



## 2021 Year in Review

**This year there have been thousands of research trials and articles about mechanical ventilation that makes the selection of important articles very difficult.**

**We chose some studies/articles that might have educational and clinical significance**

**We represent the abstract of those articles along a brief commentary and thoughts by our editorial team**

**We do not recommend depending on our comments but reading and critiquing the study/paper yourself and make your own decision**

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# Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial.

Ehrmann S, Li J, Ibarra-Estrada M, et al. Lancet Respir Med. 2021 Dec;9(12):1387-1395.

doi: 10.1016/S2213-2600(21)00356-8. Epub 2021 Aug 20. PMID: 34425070; PMCID: PMC8378833.

## **Abstract**

### **Background**

Awake prone positioning has been reported to improve oxygenation for patients with COVID-19 in retrospective and observational studies, but whether it improves patient-centred outcomes is unknown. We aimed to evaluate the efficacy of awake prone positioning to prevent intubation or death in patients with severe COVID-19 in a large-scale randomised trial.

### **Methods**

In this prospective, a priori set up and defined, collaborative meta-trial of six randomised controlled open-label superiority trials, adults who required respiratory support with high-flow nasal cannula for acute hypoxaemic respiratory failure due to COVID-19 were randomly assigned to awake prone positioning or standard care. Hospitals from six countries were involved: Canada, France, Ireland, Mexico, USA, Spain. Patients or their care providers were not masked to allocated treatment. The primary composite outcome was treatment failure, defined as the proportion of patients intubated or dying within 28 days of enrolment.

### **Comments**

Meta-trial: combined 6 prospective trials in multiple countries (3 countries count for 94% of subjects). Subjects included, confirmed or presumed COVID-19 with SpO<sub>2</sub>:FiO<sub>2</sub> < 315. randomly assigned to

awake prone positioning (n=567) or standard care (n=559). Average proning time 5 hrs (1.6-8.6 hrs). Findings: Treatment failure occurred in 223 (40%) of 564 patients assigned to awake prone positioning and in 257 (46%) of 557 patients assigned to standard care (relative risk 0·86 [95% CI 0·75-0·98]). The hazard ratio (HR) for intubation was 0·75 (0·62-0·91), and the HR for mortality was 0·87 (0·68-1·11) with awake prone positioning compared with standard care within 28 days of enrolment. The incidence of prespecified adverse events was low and similar in both groups. Patients with higher proning time had less failure. Patients intubated in both groups had similar mortality and LOS.

Discussion: Encouraging findings and consistent with other studies. Non blinded, Meta-trial (combining 6 different trials, with agreement on protocol) might have caused some bias in results. Morbidly obese patients (BMI > 40) were excluded 10% of the standard group were placed in prone position (unclear duration in hours or number of days). Duration of proning was not defined and highly variable. Other details of concurrent medical treatments (corticosteroids, anti-virals, anti-inflammatory) not included. Multiple funding of the trials, and multiple declaration of interest from high flow companies

**Take home point:** Awake proning is beneficial in COVID-19 patients with low side effects.

# Comparison of High-Flow Nasal Cannula and Noninvasive Ventilation in Acute Hypoxemic Respiratory Failure Due to Severe COVID-19 Pneumonia

Nair PR, Haritha D, Behera S, et al. *Respir Care*. 2021 Dec;66(12):1824-1830.

doi: 10.4187/respcare.09130. Epub 2021 Sep 28. PMID: 34584010.

## **Abstract**

**Background:** Efficacy of high-flow nasal cannula (HFNC) over noninvasive ventilation (NIV) in severe coronavirus disease 2019 (COVID-19) pneumonia is not known. We aimed to assess the incidence of invasive mechanical ventilation in patients with acute hypoxemic respiratory failure due to COVID-19 treated with either HFNC or NIV.

**Methods:** This was a single-center randomized controlled trial performed in the COVID-19 ICU of a tertiary care teaching hospital in New Delhi, India. One hundred and nine subjects with severe COVID-19 pneumonia presenting with acute hypoxemic respiratory failure were recruited and allocated to either HFNC ( $n = 55$ ) or NIV ( $n = 54$ ) arm.

Primary outcome was intubation by 48 h. Secondary outcomes were improvement in oxygenation by 48 h, intubation rate at day 7, and in-hospital mortality.

**Results:** Baseline characteristics and  $P_{aO_2}/F_{IO_2}$  ratio were similar in both the groups. Intubation rate at 48 h was similar between the groups (33% NIV vs 20% HFNC, relative risk 0.6, 95% CI 0.31–1.15,  $P = .12$ ). Intubation rate at day 7 was lower in the HFNC (27.27%) compared to the NIV group (46.29%) (relative risk 0.59, 95% CI 0.35–0.99,  $P = .045$ ), and this difference remained significant after adjustment for the incidence of chronic kidney disease and the arterial pH (adjusted OR 0.40, 95% CI 0.17–0.93,  $P = .03$ ). Hospital mortality was similar between HFNC (29.1%) and NIV (46.2%) group (relative risk 0.6, 95% CI 0.38–1.04,  $P = .06$ ).

**Conclusions:** We were not able to demonstrate a statistically significant improvement of oxygenation

parameters nor of the intubation rate at 48 h between NIV and HFNC. These findings should be further tested in a larger randomized controlled trial.

## **Comments**

Single center randomized trial in India of 109 nine patients with COVID-19 to HFNC (55) or NIV (54) Primary outcome was intubation at 48 hrs, Secondary outcomes were improvement in oxygenation at 48 hrs, intubation at 7 days, and in hospital mortality.

**Findings:** Rate of intubation at 48 hrs (33% in NIV vs 27% in HFNC) was not statistically significant, rate of intubation at 7 days was (46.29% vs 27.27 in HFNC) was statistically significant. Hospital mortality (46.2% NIV vs 29.1 in HFNC) not statistically significant.

**Discussion:** Though the intubation rate 48 hrs and in hospital mortality were not statistically significant, the trend favors HFNC. Results consistent with studies from 2020 that favors HFNC and recommended by the recently updated surviving sepsis guidelines. The study was non blinded, single center, small size of subjects. No available data on awake proning in both groups (HFNC probably had more proning per study discussion).

No mention on medical therapy on both groups (corticosteroids, anti-virals, anti-inflammatory therapies).

**Take home point:** HFNC might be slightly more beneficial than NIV in COVID-19.

## **Efficacy of non-invasive and invasive respiratory management strategies in adult patients with acute hypoxaemic respiratory failure: a systematic review and network meta-analysis**

Sakuraya M, Okano H, Masuyama T, et al. Efficacy of non-invasive and invasive respiratory management strategies in adult patients with acute hypoxaemic respiratory failure: a systematic review and network meta-analysis. *Crit Care*. 2021 Nov 29;25(1):414.

doi: 10.1186/s13054-021-03835-8. PMID: 34844655; PMCID: PMC8628281.

### **Abstract**

**Background:** Although non-invasive respiratory management strategies have been implemented to avoid intubation, patients with de novo acute hypoxaemic respiratory failure (AHRF) are high risk of treatment failure. In the previous meta-analyses, the effect of non-invasive ventilation was not evaluated according to ventilation modes in those patients. Furthermore, no meta-analyses comparing non-invasive respiratory management strategies with invasive mechanical ventilation (IMV) have been reported. We performed a network meta-analysis to compare the efficacy of non-invasive ventilation according to ventilation modes with high-flow nasal oxygen (HFNO), standard oxygen therapy (SOT), and IMV in adult patients with AHRF.

**Methods:** The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and Ichushi databases were searched. Studies including adults with AHRF and randomized controlled trials (RCTs) comparing two different respiratory management strategies (continuous positive airway pressure (CPAP), pressure support ventilation (PSV), HFNO, SOT, or IMV) were reviewed.

**Results:** We included 25 RCTs (3,302 participants; 27 comparisons). Using SOT as the reference, CPAP (risk ratio [RR] 0.55; 95% confidence interval [CI] 0.31–0.95; very low certainty) was associated significantly with a lower risk of mortality. Compared with SOT, PSV (RR 0.81; 95% CI 0.62–1.06; low certainty) and HFNO (RR 0.90; 95% CI 0.65–1.25; very low certainty) were not associated with a significantly lower risk of mortality. Compared with IMV, no non-invasive respiratory management was associated with a significantly lower risk of mortality, although all certainties of evidence were very low. The probability of being best in reducing short-term mortality among all possible interventions was higher for CPAP, followed by PSV and HFNO;

IMV and SOT were tied for the worst (surface under the cumulative ranking curve value: 93.2, 65.0, 44.1, 23.9, and 23.9, respectively).

**Conclusions:** When performing non-invasive ventilation among patients with de novo AHRF, it is important to avoid excessive tidal volume and lung injury. Although pressure support is needed for some of these patients, it should be applied with caution because this may lead to excessive tidal volume and lung injury.

### **Comments:**

Meta-analysis (25 studies with 3,302 patients) to compare different non-invasive modes of ventilation (CPAP & PSV) to High flow nasal oxygen (HFNO), standard oxygen (SO) and Invasive mechanical ventilation (IMV) in acute hypoxic respiratory failure.

**Findings:** CPAP had better mortality than SO. PSV and HFNO were not associated with decreased mortality. None had any mortality difference compared to IMV

**Discussion:** Though it is an interesting meta-analysis, the results should be interpreted with caution and can't be definitely generalized or make a statement that CPAP is superior to PSV, HFNC.

Though the authors tried to exclude studies with COPD exacerbation and cardiogenic pulmonary edema where NIV shown superiority, still there were patients included in those trials.

**Insufficient comparisons:** No studies included compared CPAP and HFNO to IMV

No studies compared CPAP to HFNO or PSV in mortality or intubation. The results were of low, to very low certainty

**Take home point:** We can't make a statement that CPAP is really more beneficial than PSV, HFNC or IMV in acute hypoxic respiratory failure.

More studies needed.

## Driving Pressure Is a Risk Factor for ARDS in Mechanically Ventilated Subjects Without ARDS

Oriol Roca, Oscar Penñuelas, Alfonso Muriel, et al. Driving Pressure Is a Risk Factor for ARDS in Mechanically Ventilated Subjects Without ARDS. *Respir Care*. 2021 Oct;66(10):1505-1513. doi: 10.4187/respcare.08587. Epub 2021 Aug 3. PMID: 34344717.

### **Abstract:**

**Background:** Driving pressure ( $\Delta P$ ) has been described as a risk factor for mortality in patients with ARDS. However, the role of  $\Delta P$  in the outcome of patients without ARDS and on mechanical ventilation has received less attention. Our objective was to evaluate the association between  $\Delta P$  on the first day of mechanical ventilation with the development of ARDS. **Methods:** This was a post hoc analysis of a multicenter, prospective, observational, international study that included subjects who were on mechanical ventilation for  $> 12$  h. Our objective was to evaluate the association between  $\Delta P$  on the first day of mechanical ventilation with the development of ARDS. To assess the effect of  $\Delta P$ , a logistic regression analysis was performed when adjusting for other potential risk factors. Validation of the results obtained was performed by using a bootstrap method and by repeating the same analyses at day 2. **Results:** A total of 1,575 subjects were included, of whom 65 (4.1%) developed ARDS. The  $\Delta P$  was independently associated with ARDS (odds ratio [OR] 1.12, 95% CI 1.07-1.18 for each cm H<sub>2</sub>O of  $\Delta P$  increase,  $P < .001$ ). The same results were observed at day 2 (OR 1.14, 95% CI 1.07-1.21;  $P < .001$ ) and after bootstrap validation (OR 1.13, 95% CI 1.04-1.22;  $P < .001$ ). When taking the prevalence of ARDS in the lowest quartile of  $\Delta P$  ( $\leq 9$  cm H<sub>2</sub>O) as a reference, the subjects with  $\Delta P > 12$ -15 cm H<sub>2</sub>O and those with  $\Delta P > 15$  cm H<sub>2</sub>O presented a higher probability of ARDS (OR 3.65, 95% CI 1.32-10.04 [ $P = .01$ ] and OR 7.31, 95% CI, 2.89-18.50 [ $P < .001$ ], respectively). **Conclusions:** In the subjects without ARDS, a higher level of  $\Delta P$  on the first day of mechanical

ventilation was associated with later development of ARDS.

### **Comments:**

With the background of less attention to the role of  $\Delta P$  in the outcome of patients without ARDS, the association between  $\Delta P$  on the first day of mechanical ventilation and the development of ARDS was evaluated. Through a post hoc analysis of multicenter, prospective, observational, international study a logistic regression analysis was performed in adjusting for other potential risk factors to assess the effect of  $\Delta P$ . Validation of the results obtained was performed by using a bootstrap method. The level of  $\Delta P$  on the first day of mechanical ventilation was associated with later development of ARDS and mortality. The subjects with  $\Delta P > 12$  cm H<sub>2</sub>O presented higher possibility of developing ARDS.

**Findings:** Each cm H<sub>2</sub>O increase of  $\Delta P$  increased the risk of ARDS by 10%, and the risk of ICU and hospital death by 3%. The subjects with  $\Delta P > 12$  cm H<sub>2</sub>O presented higher possibility of developing ARDS.

**Discussion:** This study shows higher  $\Delta P$  was associated with an increased risk of ARDS; the  $\Delta P$  at day 1 was associated with higher ICU and hospital mortality. Although this study was observational and the results did not necessarily imply causality, there was a physiologic plausibility that linked a high  $\Delta P$  to ARDS development. These results provide a rationale for assessing the effectiveness of reducing  $\Delta P$  in patients without ARDS.

**Take home point:** the less applied inspiratory pressure is better.

## Transpulmonary Pressure-Guided Lung-Protective Ventilation Improves Pulmonary Mechanics and Oxygenation Among Obese Subjects on Mechanical Ventilation

Rowley DD, Arrington SA, Enfield KB, et al. *Respir Care* 2021;66(7):1049–1058. doi: 10.4187/respcare.08686. Epub 2021 Apr 20. PMID: 33879565.

### **Abstract**

**Background:** Transpulmonary pressure ( $P_L$ ) is used to assess pulmonary mechanics and guide lung-protective mechanical ventilation (LPV).  $P_L$  is recommended to individualize LPV settings for patients with high pleural pressures and hypoxemia. We aimed to determine whether  $P_L$ -guided LPV settings, pulmonary mechanics, and oxygenation improve and differ from non- $P_L$ -guided LPV among obese patients after 24 h on mechanical ventilation. Secondary outcomes included classification of hypoxemia severity, count of ventilator-free days, ICU length of stay, and overall ICU mortality.

**Methods:** This is a retrospective analysis of data. Ventilator settings, pulmonary mechanics, and oxygenation were recorded on the initial day of  $P_L$  measurement and 24 h later.  $P_L$ -guided LPV targeted inspiratory  $P_L < 20$  cm H<sub>2</sub>O and expiratory  $P_L$  of 0–6 cm H<sub>2</sub>O. Comparisons were made to repeat measurements.

**Results:** Twenty subjects (13 male) with median age of 49 y, body mass index 47.5 kg/m<sup>2</sup>, and SOFA score of 8 were included in our analysis. Fourteen subjects received care in a medical ICU.

$P_L$  measurement occurred 16 h after initiating non- $P_L$ -guided LPV.  $P_L$ -guided LPV resulted in higher median PEEP (14 vs 18 cm H<sub>2</sub>O,  $P = .009$ ), expiratory  $P_L$  (-3 vs 1 cm H<sub>2</sub>O,  $P = .02$ ), respiratory system compliance (30.7 vs 44.6 mL/cm H<sub>2</sub>O,  $P = .001$ ), and [Formula: see text] (156 vs 240 mm Hg,  $P = .002$ ) at 24 h.  $P_L$ -guided LPV resulted in lower [Formula: see text] (0.53 vs 0.33,  $P < .001$ ) and lower  $P_L$  driving pressure (10 vs 6 cm H<sub>2</sub>O,  $P = .001$ ). Tidal volume (420 vs 435 mL,  $P = .64$ ) and inspiratory  $P_L$  (7 vs 7 cm H<sub>2</sub>O,  $P = .90$ ) were similar. Subjects had a median of 7 ventilator-free days, and median ICU length of stay was 14 d. Three of 20 subjects died within 28 d after ICU admission.

**Conclusions:**  $P_L$ -guided LPV resulted in higher PEEP, lower [Formula: see text], improved pulmonary mechanics, and greater oxygenation then

compared to non- $P_L$ -guided LPV settings in adult obese subjects.

### **Comments:**

Parameters of pulmonary mechanics and oxygenation were compared before and 16 hours after initiating transpulmonary pressure-guided lung-protective ventilation (LPV) for 20 obese patients. Mechanical ventilator settings were adjusted to target an inspiratory transpulmonary pressure (PL) <20cmH<sub>2</sub>O and expiratory PL target of 0–6cm H<sub>2</sub>O. A FiO<sub>2</sub>/ PL table was used to determine optimal expiratory PL in relationship to set FiO<sub>2</sub>.

**Findings:** For adjustments of ventilator settings, median set PEEP increased significantly from 14 to 18cmH<sub>2</sub>O and median FiO<sub>2</sub> decreased from 0.53 to 0.33. Median Vt and median inspiratory PL did not change significantly after PL -guided set PEEP or Vt increase. As a result, median respiratory system compliance increased significantly from 30.7 to 44.6 ml/cmH<sub>2</sub>O, median PL driving pressure decreased significantly from 10 to 6 cmH<sub>2</sub>O, and median PaO<sub>2</sub>/FiO<sub>2</sub> ratio increased significantly from 156 to 240.

**Discussion:** In this study oxygenation and respiratory system compliance improved after initiating transpulmonary pressure-guided lung-protective ventilation (LPV) for obese patients. Research and studies to find optimal PEEP and optimal mechanical ventilator settings for obesity have been limited. Through LPV, PEEP is recognized not only for recruitment method of alveoli but also stabilize dependent lung region against atelectasis when pleural pressure exceeds alveolar pressure at the end of exhalation especially for obesity. Further studies are required to have control group with high PEEP/FiO<sub>2</sub> table or electrical impedance tomography to determine if there is beneficial to utilize LPV for obese patients.

**Take home point:** using esophageal balloon monitoring during mechanical ventilation is helpful and should be adopted.

## **Intracycle power and ventilation mode as potential contributors to ventilator-induced lung injury**

Marini JJ, Crooke PS, Tawfik P, et al. Intracycle power and ventilation mode as potential contributors to ventilator-induced lung injury. *Intensive Care Med Exp*. 2021 Nov 1;9(1):55. doi: 10.1186/s40635-021-00420-9. PMID: 34719749; PMCID: PMC8557972.

### **Abstract**

**Background:** High rates of inflation energy delivery coupled with transpulmonary tidal pressures of sufficient magnitude may augment the risk of damage to vulnerable, stress-focused units within a mechanically heterogeneous lung. Apart from flow amplitude, the clinician-selected flow waveform, a relatively neglected dimension of inflation power, may distribute inflation energy of each inflation cycle non-uniformly among alveoli with different mechanical properties over the domains of time and space. In this initial step in modeling intracycle power distribution, our primary objective was to develop a mathematical model of global intracycle inflation power that uses clinician-measurable inputs to allow comparisons of instantaneous ICP profiles among the flow modes commonly encountered in clinical practice: constant, linearly decelerating, exponentially decelerating (pressure control), and spontaneous (sinusoidal).

**Methods:** We first tested the predictions of our mathematical model of passive inflation with the actual physical performance of a mechanical ventilator-lung system that simulated ventilation to three types of patients: normal, severe ARDS, and severe airflow obstruction. After verification, model predictions were then generated for 5000 'virtual ARDS patients'. Holding constant the tidal volume and inflation time between modes, the validated model then varied the flow profile and quantitated the resulting intensity and timing of potentially damaging 'elastic' energy and intracycle power (pressure-flow product) developed in response to random combinations of machine settings and severity levels for ARDS.

**Results:** Our modeling indicates that while the varied flow patterns ultimately deliver similar total

amounts of alveolar energy during each breath, they differ profoundly regarding the potentially damaging pattern with which that energy distributes over time during inflation. Pressure control imposed relatively high maximal intracycle power.

**Conclusions:** Flow amplitude and waveform may be relatively neglected and modifiable determinants of VILI risk when ventilating ARDS.

### **Comments:**

The authors developed an interesting conceptual theory of VILI called the Intra-Cyclic power (ICP) which is described as pressure-flow product. This is a mathematical simulation equation and tested it in a lung simulator on 3 passive different respiratory mechanics (Normal, ARDS, airflow obstruction) using different flow waveforms (sinusoidal, constant, linear, and exponential deceleration).

**Findings:** is not only the flow amplitude, but different flow waveforms dissipate energy to alveoli differently.

**Discussion:** The article is very technical and mathematical which makes it difficult to follow but that doesn't lessen its importance. The study is a bench study with the inherent limitations of such studies like not on real active patients with unknown patient-ventilator interactions. The threshold chosen was empiric not based on accepted studied threshold.

**Take home message:** the study adds to our knowledge about VILI and to think about other modifiable parameters like flow amplitude, waveforms that might contribute to VILI. The results need to be verified in animal/human studies before adopting this theory.

## **Programmed Multi-Level Ventilation: A Strategy for Ventilating Non-Homogenous Lungs**

Depta F, Torok P, Reeves V, et al. Programmed Multi-Level Ventilation: A Strategy for Ventilating Non-Homogenous Lungs. *Med Devices (Auckl)*. 2021 Sep 21;14:277-285. doi: 10.2147/MDER.S329352. PMID: 34584466; PMCID: PMC8464363.

### **Abstract**

Mechanical ventilation (MV) has been an integral method used in ICU care for decades. MV is typically viewed as a life-supporting intervention. However, it can also contribute to lung injury through stress and strain, as evidenced by ventilator-induced lung injury (VILI), even in previously healthy lungs. The negative impact may be worsened when significant lung non-homogeneity is present, eg. ALI and ARDS. Protective lung strategies to minimize VILI are to use low tidal volumes ( $V_t$  4-6 mL/kg/PBW), plateau pressures ( $P_{plat}$ ) <30 cmH<sub>2</sub>O and relatively high positive end-expiratory pressures (PEEP). Yet, use of constantly high PEEP levels is well recognized to result in hemodynamic compromise of the right ventricle, increased stress and strain through high mechanical energy impact on the lung and overdistension of relatively healthy lung tissue. Taking these issues into consideration, a different approach to mechanical ventilation was developed specifically for patients with non-homogeneity. This review focuses on a feature called programmed multi-level ventilation (PMLV). It is not a ventilation mode per se, but rather a form of extension that adjusts and modifies any ventilation mode (eg PCV, PSV, VCV, SIMV, etc.). PMLV is based on measured time constants

( $\tau$ ) of the whole respiratory system, including artificial airways, breathing circuits, humidification devices and mechanical ventilator. Using a physiology-based approach presents a method to ventilate non-homogenous lungs through cyclic changes of different PEEP levels; recruitment takes place in lung areas with long time constants but protects relatively healthy lung areas from overdistension thus minimizing excessive mechanical power to the lung tissue.

### **Comments:**

Very interesting theory for mechanical ventilation inhomogeneous lung disease with different levels of PEEP, Frequencies which might reduce VILI in forms of alveolar over and under distention. The algorithm the authors use is based on mathematical model and measuring expiratory time constant. The authors quote 2 small clinical trials from 2013 and 2014. More robust studies need to be performed with better monitoring of inhomogeneity and oxygenation/ventilation indices. Also would be helpful in comparing this strategy to other modes that adjusts respiratory frequency and tidal volumes based on expiratory time constant.

**Take home points:** a promising technique for understanding and ventilating inhomogeneous lungs.



## **Flow Index: a novel, non-invasive, continuous, quantitative method to evaluate patient inspiratory effort during pressure support ventilation**

Albani, F., Pisani, L., Ciabatti, G. et al. Flow Index: a novel, non-invasive, continuous, quantitative method to evaluate patient inspiratory effort during pressure support ventilation. Crit Care 25, 196 (2021). <https://doi.org/10.1186/s13054-021-03624-3>

### **Abstract:**

**Background:** The evaluation of patient effort is pivotal during pressure support ventilation, but a non-invasive, continuous, quantitative method to assess patient inspiratory effort is still lacking. We hypothesized that the concavity of the inspiratory flow-time waveform could be useful to estimate patient's inspiratory effort. The purpose of this study was to assess whether the shape of the inspiratory flow, as quantified by a numeric indicator, could be associated with inspiratory effort during pressure support ventilation.

**Methods:** Twenty-four patients in pressure support ventilation were enrolled. A mathematical relationship describing the decay pattern of the inspiratory flow profile was developed. The parameter hypothesized to estimate effort was named Flow Index. Esophageal pressure, airway pressure, airflow, and volume waveforms were recorded at three support levels (maximum, minimum and baseline). The association between Flow Index and reference measures of patient effort (pressure time product and pressure generated by respiratory muscles) was evaluated using linear mixed effects models adjusted for tidal volume, respiratory rate and respiratory rate/tidal volume.

**Results:** Flow Index was different at the three pressure support levels and all group comparisons were statistically significant. In all tested models, Flow Index was independently associated with patient effort ( $p < 0.001$ ). Flow Index prediction of

inspiratory effort agreed with esophageal pressure-based methods.

**Conclusions:** Flow Index is associated with patient inspiratory effort during pressure support ventilation, and may provide potentially useful information for setting inspiratory support and monitoring patient-ventilator interactions.

### **Comments:**

Interesting well performed clinical study that evaluate the shape of the flow-time curve and that the concavity of the flow curve is influenced and correlated by patient effort. The authors made a calculation very similar to the stress index of airway pressure. The hypothesis is not new but it is the first time to be evaluated quantitatively.

**Finding:** the Flow index correlated well with the pressure-time product, esophageal pressure drop, Pmus.

**Discussion:** as PSV uses the linear deceleration waveform, the index will be usually 1 in patients with low effort and might be misleading as could be secondary to weakness. The study was in small patient cohort. It didn't include the correlation of this index on weaning success. It is difficult to calculate such indices in clinical practice but visual qualitative assessment might be close.

**Take home point:** Evaluation of the flow curves are important to estimate patient effort especially during the SBT trials.

## **Prediction of extubation outcome in critically ill patients: a systematic review and meta-analysis**

Torrini F, Gendreau S, Morel J, et al. Prediction of extubation outcome in critically ill patients: a systematic review and meta-analysis. *Crit Care* 25, 391 (2021). <https://doi.org/10.1186/s13054-021-03802-3>

### **Abstract:**

**Background:** Extubation failure is an important issue in ventilated patients and its risk factors remain a matter of research. We conducted a systematic review and meta-analysis to explore factors associated with extubation failure in ventilated patients who passed a spontaneous breathing trial and underwent planned extubation. This systematic review was registered in PROPERO with the Registration ID CRD42019137003.

**Methods:** We searched the PubMed, Web of Science and Cochrane Controlled Register of Trials for studies published from January 1998 to December 2018. We included observational studies involving risk factors associated with extubation failure in adult intensive care unit patients who underwent invasive mechanical ventilation. Two authors independently extracted data and assessed the validity of included studies.

**Results:** Sixty-seven studies (involving 26,847 participants) met the inclusion criteria and were included in our meta-analysis. We analyzed 49 variables and, among them, we identified 26 factors significantly associated with extubation failure. Risk factors were distributed into three domains (comorbidities, acute disease severity and characteristics at time of extubation) involving mainly three functions (circulatory, respiratory and neurological). Among these, the physiological respiratory characteristics at time of extubation

were the most represented. The individual topic of secretion management was the one with the largest number of variables. By Bayesian multivariable meta-analysis, twelve factors were significantly associated with extubation failure: age, history of cardiac disease, history of respiratory disease, Simplified Acute Physiologic Score II score, pneumonia, duration of mechanical ventilation, heart rate, Rapid Shallow Breathing Index, negative inspiratory force, lower PaO<sub>2</sub>/FiO<sub>2</sub> ratio, lower hemoglobin level and lower Glasgow Coma Scale before extubation, with the latest factor having the strongest association with extubation outcome.

**Conclusions:** Numerous factors are associated with extubation failure in critically ill patients who have passed a spontaneous breathing trial. Robust multiparametric clinical scores and/or artificial intelligence algorithms should be tested based on the selected independent variables in order to improve the prediction of extubation outcome in the clinical scenario.

### **Comments:**

This metanalysis identified multiple factors that might contribute to failing liberation of mechanical ventilation as outlined in the abstract. However non of this information are new and most of the factors associated can be modifiable.

**Take home points:** it is important to be aware of the factors that can cause extubation failures. We need better indices and prediction models for future research.

## **Discriminant Accuracy of the SOFA Score for Determining the Probable Mortality of Patients With COVID-19 Pneumonia Requiring Mechanical Ventilation**

Raschke RA, Agarwal S, Rangan P, et al. Discriminant Accuracy of the SOFA Score for Determining the Probable Mortality of Patients With COVID-19 Pneumonia Requiring Mechanical Ventilation. JAMA. 2021 Apr 13;325(14):1469-1470. doi: 10.1001/jama.2021.1545. PMID: 33595630; PMCID: PMC7890534.

### **Abstract:**

The COVID-19 pandemic has raised concern regarding the capacity to provide care for a surge of critically ill patients that might require excluding patients with a low probability of short-term survival from receiving mechanical ventilation.<sup>1</sup> A survey identified 26 unique COVID-19 triage policies, of which 20 used some form of the Sequential Organ Failure Assessment (SOFA) score.

However, studies performed in 2016 and 2017 have shown only moderate discriminant accuracy of the SOFA score for predicting survival in intensive care unit (ICU) patients with sepsis and an area under the receiver operating characteristic curve (AUROC) of 0.74 to 0.75.<sup>3,4</sup> We hypothesized that the SOFA score might be less accurate in patients

requiring mechanical ventilation for COVID-19 pneumonia because such patients generally have severe single-organ dysfunction and less variation in SOFA scores.

### **Comments:**

A retrospective study in a single center that tried to investigate the predictive accuracy of the SOFA score on mortality in COVID-19 patients.

Findings: the SOFA score did not correlate with mortality.

Discussion: Retrospective study in single center, there was lots of missing data almost 33% of patients.

Take home points: there is a need for a better specific score for patients with COVID-19 presenting with respiratory failure and requiring mechanical ventilatory support.

# Reviews

## **A Taxonomy for Patient-Ventilator Interactions and a Method to Read Ventilator Waveforms**

Mireles-Cabodevila E, Siuba MT, Chatburn RL. A Taxonomy for Patient-Ventilator Interactions and a Method to Read Ventilator Waveforms. *Respir Care*. 2021 Sep 1:respcare.09316.  
doi: 10.4187/respcare.09316. Epub ahead of print. PMID: 34470804.

### **Abstract**

Mechanical ventilators display detailed waveforms which contain a wealth of clinically relevant information. Although much has been written about interpretation of waveforms and patient-ventilator interactions, variability remains on the nomenclature (multiple and ambiguous terms) and waveform interpretation. There are multiple reasons for this variability (legacy terms, language, multiple definitions). In addition, there is no widely accepted

systematic method to read ventilator waveforms. We propose a standardized nomenclature and taxonomy along with a method to interpret mechanical ventilator displayed waveforms.

### **Comments**

A great review about how to read ventilator waveforms and classification of mechanical ventilation modes. A new taxonomy of patient-ventilator asynchronies

## **Four Truths of Mechanical Ventilation and the Ten-Fold Path to Enlightenment**

Chatburn RL. Four Truths of Mechanical Ventilation and the Ten-Fold Path to Enlightenment. J Mech Vent 2021; 2(3):73-78.

Abstract:

The Four Truths

1. The truth of confusion
2. The truth of the origin of confusion
3. The truth of the cessation of confusion
4. The truth of the path leading to the cessation of confusion

The 10-Fold Path

1. A breath is one cycle of positive flow (inspiration) and negative flow (expiration) defined in terms of the flow-time curve.
2. A breath is assisted if the ventilator does work on the patient.
3. A ventilator assists breathing using either pressure control or volume control based on the equation of motion for the respiratory system.
4. Breaths are classified by the criteria that trigger (start) and cycle (stop) inspiration
5. Trigger and cycle events can be initiated by the patient or the machine.

6. Breaths are classified as spontaneous or mandatory based on both the trigger and cycle events.

7. There are 3 breath sequences: Continuous mandatory ventilation (CMV), Intermittent Mandatory Ventilation (IMV), and Continuous Spontaneous Ventilation (CSV).

8. There are 5 basic ventilatory patterns: VC-CMV, VC-IMV, PC-CMV, PC-IMV, and PC-CSV:

9. Within each ventilatory pattern there are several variations that can be distinguished by their targeting scheme(s).

10. A mode of ventilation is classified according to its control variable, breath sequence, and targeting scheme(s)

### **Comments:**

Another great review to understand mechanical ventilation, modes, patient-ventilator interactions.

## **Mechanical Power: A New Concept in Mechanical Ventilation**

Paudel R, Trinkle CA, Waters CM, et al. Mechanical Power: A New Concept in Mechanical Ventilation. Am J Med Sci. 2021 Dec;362(6):537-545. doi: 10.1016/j.amjms.2021.09.004. Epub 2021 Sep 28. PMID: 34597688; PMCID: PMC8688297.

### **Abstract**

Mechanical ventilation is a potentially life-saving therapy for patients with acute lung injury, but the ventilator itself may cause lung injury. Ventilator-induced lung injury (VILI) is sometimes an unfortunate consequence of mechanical ventilation. It is not clear however how best to minimize VILI through adjustment of various parameters including tidal volume, plateau pressure, driving pressure, and positive end expiratory pressure (PEEP). No single parameter provides a clear indication for onset of lung injury attributable exclusively to the ventilator. There is currently interest in quantifying how static and dynamic parameters contribute to VILI. One concept that has emerged is the consideration of the amount of energy transferred from the ventilator to the respiratory system per unit time, which can be quantified as mechanical power. This review article reports on recent literature in this emerging field and future roles for mechanical power assessments in prospective studies.

### **Comment:**

Excellent review of the concept of mechanical power and its role and the future in VILI.