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#### **ORIGINAL RESEARCH**

# Ventilator Weaning and Spontaneous Breathing Trials; an Educational Review

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#### **Abstract:**

The term "weaning" is used to describe the gradual process of decreasing ventilator support. It is estimated that 40% of the duration of mechanical ventilation is dedicated to the process of weaning. Spontaneous breathing trial (SBT) assesses the patient's ability to breathe while receiving minimal or no ventilator support. The collective task force in 2001 stated that the process of SBT and weaning should start by assessing whether the underlying cause of respiratory failure has been resolved or not. Weaning predictors are parameters that are intended to help clinicians predict whether weaning attempts will be successful or not. Although the international consensus conference in 2005 did not recommend their routine use for clinical decision making, researchers did not stop working in this area. In the present article, we review some of the recent studies about weaning predictors, criteria, procedure, as well as assessment for extubation a mechanically ventilated patient.

**Keywords:** Ventilator weaning; mechanical ventilation; emergency service, hospital; airway extubation; ventilator induced lung injury

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# 1. Introduction

he term "weaning" is used to describe the gradual process of decreasing ventilator support. It is estimated that 40% of the duration of mechanical ventilation is dedicated to the process of weaning (1). Delayed weaning can lead to complications such as ventilator induced lung injury (VILI), ventilator associated pneumonia (VAP), and ventilator induced diaphragmatic dysfunction (2-4). On the other hand, premature weaning can lead to complications like loss of the airway, defective gas exchange, aspiration and respiratory muscle fatigue (5-7). Spontaneous breathing trial (SBT) assesses the patient's ability to breathe while receiving minimal or no ventilator support. The collective task force in 2001 stated that the process of SBT and weaning should start by assessing whether the underlying cause of respiratory failure has been resolved or not (2). There is no consensus about what criteria should be used to assess reversal of the

The process of weaning leads to changes in the hemodynamic and autonomic nervous systems. Two prospective observational studies showed that reduced heart rate variability

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underlying condition. A combination of subjective and objective criteria is usually used to determine disease reversal. Usually the criteria used are improvement of gas exchange, improvement of mental status, neuromuscular functional assessment and radiographic signs (7). However, it should be kept in mind that some patients who don't meet these criteria are eventually successfully weaned (8). Weaning predictors are parameters that are intended to help clinicians predict whether weaning attempts will be successful or not. Although the international consensus conference in 2005 did not recommend their routine use for clinical decision making, researchers did not stop working in this area (9). In the present article, we review some of the recent studies about weaning predictors, criteria, procedure, as well as assessment for extubation a mechanically ventilated patient.

<sup>2.</sup> Weaning predictors
2.1. Heart rate variability

during spontaneous breathing trials (SBT) was significantly associated with extubation failure (10-12). Acrentales et al. found that spectral coherence between heart rate variability and respiratory flow signals could predict extubation failure with good sensitivity and specificity (13). However, all these results still need validation in larger groups of patients.

# 2.2. Sleep quality

Poor quality of sleep may affect the function of the respiratory muscles and weaning outcome. In a cross sectional study, Chen et al. assessed the quality of sleep using the Verran and Snyder-Halpern Sleep Scale and found that poor quality of sleep was significantly associated with weaning failure (14).

# 2.3. Hand grip strength

Muscle weakness can negatively affect the weaning outcome (15). Cottereau et al. assessed handgrip strength by a handheld dynamometer and found that handgrip strength was significantly associated with difficult or prolonged weaning but not with extubation failure (16).

# 2.4. Diaphragmatic dysfunction

The acquired diaphragmatic dysfunction following prolonged mechanical ventilation can affect the weaning outcome (17). DiNino et al. assessed diaphragmatic dysfunction by measuring the difference between diaphragm thickness at the end of inspiration and expiration using ultrasonography to view the diaphragm in the zone of apposition. They found that a difference of 30% or more could predict extubation failure with a sensitivity of 88% and a specificity of 71% (18).

#### 2.5. Oxidative stress markers

Oxidative stress is a key mechanism involved in ventilator induced respiratory muscle dysfunction. Verona et al. estimated the plasma levels of oxidative stress markers before and after SBT. They found higher plasma concentration of malondialdehyde and vitamin C, and lower level of nitric oxide in plasma were significantly associated with SBT failure (19).

# 3. Weaning criteria

Table 1 shows some of derivate criteria of readiness for weaning trial (20, 21). According to the international consensus conference recommendations in 2005, these criteria should be thought of as considerations rather than as rigid thresholds that patients must meet all of them to be successfully weaned. Because many patients were successfully discontinued from the ventilator although they didn't meet one or more of them (9).

Table 1: Criteria of readiness for weaning trial

#### Criteria

#### Subjective assessment

Adequate cough

No neuromuscular blocking agents

Absence of excessive trachea-bronchial secretion

Reversal of the underlying cause for respiratory failure

No continuous sedation infusion or adequate mentation on sedation

#### Objective measurements

Stable cardiovascular status

Heart rate ≤ 140 beat/minute

No active myocardial ischemia

Adequate hemoglobin level (≥8 g/dl)

Systolic blood pressure 90-160 mmHg

Afebrile (36° C < temperature < 38° C)

No or minimal vasopressor or inotrope

( $< 5 \mu g/kg/minute$  dopamine or dobutamine)

#### Adequate oxygenation

Tidal volume > 5 mL/kg

Vital capacity >10 mL/kg

Proper inspiratory effort

Respiratory rate ≤ 35/minute

 $PaO_2 \ge 60$  and  $PaCO_2 \le 60$  mmHg

Positive end expiratory pressure  $\leq 8 \text{ cmH}_2\text{O}$ 

Positive end expiratory pressure ≤ 8 cmm<sub>2</sub>O

No significant respiratory acidosis (pH  $\geq$  7.30)

Maximal inspiratory pressure (MIP)  $\leq$  -20 – -25 cmH<sub>2</sub>O O<sub>2</sub> saturation > 90% on FIO<sub>2</sub>  $\leq$  0.4 (or PaO<sub>2</sub>/FIO<sub>2</sub>  $\geq$  200)

Rapid Shallow Breathing Index

(respiratory Frequency/Tidal Volume) < 105

# 4. Weaning procedure

# 4.1. Planning

#### Step1:

A weaning plan starts with assessing the ability of the patient for spontaneous breathing. Three main strategies are used by clinicians to perform SBT.

#### **SBT Strategies**

- \* T-piece trial, in which only supplemental oxygen is supplied through a T-piece connected to an endotracheal tube.
- \* Continuous positive airway pressure (CPAP) trial using a CPAP level equal to the previous positive end-expiratory pressure (PEEP) level.
- \* Invasive ventilation with low level of pressure support (5-8 cmH<sub>2</sub>O) or automatic tube compensation. There is no current evidence suggesting that one of these approaches is superior to the others (22, 23). A recent Cochrane systematic review concluded that there is no difference between T-piece trials and pressure support trials regarding extubation failure and mortality with low quality of evidence. However, pressure support was found to be superior to T-piece in the proportion of successful SBT in patients considered to have simple weaning with moderate quality of evidence (relative risk 1.09; 95%CI: 1.02-1.17) (24). Neil R MacIntyre suggested



that the T-piece approach may be considered if there is borderline performance with other techniques or there are concerns that loss of PEEP would precipitate latent cardiac dysfunction or lung failure (7).

#### **SBT Duration**

Based on strong evidence, the collective task force in 2001 recommended that the duration of SBT should be at least 30 minutes and not longer than 120 minutes (2). This means that physicians should wait at least 30 minutes to judge tolerance of the SBT, but they shouldn't wait longer than 120 minutes if tolerance of the SBT is not clear (7). The initial few minutes of the SBT should be monitored closely before judgment is made to continue the SBT. There are some evidence regarding the harmful effects of respiratory muscle fatigue, if they occur early in failing SBTs (7, 25-27).

#### Criteria of successful SBT

Table 2 illustrates the criteria used by clinicians to judge tolerance of SBTs (20). According to Neil R MacIntyre, these criteria should be interpreted in the context of each other and as changes from baseline, not as rigid thresholds (7).

#### Definition of weaning outcome based on SBT

The International Consensus Conference in 2005 suggested a new classification of weaning outcomes (table 3). This classification has been shown in multiple observational studies to have prognostic value. Some studies showed that only the prolonged weaning group significantly had higher mortality and longer hospital stay compared to the other two groups (28-31). Jeong et al. concluded that ventilator free days, extubation failure, tracheostomy, and mortalities increased significantly across groups (32). Funk et al. also concluded that ventilator free days and intensive care unit (ICU) free days increased significantly in the difficult and prolonged classes (31).

#### Step 2:

If SBT was successful, step 2 would be assessment for airway removal. But, if SBT was unsuccessful, the collective task force in 2001 (2) recommended the following processes as step 2:

\* Searching for an underlying cause of respiratory failure and

 Table 2:
 Criteria of successful spontaneous breathing trials

Respiratory rate < 35 breaths/minute
Good tolerance to spontaneous breathing trials
Heart rate < 140 /minute or heart rate variability of >20%
Arterial oxygen saturation >90% or PaO<sub>2</sub> > 60 mmHg on
FiO<sub>2</sub><0.4

80 < Systolic blood pressure < 180 mmHg or < 20% change from baseline

No signs of increased work of breathing or distress \*

\* Accessory muscle use, paradoxical or asynchronous rib cageabdominal movements, intercostal retractions, nasal flaring, profuse diaphoresis, agitation. correcting it if possible.

- \* Using a comfortable non-fatiguing form of respiratory support. Neil R MacIntyre showed that this support should be interactive and well synchronized with the patient effort (33).
- \* Screen every 24 hours for readiness for another SBT.

### 4.2. Options

### Protocolized versus non-protocolized weaning

Weaning protocols usually consist of 3 parts: 1) objective criteria to judge readiness to wean; 2) guidelines to decrease support gradually; and 3) criteria to assess readiness for extubation (34). The latest Cochrane systematic review showed that the use of protocols led to shorter total duration of mechanical ventilation and no extra side effects with moderate quality of evidence. It also showed that protocols led to shorter duration of weaning and ICU length of stay with low quality of evidence. There were considerable variations in the types of protocols used, types of patients and usual practices in ICUs, therefore the reviewers could not recommend a certain protocol for general use (35).

#### Automated versus non automated weaning

Automated systems use closed loop circuits to automatically adjust the level of support given to the patient. The latest Cochrane systematic review showed that automated systems were associated with shorter duration of weaning (36). However there was substantial heterogeneity in the result (87%). It also showed that automated systems led to shorter duration of mechanical ventilation, length of ICU stay with moderate heterogeneity. It did not show the automated systems to be beneficial in reducing the length of hospital stay, mortality rates, or need for re-intubation. Compared to usual protocolized systems, automated systems showed shorter duration of weaning and shorter total duration of mechanical ventilation.

#### 4.3. Sedation optimization strategies

Excessive sedation can result in poor performance in SBTs and prolong the duration of mechanical ventilation (7). The

Table 3: classification of weaning outcomes

#### Outcome definitions

Simple

Successful SBT after the first attempt

Difficult

Failed SBT at first attempt and Required up to three trials or

Required <7days to reach successful SBT

**Prolonged** 

Required >7days to reach successful SBT

profuse diaphoresis, agitation.



most important sedation strategies are aiming at reducing the duration of mechanical ventilation and daily sedation interruption. Atiken et al. investigated the benefits of protocolized sedation versus non-protocolized sedation in a Cochrane systematic review including 633 patients and found that protocolized sedation did not result in a reduction in the duration of mechanical ventilation, ICU length of stay, hospital length of stay or mortality rates. However they graded the quality of evidence as low due to the conflicting results from the two included studies (37). Another Cochrane systematic review investigated the benefits of daily sedation interruption versus no interruption. It found that there is no strong evidence that daily sedation interruption reduced the duration of mechanical ventilation, length of hospital or ICU stay or mortality. In a subgroup analysis of studies performed in North America, they found that daily sedation interruption reduced the total duration of mechanical ventilation. However, the authors advised that the study results should be used cautiously as the studies were heterogeneous in the patients and methods (38). These results show that further well-reported randomized clinical trials with large number of patients and uniform interventions are needed to judge the usefulness of these strategies.

#### 5. Assessment for extubation

After successful SBT, the patient should undergo assessment for removal of the airway. Assessment includes factors leading to extubation failure. Extubation failure is defined as reintubation within 48 hours of extubation. Re-intubation is associated with prolonged hospital and ICU stay and more tracheostomies (39). Re-intubation rate is commonly used as an indicator of the aggressiveness of weaning behavior in ICU units. It equals number of re-intubated patients divided by total number of extubated patients. A value too high suggests that weaning is done too early, and a value too low suggests unnecessary conservative practices. Neil R MacIntyre suggested that a value of 5-20% is generally accepted (7). However, no significant differences were found between the ranges of 7-15% and <7%. Table 4 shows factors leading to extubation failure(34).

#### Stridor at extubation

Stridor at extubation occurs due to narrowing of the upper airways. Cuff leak test has been introduced as a predictor of stridor after extubation (40). The amount of air leaking through the airway after deflating the cuff of the endotracheal tube is measured. The average of three values of 6 consecutive breaths during continuous mandatory ventilation 24 hours before extubation is taken. A value of <110 ml is considered to identify patients at high risk for stridor after extubation (41). However, it should be kept in mind that low values may be due to crusts of secretions around the tube (7).

Table 4: Risk factors of extubation failure

Failure of two or more consecutive spontaneous breathing trials Chronic heart failure

Partial pressure of arterial carbon dioxide > 45 mmHg after extubation  $\,$ 

More than one coexisting condition other than heart failure Weak cough

Upper-airway stridor at extubation

Age ≥ 65 years

APACHE II score >12 on the day of extubation
Patients in medical, pediatric or multispecialty ICU\*
Pneumonia as a cause of respiratory failure

\* Intensive care unit.

Steroids and/or epinephrine can treat post extubation stridor. It is also possible to give steroids and/or epinephrine 24 hours before extubation for patients with low cuff leak values (42).

#### Airway protection capacity

The ability of the patient to protect his airway from excessive secretions by effective cough is evaluated. This includes noting the quality of cough with airway suctioning, the amount of secretions and the frequency of suctioning (4, 43, 44). Patients judged to be not capable of protecting their airway effectively should not be extubated (45).

#### Mental status

It is controversial whether patients should have intact cognitive functions before extubation. A literature review showed that a Glasgow coma score > 8 was associated with successful extubation, if airway protection capacity is adequate (46).

# The role of non-invasive ventilation (NIV)

Agarwal et al. conducted a meta-analysis of RCTs comparing NIV with standard medical therapy in extubation failure (47). It showed that NIV when used prophylactically in patients with high risk for extubation failure was associated with lower risk for re-intubation and ICU mortality. However, when patients already developed respiratory distress, NIV didn't show the same benefits.

#### The role of high flow nasal cannula (HFNC)

Modern HFNC devices provide gas flow with a high rate up to 70 Litter/minutr and thus can provide oxygen with a high FiO2 up to 100%. Maggiore et al. conducted an RCT of HFNC versus conventional venture mask for oxygen delivery after extubation and found that HFNC was associated with better oxygenation and lower re-intubation rate (48). Bortfain et al. found that HFNC was associated with better oxygenation, more ventilator free days and lower re-intubation rate (49).



# 6. Appendix

# 6.1. Acknowledgements

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#### 6.2. Author's contributions

All the authors have contributed to drafting/revising the manuscript, study concept, or design, as well as data interpretation.

# 6.3. Conflict of interest

All authors declare that there is no conflict of interest in this study.

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# References

- Esteban A, Ferguson ND, Meade MO, Frutos-Vivar F, Apezteguia C, Brochard L, et al. Evolution of mechanical ventilation in response to clinical research. American journal of respiratory and critical care medicine. 2008;177(2):170-7.
- 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-95s.
- 3. Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. The New England journal of medicine. 1996;335(25):1864-9.
- 4. Fagon JY, Chastre J, Hance AJ, Montravers P, Novara A, Gibert C. Nosocomial pneumonia in ventilated patients: a cohort study evaluating attributable mortality and hospital stay. The American journal of medicine. 1993;94(3):281-8.
- 5. 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):906-15.
- Tobin MJ, Guenther SM, Perez W, Lodato RF, Mador MJ, Allen SJ, et al. Konno-Mead analysis of ribcage-

- abdominal motion during successful and unsuccessful trials of weaning from mechanical ventilation. The American review of respiratory disease. 1987;135(6):1320-8.
- 7. MacIntyre NR. The ventilator discontinuation process: an expanding evidence base. Respiratory care. 2013;58(6):1074-86.
- 8. Ely EW, Baker AM, Evans GW, Haponik EF. The prognostic significance of passing a daily screen of weaning parameters. Intensive care medicine. 1999;25(6):581-7.
- 9. 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):1033-56.
- Huang CT, Tsai YJ, Lin JW, Ruan SY, Wu HD, Yu CJ. Application of heart-rate variability in patients undergoing weaning from mechanical ventilation. Critical care (London, England). 2014;18(1):R21.
- Seely AJ, Bravi A, Herry C, Green G, Longtin A, Ramsay T, et al. Do heart and respiratory rate variability improve prediction of extubation outcomes in critically ill patients? Critical care (London, England). 2014;18(2):R65.
- 12. Hammash MH, Moser DK, Frazier SK, Lennie TA, Hardin-Pierce M. Heart rate variability as a predictor of cardiac dysrhythmias during weaning from mechanical ventilation. American journal of critical care: an official publication, American Association of Critical-Care Nurses. 2015;24(2):118-27.
- Arcentales A, Caminal P, Diaz I, Benito S, Giraldo BE Classification of patients undergoing weaning from mechanical ventilation using the coherence between heart rate variability and respiratory flow signal. Physiological measurement. 2015;36(7):1439-52.
- Chen CJ, Hsu LN, McHugh G, Campbell M, Tzeng YL. Predictors of sleep quality and successful weaning from mechanical ventilation among patients in respiratory care centers. The journal of nursing research: JNR. 2015;23(1):65-74.
- Hermans G, De Jonghe B, Bruyninckx F, Van den Berghe G. Clinical review: Critical illness polyneuropathy and myopathy. Critical care (London, England). 2008;12(6):238.
- 16. Cottereau G, Dres M, Avenel A, Fichet J, Jacobs FM, Prat D, et al. Handgrip Strength Predicts Difficult Weaning But Not Extubation Failure in Mechanically Ventilated Subjects. Respiratory care. 2015.
- 17. Hermans G, Agten A, Testelmans D, Decramer M, Gayan-Ramirez G. Increased duration of mechanical ventilation is associated with decreased diaphragmatic force: a prospective observational study. Critical care (London, England). 2010;14(4):R127.
- 18. DiNino E, Gartman EJ, Sethi JM, McCool FD. Diaphragm ultrasound as a predictor of successful extubation from mechanical ventilation. Thorax. 2014;69(5):423-7.



- 19. Verona C, Hackenhaar FS, Teixeira C, Medeiros TM, Alabarse PV, Salomon TB, et al. Blood markers of oxidative stress predict weaning failure from mechanical ventilation. Journal of cellular and molecular medicine. 2015;19(6):1253-61.
- 20. Penuelas O, Thille AW, Esteban A. Discontinuation of ventilatory support: new solutions to old dilemmas. Current opinion in critical care. 2015;21(1):74-81.
- 21. Boles J-M, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. European Respiratory Journal. 2007;29(5):1033-56.
- 22. Bailey CR, Jones RM, Kelleher AA. The role of continuous positive airway pressure during weaning from mechanical ventilation in cardiac surgical patients. Anaesthesia. 1995;50(8):677-81.
- 23. Jones DP, Byrne P, Morgan C, Fraser I, Hyland R. Positive end-expiratory pressure vs T-piece. Extubation after mechanical ventilation. Chest. 1991;100(6):1655-9.
- 24. Ladeira Magdaline T, Vital Flavia MR, Andriolo Regis B, Andriolo Brenda NG, Atallah Alvaro N, Peccin Maria S. Pressure support versus T-tube for weaning from mechanical ventilation in adults. Cochrane Database of Systematic Reviews [Internet]. 2014; (5). Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.C D006056.pub2/abstract.
- 25. Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. The New England journal of medicine. 1991;324(21):1445-50.
- 26. Dojat M, Harf A, Touchard D, Laforest M, Lemaire F, Brochard L. Evaluation of a knowledge-based system providing ventilatory management and decision for extubation. American journal of respiratory and critical care medicine. 1996;153(3):997-1004.
- 27. Liu L, Liu H, Yang Y, Huang Y, Liu S, Beck J, et al. Neuroventilatory efficiency and extubation readiness in critically ill patients. Critical care (London, England). 2012;16(4):R143.
- 28. Sellares J, Ferrer M, Cano E, Loureiro H, Valencia M, Torres A. Predictors of prolonged weaning and survival during ventilator weaning in a respiratory ICU. Intensive care medicine. 2011;37(5):775-84.
- 29. Tonnelier A, Tonnelier JM, Nowak E, Gut-Gobert C, Prat G, Renault A, et al. Clinical relevance of classification according to weaning difficulty. Respiratory care. 2011;56(5):583-90.
- 30. 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):430-7.
- 31. Funk GC, Anders S, Breyer MK, Burghuber OC, Edel-

- mann 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.
- 32. 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.
- 33. MacIntyre NR. Patient-ventilator interactions: optimizing conventional ventilation modes. Respiratory care. 2011;56(1):73-84.
- 34. McConville JF, Kress JP. Weaning Patients from the Ventilator. New England Journal of Medicine. 2012;367(23):2233-9.
- 35. Blackwood B, Burns KE, Cardwell CR, O'Halloran P. Protocolized versus non-protocolized weaning for reducing the duration of mechanical ventilation in critically ill adult patients. The Cochrane database of systematic reviews. 2014;11:Cd006904.
- 36. Rose L, Schultz MJ, Cardwell CR, Jouvet P, McAuley DF, Blackwood B. Automated versus non-automated weaning for reducing the duration of mechanical ventilation for critically ill adults and children: a cochrane systematic review and meta-analysis. Critical care (London, England). 2015;19(1):48.
- 37. Aitken Leanne M, Bucknall T, Kent B, Mitchell M, Burmeister E, Keogh Samantha J. Protocol-directed sedation versus non-protocol-directed sedation to reduce duration of mechanical ventilation in mechanically ventilated intensive care patients. Cochrane Database of Systematic Reviews [Internet]. 2015; (1). Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.C D009771.pub2/abstract.
- 38. Burry L, Rose L, McCullagh Iain J, Fergusson Dean A, Ferguson Niall D, Mehta S. Daily sedation interruption versus no daily sedation interruption for critically ill adult patients requiring invasive mechanical ventilation. Cochrane Database of Systematic Reviews [Internet]. 2014; (7). Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.C D009176.pub2/abstract.
- 39. Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L. Outcomes of extubation failure in medical intensive care unit patients. Critical care medicine. 2011;39(12):2612-8.
- 40. Fisher MM, Raper RF. The 'cuff-leak' test for extubation. Anaesthesia. 1992;47(1):10-2.
- 41. Miller RL, Cole RP. Association between reduced cuff leak volume and postextubation stridor. Chest. 1996;110(4):1035-40.
- 42. Jaber S, Jung B, Chanques G, Bonnet F, Marret E. Effects of steroids on reintubation and post-extubation stridor



- in adults: meta-analysis of randomised controlled trials. Critical care (London, England). 2009;13(2):R49.
- 43. Hilberman M, Dietrich HP, Martz K, Osborn JJ. An analysis of potential physiological predictors of respiratory adequacy following cardiac surgery. The Journal of thoracic and cardiovascular surgery. 1976;71(5):711-20.
- 44. Bach JR, Saporito LR. Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure. A different approach to weaning. Chest. 1996;110(6):1566-71.
- 45. Salam A, Tilluckdharry L, Amoateng-Adjepong Y, Manthous CA. Neurologic status, cough, secretions and extubation outcomes. Intensive care medicine. 2004;30(7):1334-9.
- 46. King CS, Moores LK, Epstein SK. Should patients be able to follow commands prior to extubation? Respiratory care. 2010;55(1):56-65.

- 47. Agarwal R, Aggarwal AN, Gupta D, Jindal SK. Role of non-invasive positive-pressure ventilation in postextubation respiratory failure: a meta-analysis. Respiratory care. 2007;52(11):1472-9.
- 48. Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F, et al. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. American journal of respiratory and critical care medicine. 2014;190(3):282-8.
- 49. Brotfain E, Zlotnik A, Schwartz A, Frenkel A, Koyfman L, Gruenbaum SE, et al. Comparison of the effectiveness of high flow nasal oxygen cannula vs. standard nonrebreather oxygen face mask in post-extubation intensive care unit patients. The Israel Medical Association journal: IMAJ. 2014;16(11):718-22.

