Disease specific thresholds for determining extubation readiness: The optimal negative inspiratory force for chronic obstructive pulmonary disease patients

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ABSTRACT

Objectives: The negative inspiratory force (NIF) has been used to help clinicians predict a patient’s likelihood of successful liberation from mechanical ventilation (MV). However, the utility of the traditional threshold of ≤−30 cmH₂O may not be appropriate for patients with chronic obstructive pulmonary disease (COPD). This study aims to define the optimal predictive NIF threshold for COPD patients.

Methods: A prospective-observational multi-center study was conducted in intensive care units of six academic medical centers. All patients had COPD and were intubated for hypercapnic respiratory failure. The process of weaning from MV was conducted according to the defined hospital protocol. NIF was measured after 120 min of spontaneous breathing trial (SBT). The sensitivity, specificity, positive, and negative predictive value (PPV, NPV), positive and negative likelihood ratios (LR+, LR−) were calculated, and the diagnostic accuracy recorded.

Results: A total of 90 patients with COPD (39 males and 51 females) were included. Of these, 43 patients (47.8%) were successfully extubated whereas 47 patients (52.2%) failed SBT or required re-intubation (P = 0.654). The threshold value of ≤−25 cmH₂O offered the optimal performance in COPD patients: area under the receiver operating characteristic (ROC) curves ROC curves 0.836, sensitivity 95.0%, specificity 86.0%, PPV 84.4%, and NPV 95.6%, LR+ 6.79, LR− 0.06, and the diagnostic accuracy 90.7%.

Conclusions: In mechanically ventilated COPD patients with hypercapnic respiratory failure, the NIF threshold of ≤−25 cmH₂O was a moderate-to-good predictor for successful ventilator liberation, and outperforms the traditional threshold of ≤−30 cmH₂O.

Key Words: Airway extubation, artificial, chronic obstructive, critical care, pulmonary disease, respiration

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of global morbidity and mortality, affecting 251 million people worldwide.[1-3] COPD ranked 8th in terms of disability-adjusted life years globally from 1990 to 2015.[3,4] It is a leading cause of death in the US and is projected to be the third leading cause of death globally by 2020.[5,6]
COPD is a chronic lower respiratory disease characterized by persistent respiratory symptoms and chronic airflow limitation due to small airways disease and parenchymal destruction.\[^{[7]}\] In patients with appropriate symptoms and significant exposures to noxious stimuli, the diagnosis of COPD is made with formal spirometry and is defined by The Global Initiative for Chronic Obstructive Lung Disease (GOLD) schema as the presence of a postbronchodilator forced expiratory volume in one second (FEV\(_1\)) to forced vital capacity ratio <0.70.\[^{[7]}\] Disease severity (GOLD criteria) is graded using FEV\(_1\) as a percent of predicted.\[^{[7,8]}\]

COPD may be punctuated by periods of acute worsening of respiratory symptoms termed exacerbations, which account for the majority COPD-associated mortality and health-care spending.\[^{[3]}\] Up to 80\% of COPD exacerbations are caused by respiratory infections, with viral infections generally inducing worse hypoxemia, longer hospital length-of-stay (LOS), and greater deterioration of lung function than bacterial infections.\[^{[9,13]}\] Exacerbations may lead to acute respiratory failure requiring noninvasive ventilation (NIV) or, in more severe cases, invasive mechanical ventilation (IMV). Although various prognostication tools have attempted to predict IMV needs,\[^{[14]}\] this remains largely a clinical decision. IMV is associated with a myriad of complications for patients, including increased exposure to nosocomial infections,\[^{[15]}\] barotrauma and ventilatory-induced lung injury,\[^{[16,17]}\] hemodynamic compromise,\[^{[18,19]}\] diaphragmatic and limb muscle weakness,\[^{[20-22]}\] organ dysfunction,\[^{[23-25]}\] neurological and psychological sequelae,\[^{[26,27]}\] protracted hospital and intensive care unit (ICU) LOS, and increased mortality.\[^{[28-32]}\] These risks increase with IMV duration. As such, a timely assessment of extubation readiness and ventilatory weaning is of utmost importance.\[^{[28]}\]

That said, premature weaning and failed extubation are not without their complications, including increased mortality, higher rates of tracheostomy dependence, and increased ICU and hospital LOS, and higher transfer rates to long-term-care facilities.\[^{[33-35]}\]

Given the importance of accurate assessment of extubation readiness, a multitude of factors have been studied for the prediction of extubation success including clinical gestalt, tidal volume (V\(_T\)), respiratory rate (RR), minute ventilation, rapid shallow breathing index (RSBI; defined as RR/V\(_T\) breaths/min/L), and negative inspiratory force (NIF). NIF, also known as negative inspiratory pressure or maximal inspiratory pressure, is a commonly used clinical parameter to assess extubation readiness by assessing diaphragmatic strength during the inspiratory phase.\[^{[36]}\] This metric is simple to obtain at the bedside. An early study indicated that a NIF of ≤−30 cmH\(_2\)O predicted successful weaning, whereas ≥−20 cmH\(_2\)O predicted weaning failure.\[^{[37]}\] Unfortunately, subsequent studies did not support these thresholds due to high false-positive and false-negative results.\[^{[38]}\] As studies across heterogeneous populations have shown, there is not a single threshold that will predict extubation success; however, its utility for homogeneous subpopulations remains unclear and more granular data is needed.\[^{[36,39]}\] The objective of this study was to determine if in COPD patients on IMV ≥24 h (population), what NIF threshold performs best to identify patients at the highest likelihood of successful extubation (primary outcome).

### METHODS

A prospective observational study was conducted in the closed mixed medical-surgical ICUs at six academic medical centers in a resource-limited setting from January 1, 2013, to February 28, 2017. The study was approved by the Investigational Review Board at Baqiyatallah University of the Medical Sciences (340/5/5904) and Shahid Beheshti University of the Medical Sciences (SBMU1/REC/1393/89), and these approvals were accepted by each of the enrolling centers: Baqiyatallah Hospital, Shariati hospital, Loghman Hakim Hospital, Besat Hospital, Masih Daneshvari Hospital, and Talaghan Hospital. All study parts were reviewed according to the Strengthening the Reporting of Observational Studies in Epidemiology “STROBE.”\[^{[40]}\] Consent was required and covered both study participation and publication of de-identified aggregate findings. Surrogate consent from the patient’s legal guardian or designated health proxy was permitted in cases where the subject lacked decision-making capacity. All patients that survived and regained their faculties were informed of the project. All data generated or analyzed during this study are included in this article. De-identified individual subject data may be available from the corresponding author on a reasonable request.

Patients were eligible for study participation if: (1) established COPD diagnosis before hospitalization; (2) admitted with hypercapnic respiratory failure; (3) age ≥50 years; (4) IMV for ≥24 h (any mode except high-frequency percussive ventilation or high-frequency oscillatory ventilation); (5) no sedatives or low dose sedation (1–2 mg midazolam per hour or 25–100 mcg fentanyl per hour);\[^{[41]}\] and (6) meeting the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines to participate in a weaning trial.\[^{[42]}\] Pre-defined weaning criteria included: (1) patent upper airway; (2) ability to protect airway (Glasgow Coma Score <10; adequate gag and cough reflexes); (3) ability to clear secretions; (4) secretion burden not requiring suction more frequently than every 2 h; (5) level of support (fraction of inspired oxygen [F\(_{\text{O}_2}\]) <50%; positive end-expiratory pressure [PEEP] ≤5 cm H\(_2\)O); and (6) hemodynamic stability not requiring chemical (vasopressors, inotropes) or mechanical (e.g. intra-aortic balloon pump, extracorporeal life support) circulatory support.
Patients were excluded if they did not meet the predefined weaning criteria, self-extubation, history of neuromuscular disease, acute coronary syndrome, overt cardiac failure, end-stage renal disease, hemodynamic instability, or for signs of systemic infection during the weaning process.

All patients were ventilated using Dräger Evita® XL or Evita® 4 ventilators (Dräger Medical, Inc., Lubeck, Germany). Weaning and extubation readiness was determined by the respiratory therapist (RT) using pre-defined criteria and the result of a spontaneous breathing trial (SBT). The SBT consisted of pressure support (PS) ventilation mode with PS ≤12 cmH2O, PEEP ≤8 cmH2O, and FIO2 ≤ 0.4, adjusted to achieve an arterial pH ≥ 7.35, arterial oxygen saturation (SaO2) ≥ 92%, RR 10–25 breaths/min, and without arrhythmias. NIF measurements were taken as one measurement following best effort and performed following a hold maneuver on the ventilator.

The decision to return to MV was made by jointly by the RT and the attending physician (both blinded to NIF results) based on signs of poor tolerance: S O2 < 90% with FIO2 > 0.4; P CO2 > 55 mmHg or increased by ≥10 mmHg; arterial pH ≤ 7.33; RR > 35 breaths/min or increased by 50% for ≥5 min; heart rate (HR) > 140 beats/min or increased/ decreased by >20%; mean arterial pressure >130 mmHg or <70 mmHg; or the presence of agitation, diaphoresis, disorientation, or depressed mental status. The patients who demonstrated one of these signs during the SBT were considered a failed wean and returned to ventilatory support.

**Data collection**

Patients were selected consecutively among admitted COPD patients meeting inclusion criteria. The data collection tool consisted of a two-part checklist including demographic variables (age, sex, marital status, and smoking) and ventilatory parameters (intubation hours, hospitalization hours, spontaneous RR, spontaneous V̇E, systolic blood pressure (BP), diastolic BP, HR, static and dynamic compliance).

**Statistical analysis**

Parametric data were expressed as mean ± standard deviation (SD), while nonparametric data were expressed as number and percentage. Receiver operating characteristic (ROC) curves were used to determine the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, LR+, and LR− of NIF at select cutoffs for predicting successful ventilator liberation. Statistical significance was set at P < 0.05. Statistical analyses were performed using IBM® Statistical Package for Social Sciences version 22.0 (IBM Corp., Chicago, IL, USA).

**RESULTS**

Ninety patients were included in the final analysis, of which 51 (56.7%) were women. The mean (±SD) age of the patients was 69.81 (±10.66) years. Patient demographics are depicted in Table 1. Forty-three (47.8%) patients were extubated successfully (P = 0.654).

The area under the ROC curves (AUC) of 0.836 for the NIF threshold of ≤−25 cmH2O offered the optimal performance in COPD patients: sensitivity 95.0%, specificity 86.0%, PPV 84.4%, NPV 95.6%, LR+ 6.79, LR− 0.06, and diagnostic accuracy 91.7% [Table 2]. The influence of intubation duration and hospital LOS on NIF index performance at the ≤−25 cm H2O threshold is shown in Table 3.

A comparison was made between patients with a duration of intubation (DoI) of ≤105 versus >105 h. The sensitivity was lower both in patients with DoI ≤105 h (by ≥28.3 h)

**Table 1: Patient demographics and characteristics**

| Variable                        | Value (n= 90) |
|---------------------------------|---------------|
| Age *                           | 61.40 ± 12.83 |
| Duration of intubation (h)*     | 108.50 ± 24.37 |
| Duration of hospitalization (day)* | 15.07 ± 16.41 |
| Spontaneous respiratory rate (bpm)* | 29.54 ± 3.56  |
| Spontaneous tidal volume (ml)*  | 294.18 ± 34.91 |
| Systolic blood pressure (mmHg)* | 126.00 ± 13.84 |
| Diastolic blood pressure (mmHg)* | 73.72 ± 10.17  |
| Heart rate (bpm)*               | 89.91 ± 11.36  |
| Temperature (°C)                | 36.98 ± 0.32   |
| Static compliance (ml/cmH2O)    | 75.50 ± 3.94   |
| Dynamic compliance (ml/cmH2O)   | 59.94 ± 5.04   |
| Gender, n (%)                   |               |
| Male                            | 39 (43.3)      |
| Female                          | 51 (56.7)      |
| Marital status, n (%)           |               |
| Single                          | 8 (20.0)       |
| Married                         | 72 (80.00)     |
| Smoking, n (%)                  |               |
| >1 pack/month                   | 61 (67.8)      |
| ≤1 pack/month                   | 29 (32.2)      |

*Mean ± SD. SD: Standard deviation

**Table 2: Performance of negative inspiratory force index at cutoff ≤ −25 cmH2O in chronic obstructive pulmonary disease patients**

| Parameter                              | NIF                        |
|----------------------------------------|----------------------------|
| Sensitivity (%)                        | 95.00                      |
| Specificity (%)                        | 86.00                      |
| PPV (%)                                | 84.44                      |
| NPV (%)                                | 95.56                      |
| +LR (%)                                | 6.79                       |
| −LR (%)                                | 0.06                       |
| DA (%)                                 | 90.67                      |
| Probability of the weaning success if test is negative (P [W + /T−]) (%) | 4.44                       |
| Probability of the weaning success if test is positive (P [W− /T+]) (%) | 84.44                      |
| AUC ± SE (%)                           | 0.836 ± 0.06               |

NIF: Negative inspiratory force, PPV: Positive predictive value, NPV: Negative predictive value, +LR: Likelihood ratio of positive test, −LR: Likelihood ratio of negative test, DA: Diagnostic accuracy, AUC: Area under the curve, SE: Standard error
and DOI >105 h (by ≤59.52 h) when compared to the uncategorized NIF. The specificity was lower in patients with DOI ≤105 h (by ≥21.29), but higher in patients requiring >105 h of intubation (by ≥6.31) when compared to the uncategorized NIF. The LR+ was lower both in patients with DOI ≤105 h (by ≤4.9) and DOI >105 h (by ≤2.18) when compared to the uncategorized NIF. The LR− was higher both in patients with DOI ≤105 h (by ≥0.46) and DOI >105 h (by ≥0.64) when compared to the uncategorized NIF. The AUC was lower both in patients with DOI ≤105 h (0.689) and DOI >105 h (0.654) when compared to the uncategorized NIF (0.836).

Similarly, a comparison was made between patients with ICU LOS ≤9 days and >9 days. The sensitivity was lower both in patients with ICU LOS ≤9 days (by ≤50.0) and ICU LOS >9 days (by ≤29.8) when compared to the uncategorized NIF. The specificity was lower both in patients with ICU LOS ≤9 days (by ≤15.63) and ICU LOS >9 days (by ≤26.0) when compared to the uncategorized NIF. The LR+ was lower both in patients with ICU LOS ≤9 days (by ≤5.27) and ICU LOS >9 days (by ≤5.16) when compared to the uncategorized NIF. The LR− was lower both in patients with ICU LOS ≤9 days (by ≥0.72) and ICU LOS >9 days (by ≥0.52) when compared to the uncategorized NIF. The AUC was lower both in patients with ICU LOS ≤9 days (0.565) and ICU LOS >9 days (0.639) when compared to the uncategorized NIF (0.836).

### DISCUSSION

COPD is a complex disease with high socio-economic impact, morbidity, and mortality.\(^{[1-6]}\) Increased severity, as measured by GOLD class, is associated with increased complications related to ventilator associated pneumonias,\(^{[41]}\) IMV duration\(^{[44]}\) and overall ICU LOS.\(^{[45]}\) In-hospital mortality rates for ventilated COPD patients have been reported as high as 24%, with 1-year mortality rates up to 59%.\(^{[32,46,47]}\) For those on IMV, ventilator liberation and recovery rates range 60%–90%.\(^{[32,46]}\) Early and aggressive ventilator weaning is paramount for limiting complications.

Various weaning parameters have been proposed to predict extubation success in ICU populations. The RSBI is among the most commonly used indices in non-homogeneous populations for predicting successful ventilator liberation.\(^{[38,48-50]}\) The accuracy of this measurement, however, has been questioned in the setting of sepsis, fever, supine position, restrictive physiology, and patient anxiety.\(^{[51]}\) One study reported that including the RSBI into a weaning protocol after a decision was made to attempt an SBT prolonged weaning and IMV for an additional day without reducing the number of failed extubations or tracheostomy placements.\(^{[52]}\) Unfortunately, RSBI underperforms as a predictor of extubation readiness in patients with COPD, with several studies citing low sensitivity and specificity for detecting extubation readiness in COPD patients.\(^{[53-55]}\) Additionally, RSBI may overestimate the ability to liberate COPD patients from IMV using the traditional threshold of <105 breaths/min/L.\(^{[55,56]}\) Moreover, in the COPD population, an RSBI threshold of ≤85 breaths/min/L outperformed the widely used threshold <105 breaths/min/L, yielding a 95.5% probability of extubation success.\(^{[50]}\)

NIF is a relatively simple and noninvasive test to assess for extubation readiness. Patients are asked to perform a forceful inspiration after expiring to a residual volume level against an occluded mouthpiece.\(^{[56,57]}\) NIF hypothetically reflects diaphragmatic strength and hence global inspiratory muscle strength with resultant alveolar ventilation.\(^{[32,36]}\) In a COPD patient with exacerbation, this may then represent an early surrogate of respiratory failure and recovery.

Early studies that established NIF normative values had little standardization of equipment and patient population, making it difficult to generalize values to
specific subgroups such as COPD patients.\textsuperscript{[58,59]} In an attempt to standardize respiratory muscle testing, the ATS/ERS released a joint statement to this effect in 2002.\textsuperscript{[60]} A subsequent meta-analysis reported that many of the studies that have been used to derive NIF datasets have suffered from similar methodologic limitations,\textsuperscript{[56]} and to date, a validated NIF threshold for COPD patients has not been reported.

NIF is determined by the force-length of the diaphragmatic muscles, and as such, has a degree of variability at different residual volumes. Inspiratory efforts are maximized at low lung volumes, whereas expiratory efforts are maximized at higher lung volumes.\textsuperscript{[60]} As COPD-patients have inherently higher functional residual capacities (FRC), a low NIF may more reflect a shortened inspiratory fiber length than a reduction in diaphragmatic strength.\textsuperscript{[60]} This may explain in part why the optimal NIF threshold in this COPD population varied from prior reports in heterogeneous populations that may be functioning at a lower FRC. This study demonstrated that the NIF threshold of ≤−25 cmH\textsubscript{2}O performed optimally in COPD patients to predict successful weaning and ventilator liberation. More negative thresholds may not be as discriminatory in COPD patients.

CONCLUSIONS

In mechanically ventilated COPD patients with hypercapnic respiratory failure, the NIF threshold of ≤−25 cmH\textsubscript{2}O performed optimally as a moderate-to-good predictor for successful ventilator weaning and liberation. More negative thresholds may not be as discriminatory in COPD patients.

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Conflicts of interest
There are no conflicts of interest.

Research quality and ethics statement
The authors of this manuscript declare that this scientific work complies with reporting quality, formatting and reproducibility guidelines set forth by the EQUATOR Network (http://www.equator-network.org/). The study was approved by the Investigational Review Board at Baqiyatallah University of the Medical Sciences (340/5/5904) and Shahid Beheshti University of the Medical Sciences (SBMU1/REC/1393/89), and these approvals were accepted by each of the enrolling centers: Baqiyatallah Hospital, Shariati hospital, Loghman Hakim Hospital, Besat Hospital, Masih Daneshvari Hospital, and Talaghan Hospital. Trial registration was not indicated for this study type.

REFERENCES

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095-128.
2. Kochanek K, Murphy S, Xu J, Arias E. Mortality in the United States, 2016. NCHS Data Brief 2017;7:1-8.
3. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390:1211-59.
4. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med 2017;5:691-706.
5. Guarascio AF, Ray SM, Finch CK, Self TH. The clinical and economic burden of chronic obstructive pulmonary disease in the USA. Clinicoecon Outcomes Res 2013;5:235-45.
6. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3:e442.
7. Global Initiative for Chronic Obstructive Lung Disease. Pocket Guide to COPD Diagnosis, Management, and Prevention: A Guide for Health Care Professionals. 17th ed. Fontana, WI, USA: Global Initiative for Chronic Obstructive Lung Disease; 2017. p. 37.
8. Marçôa R, Rodrigues DM, Dias M, Ladeira I, Vaz AP, Lima R, et al. Classification of chronic obstructive pulmonary disease (COPD) according to the new Global Initiative for chronic obstructive lung disease (GOLD) 2017: Comparison with GOLD 2011. COPD 2018;15:21-6.
9. Ball P. Epidemiology and treatment of chronic bronchitis and its exacerbations. Chest 1995;108:435-525.
10. Ko FW, Chan KP, Hui DS, Goddard JR, Shaw JG, Reid DW, et al. Acute exacerbation of COPD. Respiriolo 2016;62:1152-65.
11. Sapey E, Stockley RA. COPD exacerbations. 2: Aetiolo. Thorax 2006;61:250-8.
12. Mohan A, Chandra S, Agarwal D, Guleria R, Broor S, Gaur B, et al. Prevalence of viral infection detected by PCR and RT-PCR in patients with acute exacerbation of COPD: a systematic review. Respirology 2010;15:536-42.
13. Bhatia A, Kant S, Jain A, Prakash V, Verma A. A study of the relation of microbiological etiology with analytical and clinical parameters in exacerbation of COPD. Eur Respir J 2016;48 Suppl 60:PA2618.
14. Elshokkary R, Ghanem M, Metwally M, Abdelaleem N. Assessment of in-hospital mortality and the need for mechanical ventilation in acute exacerbations COPD: A 2-years prospective in-hospital observational study. Chest 2015;148:756B.
15. Kalil AC, Metersky ML, Kompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2018;66:e81-111.
16. Pistillo N, Farfita O. Driving airway and transpulmonary pressure are correlated to VILI determinants during controlled ventilation. Intensive Care Med 2018;44:674-5.
17. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 2015;372:747-55.
18. Guyton AC, Lindsey AW, Abernathy B, Richardson T. Venous return at various right atrial pressures and the normal venous return curve. Am J Physiol 1957;189:609-15.
19. Meumont Dessap A, Bouissier F, Charron C, Béguet E, Repesse X, Legras A, et al. Acute cor pulmonale during protective ventilation for acute respiratory distress syndrome: prevalence, predictors, and clinical impact. Intensive Care Med 2016;42:862-70.
20. Gea J, Pascual S, Casadevall C, Orozco-Levi M, Barreiro E. Muscle dysfunction in chronic obstructive pulmonary disease: update on causes and biological findings. J Thorac Dis 2015;7:E418-38.
21. Jaitovich A, Barreiro E. Skeletal muscle dysfunction in chronic obstructive
pulmonary disease (COPD): what we know and can do for our patients. Am J Respir Crit Care Med 2018;198:175-86.
22. Dres M, Dubé BP, Mayaux J, Delemazure J, Reuter D, Brochard L, et al. Coexistence and impact of limb muscle and diaphragm weakness at time of liberation from mechanical ventilation in medical intensive care unit patients. Am J Respir Crit Care Med 2017;195:57-66.
23. Dryer DR, Henry JP, Goodman J. The effects of continuous pressure breathing on kidney function. J Clin Invest 1947;26:945-51.
24. Koyner JL, Murray PT. Mechanical ventilation and the kidney. Blood Purif 2010;29:52-68.
25. Mohebbi L, Hesch K. Stress ulcer prophylaxis in the intensive care unit. Proc (Bayl Univ Med Cent) 2009;22:373-6.
26. Griffiths J, Fortune G, Barber V, Young JD. The prevalence of post traumatic stress disorder in survivors of ICU treatment: a systematic review. Intensive Care Med 2007;33:1506-18.
27. Busk KM, Ouyang B, Boland TA, Pollandt S, Temes RE. Prolonged mechanical ventilation is associated with pulmonary complications, increased length of stay, and unfavorable discharge destination among patients with subdural hematoma. J Neurosurg Anesthesiol 2015;27:31-6.
28. Scheinholm DJ, Hasenplug MS, Votto JJ, Chao DC, Epstein SK, Doig GS, et al. Post-ICU mechanical ventilation at 23 long-term care hospitals: A multicenter outcomes study. Chest 2007;131:85-93.
29. Powers SK, Kavazis AN, Levine S. Synchronized mechanical ventilation alters diaphragmatic structure and function. Crit Care Med 2009;37:S347-53.
30. Hermans G, Agten A, Testelmann D, Decramer M, Guyan-Ramirez G. Increased duration of mechanical ventilation is associated with decreased diaphragmatic force: a prospective observational study. Crit Care 2010;14:R127.
31. Talwar D, Dogra V. Weaning from mechanical ventilation in chronic obstructive pulmonary disease: Keys to success. J Assoc Chest Physicians 2016;4:43.
32. Nava S, Rubini F, Zanotti E, Ambrosino N, Bruschi C, Vitacca M, et al. Survival and prediction of successful ventilator weaning in COPD patients requiring mechanical ventilation for more than 21 days. Eur Respir J 1994;7:1645-52.
33. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. Chest 1997;112:186-92.
34. Gowdarmann JR, Huntington DR, Whiting J. The effect of extubation failure on outcome in a multidisciplinary Australian intensive care unit. Crit Care Resusc 2006;8:328-33.
35. de Lassence A, Alberti C, De Gaetano A, Gudjonsdottir M, Donner CF, et al. Impact of unplanned extubation and reintubation after weaning on nosocomial pneumonia risk in the intensive care unit: a prospective multicenter study. Anesthesiology 2002;97:148-56.
36. Sclavser Pessa OM, Franco Parreira V, Fregonetti GA, Sheel AW, Chung F, Reid WD. Reference values for maximal inspiratory pressure: a systematic review. Can Respir J 2014;21:43-50.
37. Sahn SA, Lakshminarayan S. Bedside criteria for discontinuation of mechanical ventilation. Chest 1973;63:1002-5.
38. Yang KL, Tobin MJ. A prognosis study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 1991;324:1445-50.
39. Rodrigues A, Da Silva ML, Berton DC, Cipriano G, Pitta F, O'Donnell DE, et al. Maximal inspiratory pressure: does the choice of reference values actually matter? Chest 2017;152:32-9.
40. White RG, Hakim AJ, Salganik MJ, Spiller MW, Johnston LG, Kerr L, et al. Strengthening the reporting of observational studies in epidemiology for respondent-driven sampling studies: “STROBE-RDS” statement. J Clin Epidemiol 2015;68:463-71.
41. Miller RD, Eriksson L, Fleisher L, Wiener-Kronish J, Cohen N, Young W. Miller's Anesthesia. 8th ed. Philadelphia: Elsevier Churchill Livingstone; 2015.
42. Girard TD, Alhazzani W, Kress JP, Ouellette DR, Schmidt GA, Truwit JD, et al. An Official American Thoracic Society/American College of Chest Physicians Clinical Practice Guideline: Liberation from mechanical ventilation in critically ill adults. Rehabilitation protocols, ventilator liberation protocols, and cuff leak tests. Am J Respir Crit Care Med 2017;195:120-33.
43. Rinaudo M, Ferrer M, Terraneo S, De Rosa F, Peralta R, Fernández-Barat L, et al. Impact of COPD in the outcome of ICU-acquired pneumonia with and without previous intubation. Chest 2015;147:1530-8.
44. Gursel G. Determinants of the length of mechanical ventilation in patients with COPD in the intensive care unit. Respiration 2005;72:61-7.
45. Dalal AA, Shah M, D'Souza AO, Rane P. Costs of COPD exacerbations in the emergency department and inpatient setting. Respir Med 2011;105:454-60.
46. Bergius J, Engerström L, Orwellius L, Nordlund P, Sjöberg F, Fredrikson M, et al. A prospective longitudinal multicentre study of health related quality of life in ICU survivors with COPD. Crit Care 2013;17:R211.
47. Seneff MG, Wagner DP, Wagner RB, Zimmerman JE, Knaus WA. Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of chronic obstructive pulmonary disease. JAMA 1995;274:1852-7.
48. Epstein SK. Etiology of extubation failure and the predictive value of the rapid shallow breathing index. Am J Respir Crit Care Med 1995;152:545-9.
49. Jacob B, Chatila W, Mannouh CA. The unassisted respiratory rate/tidal volume ratio accurately predicts weaning outcome in postoperative patients. Crit Care Med 1997;25:253-7.
50. Goharani R, Vahedian-Azimi A, Gulal IH, Cordeiro de Souza L, Farzanegan B, Bashar FR, et al. A rapid shallow breathing index threshold of 85 predicts extubation success in chronic obstructive pulmonary disease patients with hypercapnic respiratory failure. J Thorac Dis 2019;11:1223-32.
51. Karthika M, Al Enezi FA, Pillai LV, Arabi YM. Rapid shallow breathing index. Ann Thorac Med 2016;11:167-76.
52. Tanios MA, Nevins ML, Hendra KP, Cardinal P, Allan JE, Naumova EN, et al. A randomized, controlled trial of the role of weaning predictors in clinical decision making. Crit Care Med 2006;34:2530-5.
53. Li Y, He G, Chen R. Clinical study of weaning predictors in COPD patients with prolonged mechanical ventilation. Zhonghua Jie He He Hu Xi Za Zhi 2000;23:217-20.
54. Li ZB, Gao XJ, Wang DH, Zhang B, Zhang ZP, Hu ZM, et al. [A multicenter study of respiratory multiple index in predicting weaning from mechanical ventilation in patients with acute exacerbation of chronic obstructive pulmonary disease]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2013;25:339-42.
55. Boustou AK, Abatzioudou F, Tryfon S, Nakou C, Pitsiou G, Argyropoulou P, et al. Diagnostic accuracy of the rapid shallow breathing index to predict a successful spontaneous breathing trial outcome in mechanically ventilated patients with chronic obstructive pulmonary disease. Heart Lung 2011;40:105-10.
56. Purro A, Appendini L, De Gaetano A, Gudjonsson M, Donner CF, Rossi A. Physiologic determinants of ventilator dependence in long-term mechanically ventilated patients. Am J Respir Crit Care Med 2000;161:115-23.
57. Schoser B, Fong E, Geberhiwot T, Hughes D, Kissel JT, Madathil SC, et al. Maximum inspiratory pressure as a clinically meaningful trial endpoint for neuromuscular diseases: A comprehensive review of the literature. Orphanet J Rare Dis 2017;12:52.
58. Ringvist T. The ventilatory capacity in healthy subjects. An analysis of causal factors with special reference to the respiratory forces. Scand J Clin Lab Invest Suppl 1966;88:5-179.
59. Cook CD, Mead J, Orzalesi MM. Static volume-pressure characteristics of the respiratory system during maximal efforts. Scand J Clin Lab Invest Suppl 1966;88:5-179.
60. Girolami A, Vahidian-Azimi M, Faglia G, Mazzariol R, Pozzi F, et al. Statement on respiratory muscle testing. Am J Respir Crit Care Med 2016;193:600-14.