its assessment can be challenging at the bedside, as the tests are either invasive and/or depend on the patient's ability to understand and to cooperate. There are studies that demonstrate an association between ICU-acquired muscle weakness and longer weaning duration or failure.

2.5 ARDS

In the early stages of MV in patients with acute respiratory distress syndrome (ARDS), the use of protective-ventilation strategies is recommended, as well as the use of neuromuscular blockers, prone position and extracorporeal membrane oxygenation (ECMO) in more severe cases [42]. However, during weaning from MV in patients with ARDS, this protective-ventilation strategy may be lost, mainly due to the influence of spontaneous ventilation with higher respiratory demands [43]. The increased lung volumes, higher respiratory drive, breath stacking, pendelluft and patient-ventilator asynchrony besides to delirium and ICU-acquired paresis may influence weaning from MV and should be considered in the assessment of patients with ARDS [44].

In addition, the use of the arterial-to-inspired oxygen ($\text{PaO}_2/\text{FiO}_2$) ratio to demonstrate improvement in hypoxemia, does not always translate into improvement in inflammatory response and weaning success [45]. Then, the premise for the beginning of weaning from MV based on $\text{PaO}_2/\text{FiO}_2$ ratio (resolution or improvement of the cause that led the patient to MV) is not always a good predictor to weaning success. Moreover, the management of MV weaning in these patients through consensus on weaning from MV generally does not include this specific group of patients [20, 21, 46]. Studies have shown that a greater proportion of patients have difficult and prolonged weaning when compared to the general ICU population [29, 47]. Therefore, regarding current knowledge, the evaluation of MV weaning does not differ in general from other patients. However, this subgroup has a particular pathophysiology that can influence and delay the evolution of the withdrawal of invasive ventilatory support.

2.6 Obesity

Obese patients, with a body mass index (BMI) > 30 , have specific problems during MV. The large weight on the rib cage can cause alveolar collapse in some conditions and gravity can influence pulmonary mechanics [48]. In a study of obese patients with ARF, mortality was reduced by 50% when the choice of PEEP was guided with an esophageal catheter (EsoC) and electrical impedance tomography (EIT) [49]. During the process of weaning of MV is crucial to pay attention to the work of breathing, because the increased negative pleural pressure in these patients can lead to a compression of the diaphragm in to the rib cage and can induce atelectasis in patients with muscle weakness [49]. Therefore, obese patients may benefit from higher PEEP during the pre-extubation period, making pleural pressure more positive and preventing alveolar collapse [50]. After extubation, positive pressure in the smaller airways can be maintained through by NIV, preferably in a sitting position, to avoid abdominal cavity compression of the diaphragm and inducing collapse by undermining the mechanics of the rib cage [51].

3. Prolonged weaning and some considerations

Prolonged weaning concerns about 10% of critically ill intubated patients and is associated with a high mortality [19, 27, 52]. Patients with prolonged weaning are associated with chronic critical illness [53]. The multidisciplinary rehabilitation group is very important to treatment [54]. Physical therapy will be very important to assess the patient's tolerance and exercise. Swallowing dysfunction can complicate the extubation process and its evaluation is essential for the return to normal eating habits [55]. Short daily cuff down trials with a speaking valve are performed to induce vocal cords to exert their original function during expiration. Tracheostomy may be considered as a useful adjunct for easier care of the patient, especially for mobilization and better comfort [56, 57]. A randomized controlled trial suggested that tracheostomized patients were more rapidly separated from the ventilator by repetitive T-tube trials than with a gradual reduction of PSV without influencing survival at 12 months [58]. Assessment with the patient and family should address explicit discussion of realistic versus futile treatment goals [59].

4. Future perspectives

More recently, tools such as ultrasound, EsoC and EIT have helped to predict MV weaning. The EsoC can be useful in the objective assessment of respiratory

effort, estimating transpulmonary pressure and autoPEEP [60]. On the other hand, ultrasound can be useful in providing information through visual assessment and in obtaining objective measurements of cardiorespiratory variables at different stages of weaning. A study by Haji et al. showed that loss of pulmonary aeration and left ventricular diastolic dysfunction are more frequent in patients who fail extubation [61]. Additionally, several studies have shown that the use of the EIT can help to evaluate weaning from MV. Bickenbach et al. and Lima et al. showed loss of recruitment and lung homogeneity during SBT [62, 63]. Studies in specific populations, such as patients with COPD, are ongoing and partial results indicate that those who fail the SBT ventilate more the anterior lung regions [64].

5. Conclusions

The weaning from MV in critically ill patients is a common and fundamental process in the ICU. The understanding the withdrawal of invasive ventilatory support and identifying possible causes of weaning failure are essential. The use of SBT trial and predictors guide weaning from MV. Some subgroups should be better valued to better individualize MV weaning and avoid reintubation associated with worse outcomes.

Conflict of interest

“The authors declare no conflict of interest.”

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References

- [1] Wunsch H, Linde-Zwirble WT, Angus DC, Hartman ME, Milbrandt EB, Kahn JM. The epidemiology of mechanical ventilation use in the United States. *Critical care medicine*. 2010; 38(10):1947-1953.
- [2] Esteban A, Anzueto A, Frutos F, Alia I, Brochard L, Stewart TE, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *Jama*. 2002;287(3):345-355.
- [3] McConville JF, Kress JP. Weaning patients from the ventilator. *The New England journal of medicine*. 2012;367(23):2233-2239.
- [4] Burns KEA, Raptis S, Nisenbaum R, Rizvi L, Jones A, Bakshi J, et al. International Practice Variation in Weaning Critically Ill Adults from Invasive Mechanical Ventilation. *Annals of the American Thoracic Society*. 2018;15(4):494-502.
- [5] Frutos-Vivar F, Esteban A, Apezteguia C, Gonzalez M, Arabi Y, Restrepo MI, et al. Outcome of reintubated patients after scheduled extubation. *Journal of critical care*. 2011;26(5):502-509.
- [6] Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. *Chest*. 1997;112(1):186-192.
- [7] Esteban A, Frutos-Vivar F, Ferguson ND, Arabi Y, Apezteguia C, Gonzalez M, et al. Noninvasive positive-pressure ventilation for respiratory failure after extubation. *The New England journal of medicine*. 2004;350(24):2452-2460.
- [8] Seymour CW, Martinez A, Christie JD, Fuchs BD. The outcome of extubation failure in a community hospital intensive care unit: a cohort study. *Critical care*. 2004;8(5): R322-R327.
- [9] Torres A, Gatell JM, Aznar E, el-Ebiary M, Puig de la Bellacasa J, Gonzalez J, et al. Re-intubation increases the risk of nosocomial pneumonia in patients needing mechanical ventilation. *American journal of respiratory and critical care medicine*. 1995;152(1):137-141.
- [10] Sahn SA, Lakshminarayan S, Petty TL. Weaning from mechanical ventilation. *Jama*. 1976;235(20): 2208-2212.
- [11] Kimball WR, Leith DE, Robins AG. Dynamic hyperinflation and ventilator dependence in chronic obstructive pulmonary disease. *The American review of respiratory disease*. 1982; 126(6):991-995.
- [12] Tobin MJ, Perez W, Guenther SM, Semmes BJ, Mador MJ, Allen SJ, et al. The pattern of breathing during successful and unsuccessful trials of weaning from mechanical ventilation. *The American review of respiratory disease*. 1986;134(6):1111-1118.
- [13] Jubran A, Tobin MJ. Pathophysiologic basis of acute respiratory distress in patients who fail a trial of weaning from mechanical ventilation. *American journal of respiratory and critical care medicine*. 1997;155(3):906-915.
- [14] Milic-Emili J. Is weaning an art or a science? *The American review of respiratory disease*. 1986;134(6): 1107-1108.
- [15] Tomlinson JR, Miller KS, Lorch DG, Smith L, Reines HD, Sahn SA. A prospective comparison of IMV and T-piece weaning from mechanical ventilation. *Chest*. 1989;96(2):348-352.

- [16] Esen F, Denkel T, Telci L, Kesecioglu J, Tutuncu AS, Akpir K, et al. Comparison of pressure support ventilation (PSV) and intermittent mandatory ventilation (IMV) during weaning in patients with acute respiratory failure. *Advances in experimental medicine and biology*. 1992;317:371-376.
- [17] Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rekik N, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. *American journal of respiratory and critical care medicine*. 1994;150(4):896-903.
- [18] Esteban A, Frutos F, Tobin MJ, Alia I, Solsona JF, Valverdu I, et al. A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. *The New England journal of medicine*. 1995;332(6):345-350.
- [19] Sellares J, Ferrer M, Torres A. Predictors of weaning after acute respiratory failure. *Minerva anesthesiologica*. 2012;78(9):1046-1053.
- [20] MacIntyre NR, Cook DJ, Ely EW, Jr., Epstein SK, Fink JB, Heffner JE, et al. Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest*. 2001;120(6 Suppl):375S-395S.
- [21] Schmidt GA, Girard TD, Kress JP, Morris PE, Ouellette DR, Alhazzani W, et al. Official Executive Summary of an American Thoracic Society/American College of Chest Physicians Clinical Practice Guideline: Liberation from Mechanical Ventilation in Critically Ill Adults. *American journal of respiratory and critical care medicine*. 2017;195(1): 115-119.
- [22] Burns KE, Meade MO, Premji A, Adhikari NK. Noninvasive ventilation as a weaning strategy for mechanical ventilation in adults with respiratory failure: a Cochrane systematic review. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. 2014;186(3): E112-22.
- [23] Nava S, Ambrosino N, Clini E, Prato M, Orlando G, Vitacca M, et al. Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease. A randomized, controlled trial. *Annals of internal medicine*. 1998;128(9):721-728.
- [24] Perren A, Brochard L. Managing the apparent and hidden difficulties of weaning from mechanical ventilation. *Intensive care medicine*. 2013;39(11): 1885-1895.
- [25] Heunks LM, van der Hoeven JG. Clinical review: the ABC of weaning failure--a structured approach. *Critical care*. 2010;14(6):245.
- [26] Namen AM, Ely EW, Tatter SB, Case LD, Lucia MA, Smith A, et al. Predictors of successful extubation in neurosurgical patients. *American journal of respiratory and critical care medicine*. 2001;163(3 Pt 1):658-664.
- [27] Coplin WM, Pierson DJ, Cooley KD, Newell DW, Rubenfeld GD. Implications of extubation delay in brain-injured patients meeting standard weaning criteria. *American journal of respiratory and critical care medicine*. 2000;161(5): 1530-1536.
- [28] Thille AW, Cortes-Puch I, Esteban A. Weaning from the ventilator and extubation in ICU. *Current opinion in critical care*. 2013;19(1):57-64.
- [29] Penuelas O, Frutos-Vivar F, Fernandez C, Anzueto A, Epstein SK, Apezteguia C, et al. Characteristics and

outcomes of ventilated patients according to time to liberation from mechanical ventilation. *American journal of respiratory and critical care medicine*. 2011;184(4):430-437.

[30] Navalesi P, Frigerio P, Moretti MP, Sommariva M, Vesconi S, Baiardi P, et al. Rate of reintubation in mechanically ventilated neurosurgical and neurologic patients: evaluation of a systematic approach to weaning and extubation. *Critical care medicine*. 2008;36(11):2986-2992.

[31] Roquilly A, Cinotti R, Jaber S, Vourc'h M, Pengam F, Mahe PJ, et al. Implementation of an evidence-based extubation readiness bundle in 499 brain-injured patients. a before-after evaluation of a quality improvement project. *American journal of respiratory and critical care medicine*. 2013;188(8):958-966.

[32] Salam A, Tilluckdharry L, Amoateng-Adjepong Y, Manthous CA. Neurologic status, cough, secretions and extubation outcomes. *Intensive care medicine*. 2004;30(7):1334-1339.

[33] Landefeld CS, Palmer RM, Kresevic DM, Fortinsky RH, Kowal J. A randomized trial of care in a hospital medical unit especially designed to improve the functional outcomes of acutely ill older patients. *The New England journal of medicine*. 1995;332(20):1338-1344.

[34] De Jonghe B, Bastuji-Garin S, Sharshar T, Outin H, Brochard L. Does ICU-acquired paresis lengthen weaning from mechanical ventilation? *Intensive care medicine*. 2004;30(6):1117-1121.

[35] Witt NJ, Zochodne DW, Bolton CF, Grand'Maison F, Wells G, Young GB, et al. Peripheral nerve function in sepsis and multiple organ failure. *Chest*. 1991;99(1):176-184.

[36] Garnacho-Montero J, Madrazo-Osuna J, Garcia-Garmendia JL,

Ortiz-Leyba C, Jimenez-Jimenez FJ, Barrero-Almodovar A, et al. Critical illness polyneuropathy: risk factors and clinical consequences. A cohort study in septic patients. *Intensive care medicine*. 2001;27(8):1288-1296.

[37] Bercker S, Weber-Carstens S, Deja M, Grimm C, Wolf S, Behse F, et al. Critical illness polyneuropathy and myopathy in patients with acute respiratory distress syndrome. *Critical care medicine*. 2005;33(4):711-715.

[38] De Jonghe B, Sharshar T, Lefaucheur JP, Authier FJ, Durand-Zaleski I, Boussarsar M, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. *Jama*. 2002;288(22):2859-2867.

[39] Leijten FS, De Weerd AW, Poortvliet DC, De Ridder VA, Ulrich C, Harink-De Weerd JE. Critical illness polyneuropathy in multiple organ dysfunction syndrome and weaning from the ventilator. *Intensive care medicine*. 1996;22(9):856-861.

[40] Druschky A, Herkert M, Radespiel-Troger M, Druschky K, Hund E, Becker CM, et al. Critical illness polyneuropathy: clinical findings and cell culture assay of neurotoxicity assessed by a prospective study. *Intensive care medicine*. 2001;27(4):686-693.

[41] Garnacho-Montero J, Amaya-Villar R, Garcia-Garmendia JL, Madrazo-Osuna J, Ortiz-Leyba C. Effect of critical illness polyneuropathy on the withdrawal from mechanical ventilation and the length of stay in septic patients. *Critical care medicine*. 2005;33(2):349-354.

[42] Papazian L, Aubron C, Brochard L, Chiche JD, Combes A, Dreyfuss D, et al. Formal guidelines: management of acute respiratory distress syndrome. *Annals of intensive care*. 2019;9(1):69.

- [43] Wawrzeniak IC, Regina Rios Vieira S, Almeida Victorino J. Weaning from Mechanical Ventilation in ARDS: Aspects to Think about for Better Understanding, Evaluation, and Management. *BioMed research international*. 2018;2018:5423639.
- [44] Yoshida T, Fujino Y, Amato MB, Kavanagh BP. Fifty Years of Research in ARDS. Spontaneous Breathing during Mechanical Ventilation. Risks, Mechanisms, and Management. *American journal of respiratory and critical care medicine*. 2017;195(8): 985-992.
- [45] Spinelli E, Mauri T. Why improved PF ratio should not be our target when treating ARDS. *Minerva anestesiologica*. 2021;87(7):752-754.
- [46] Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. *The European respiratory journal*. 2007;29(5):1033-1056.
- [47] Jeong BH, Ko MG, Nam J, Yoo H, Chung CR, Suh GY, et al. Differences in clinical outcomes according to weaning classifications in medical intensive care units. *PloS one*. 2015;10(4):e0122810.
- [48] Kacmarek RM, Wanderley HV, Villar J, Berra L. Weaning patients with obesity from ventilatory support. *Current opinion in critical care*. 2021;27(3):311-319.
- [49] Obi ON, Mazer M, Bangley C, Kassabo Z, Saadah K, Trainor W, et al. Obesity and Weaning from Mechanical Ventilation-An Exploratory Study. *Clinical medicine insights Circulatory, respiratory and pulmonary medicine*. 2018;12:1179548418801004.
- [50] Teggie Droghi M, De Santis Santiago RR, Pinciroli R, Marrazzo F, Bittner EA, Amato MBP, et al. High Positive End-Expiratory Pressure Allows Extubation of an Obese Patient. *American journal of respiratory and critical care medicine*. 2018;198(4): 524-525.
- [51] Grassi L, Kacmarek R, Berra L. Ventilatory Mechanics in the Patient with Obesity. *Anesthesiology*. 2020;132(5):1246-1256.
- [52] Funk GC, Anders S, Breyer MK, Burghuber OC, Edelmann G, Heindl W, et al. Incidence and outcome of weaning from mechanical ventilation according to new categories. *The European respiratory journal*. 2010;35(1):88-94.
- [53] Macintyre NR. Chronic critical illness: the growing challenge to health care. *Respiratory care*. 2012;57(6): 1021-1027.
- [54] Mauri T, Pivi S, Bigatello LM. Prolonged mechanical ventilation after critical illness. *Minerva anestesiologica*. 2008;74(6):297-301.
- [55] Ceriana P, Carlucci A, Navalesi P, Rampulla C, Delmastro M, Piaggi G, et al. Weaning from tracheotomy in long-term mechanically ventilated patients: feasibility of a decisional flowchart and clinical outcome. *Intensive care medicine*. 2003;29(5): 845-848.
- [56] Rumbak MJ, Newton M, Truncale T, Schwartz SW, Adams JW, Hazard PB. A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. *Critical care medicine*. 2004;32(8):1689-1694.
- [57] Trouillet JL, Luyt CE, Guiguet M, Ouattara A, Vaissier E, Makri R, et al. Early percutaneous tracheotomy versus prolonged intubation of mechanically ventilated patients after cardiac surgery: a randomized trial. *Annals of internal medicine*. 2011;154(6):373-383.

[58] Jubran A, Grant BJ, Duffner LA, Collins EG, Lanuza DM, Hoffman LA, et al. Effect of pressure support vs unassisted breathing through a tracheostomy collar on weaning duration in patients requiring prolonged mechanical ventilation: a randomized trial. *Jama*. 2013;309(7):671-677.

[59] Aghabarary M, Dehghan Nayeri N. Medical futility and its challenges: a review study. *Journal of medical ethics and history of medicine*. 2016;9:11.

[60] Yoshida T, Brochard L. Ten tips to facilitate understanding and clinical use of esophageal pressure manometry. *Intensive care medicine*. 2018;44(2):220-2.

[61] Haji K, Haji D, Canty DJ, Royse AG, Green C, Royse CF. The impact of heart, lung and diaphragmatic ultrasound on prediction of failed extubation from mechanical ventilation in critically ill patients: a prospective observational pilot study. *Critical ultrasound journal*. 2018;10(1):13.

[62] Bickenbach J, Czaplik M, Polier M, Marx G, Marx N, Dreher M. Electrical impedance tomography for predicting failure of spontaneous breathing trials in patients with prolonged weaning. *Critical care*. 2017;21(1):177.

[63] Lima JNG, Fontes MS, Szmuszkowicz T, Isola AM, Maciel AT. Electrical impedance tomography monitoring during spontaneous breathing trial: Physiological description and potential clinical utility. *Acta anaesthesiologica Scandinavica*. 2019;63(8):1019-1027.

[64] Moura KBA, Bertoldi RA, Wawrzeniak IC, Balzan F, Pellegrini JAS, Pacheco E, et al. Use of Electrical Impedance Tomography and Esophageal Catheter for Weaning from Mechanical Ventilation of Patients with COPD - A Pilot Study. *American journal of respiratory and critical care medicine*. 2020;201(A5215).