Mechanical Ventilation Strategy in sepsis

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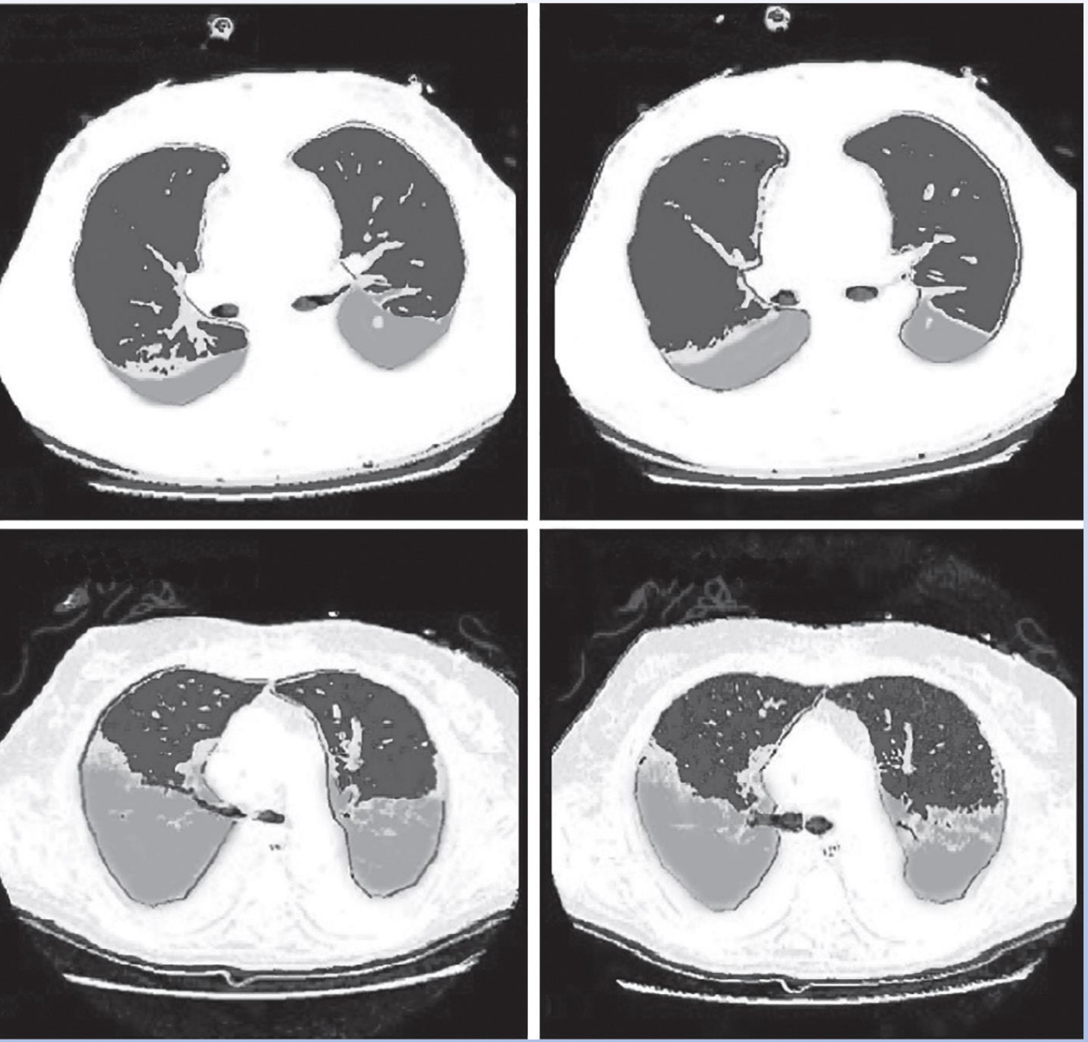
- In ARDS, mechanical ventilation supports gas exchange and **allows the respiratory system to rest** while the lung **recover from injury**.
- However, **inappropriate application** of mechanical ventilation can **worsen injury**(ventilator-induced lung injury (VILI) can develop in the form of:
- Volutrauma
- Atelectrauma
- Patient Self-Inflicted Lung Injury(P-SILI):is a form of VILI driven by a patient's own spontaneous respirations, is driven by a phenomenon called **pendelluft**, or "**swinging air**" .
- In ARDS the lungs are **heterogeneous**, and so is the flow through the airways. When **spontaneous breaths** are present, changes in pleural pressure are not uniformly transmitted through the lung, leading to **differential inflation of lung regions** where air flows from one region to another (i.e., pendelluft) and the **regional overdistension** can cause injury.



- Fig. Representative computed tomography (CT) scan slices of a patient with **a larger baby lung** component at end expiration (A) and after tidal inflation at end inspiration (B).

- A patient with **a smaller baby lung** component at end expiration (C) with **hyperinflation of the previously normally aerated lung** component after tidal inflation with **lower tidal volume delivery** (D) is shown.

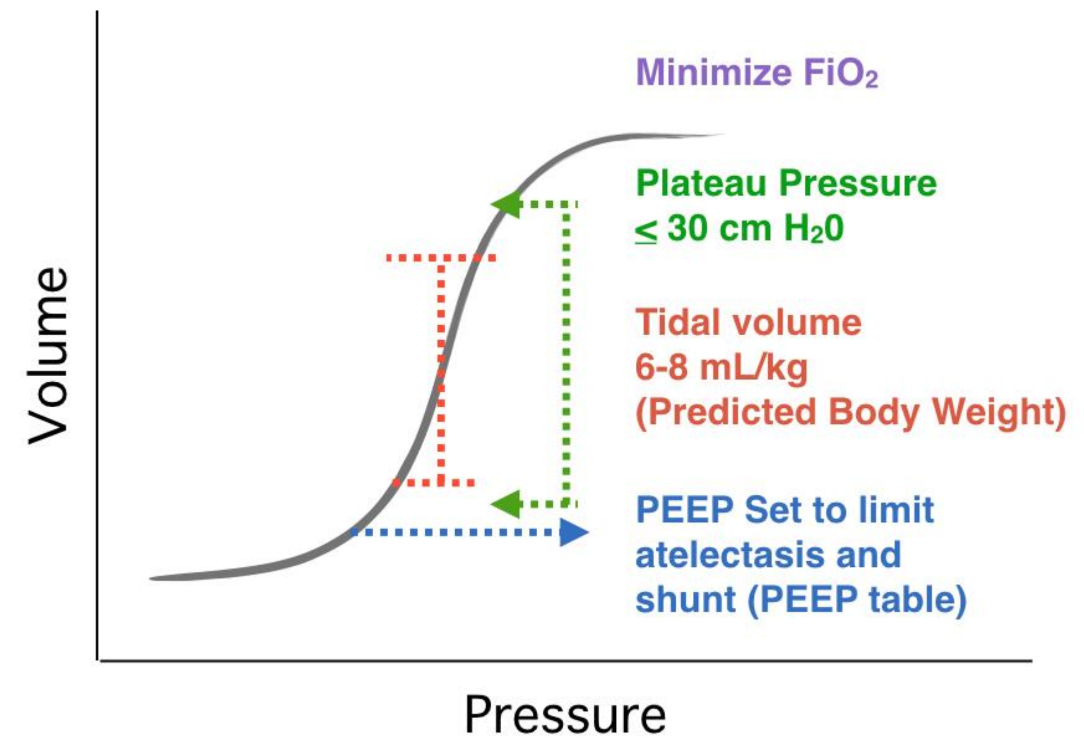
- (Modified from Terragni PP, Rosboch G, Tealdi A,et al. Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. Am J Respir Crit Care Med. 2007;175[2]:160-166.)

Conclusion

- Although the normally aerated component, **or baby lung, is still inflamed, it is functional, recruitable, and has near-normal compliance**
- **This small component** bears the stress and strain during mechanical ventilation, explaining why elevated pressures and high volumes can cause VILI

LUNG-PROTECTIVE VENTILATION

- **VILI can still occur, despite strict adherence to lung protective**, and **further reductions** in tidal **ultra-low tidal volumes(≤4 mL/kg PBW**). could potentially be beneficial, but very low tidal volumes can lead to respiratory acidosis(Hypercarbia)
- Extracorporeal carbon dioxide removal (ECCO2-R) has been suggested as a possible adjunct to lung-protective ventilation with ultra-low tidal volumes (**Ultra-lung-protective ventilation)**
- **ECMO** provides ultra-protective ventilation in patients with severe ARDS, thereby allowing the lungs to rest, and may reduce the risk of progressive VILI and subsequent multiple organ failure
- **Extracorporeal Membrane Oxygenation in Acute Respiratory Distress Syndrome:***J. Clin. Med.* **2021**, *10*(21), 4953



Components of Lung Protective Ventilation to reduce Ventilator-Associated Lung Injury (VALI) and decrease incidence of ARDS

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Ultra-lung-protective ventilation and biotrauma in severe ARDS patients on veno-venous extracorporeal membrane oxygenation: a randomized controlled study

- The pathophysiological rationale to use a ULP approach **was attractive**, but this large exploration of the biotrauma did not highlight any relevant beneficial effect of the investigated strategy.

Conclusion

- A multimodal ultra-lung-protective strategy including intermittent prone position during 48 h in severe ARDS patients supported by vv-ECMO was not associated with a decrease in the pulmonary and the systemic biotrauma as compared with the lung-protective strategy of the EOLIA trial .
- Results of future or ongoing trials exploring clinical outcomes are expected

The Assessment of Low Tidal Volume and Elevated End- Expiratory Pressure to Obviate Lung Injury

- (ALVEOLI) trial compared **high** PEEP/FiO2 and **low**-PEEP/FiO2 titration strategies. All study participants were also ventilated with LTV.
- This study was stopped early for futility and revealed no difference in in-hospital mortality between the lower-PEEP and higher-PEEP groups.

- Brower RG, Lanken PN, MacIntyre N, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med.* 2004;351(4):327-336.

- In the Lung Open Ventilation Study (LOVS), a conventional ventilation protocol with lower PEEP was compared with an open lung protocol that included higher PEEP values and RM and **there was no statistically significant difference in mortality between the groups.**
- RM involve a transient increase in transpulmonary pressure to levels higher than those achieved during tidal ventilation and can confer the same physiologic benefit as higher PEEP
- A meta-analysis of individual patient data from theALVEOLI, ExPress, LOVS trials showed that in **patients with moderate-to-severe ARDS (with a threshold PaO2/FiO2 ratio of 200 mm Hg**), the higher PEEP strategies were associated with lower mortality
- Another secondary analysis of the ExPress and LOVS trials showed that patients who **responded to increased PEEP with improved oxygenation** had lower mortality

Low tidal volume(LTV) ventilation

- In ARDS, the concept of the **baby lung** provides **a rationale** for the mortality benefit associated with LTV ventilation.
- Nearly all the studies of LTV delivered volumes based on PBW, which **is calculated based on height**.
- Predicted body weight is computed:
- in men as $50 + (0.91 \times [\text{height in centimeters} - 152.4])$
- in women as $45.5 + (0.91 \times [\text{height in centimeters} - 152.4])$

Low tidal volume(LTV) ventilation

- This approach assumes that the residual lung is a function of height, **but it may be more appropriate to deliver a volume that corresponds to the residual functional lung, or baby lung component**.
- The compliance of the respiratory system is calculated as the tidal volume divided by the change in pressure **(Pplat minus PEEP)** i.e.**the driving pressure**(**the pressure required for the alveolar opening)**
- In ARDS, **the compliance of the respiratory system correlates with the amount of the functional lung**:
- **Thus, compliance estimates the size of the baby lung.**

Driving pressure(ΔP)

- Driving pressure can be understood as the tidal volume normalized to respiratory system compliance (i.e., baby lung) and can be calculated clinically as **Pplat minus PEEP.**
- **C= VT/ ΔP (PPlat-PEEP)**
- **ΔP= VT/ C**
- [**driving pressure = Pplat – PEEP = V_T / Cstat].**
- **When the lung is recruitable(C is high), increased PEEP should decrease driving pressure,**
- **but when the lung is not recruitable (C is low), increased PEEP will lead to overdistension and will increase driving pressure.**

- **Driving pressure guided-ventilation**

- The same PEEP may decrease or increase driving pressure **according to the underlying lung pathologies or functional lung size.**

PEEP titration(individualized PEEP)

- Fixed PEEP would be inappropriate regardless of whether it is high or low.
- **Individualized PEEP** based on **driving pressure** **may be the next step of protective ventilation**.
- adjustment of PEEP and V_T has the potential to reduce driving pressure

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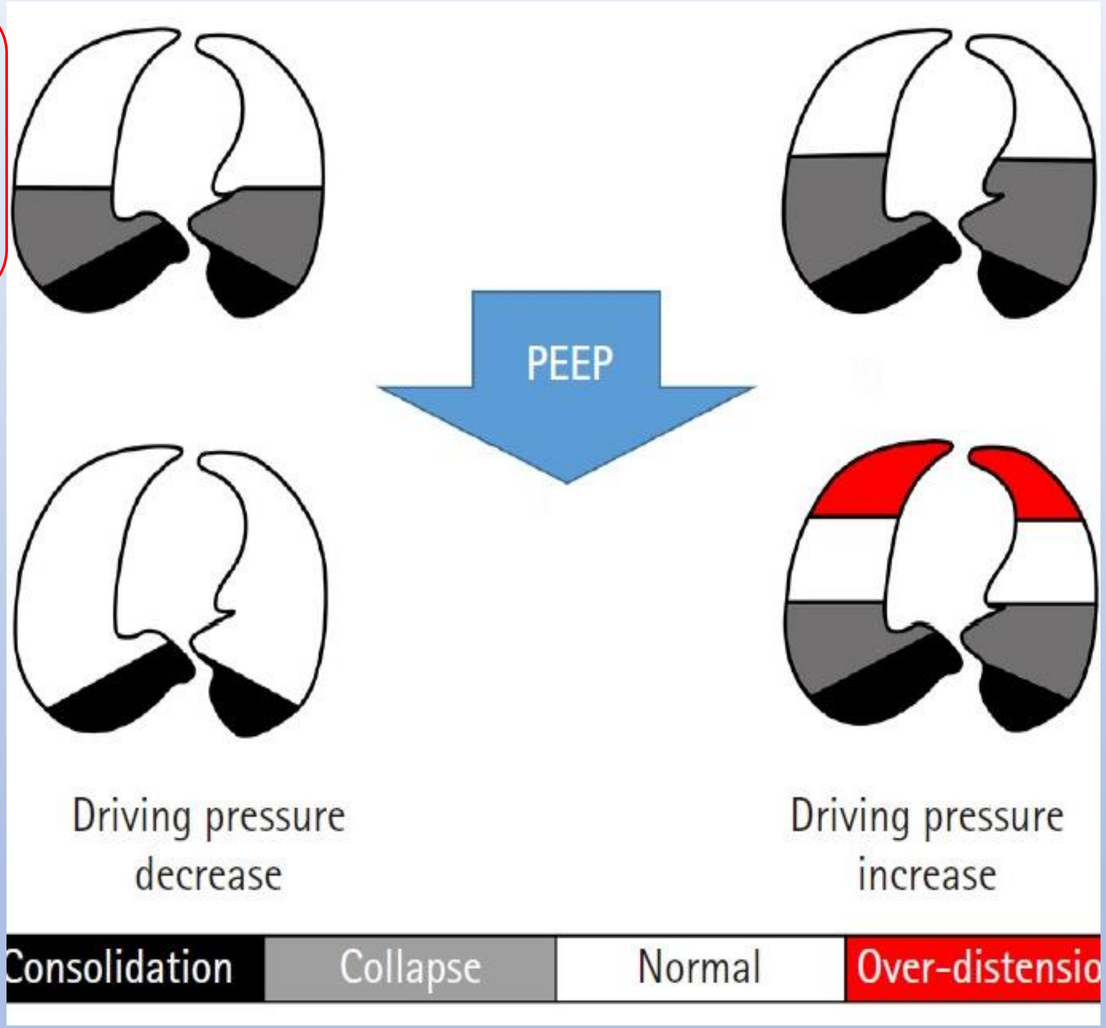


How to reduce driving pressure?

- There are no established techniques to reduce driving pressure
- yet. Driving pressure is dependent on PEEP and V_T
- [driving pressure = Pplat – PEEP = V_T / Cstat].
- Therefore, adjustment of PEEP and V_T has the potential to reduce driving pressure.
- There are few studies regarding PEEP adjustment based on driving pressure and no studies yet on the V_T titration based on driving pressure.

- In a study of individual patient data from nine ARDS trials, Amato et al. showed **that higher driving pressures were associated with increased mortality**
- **Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med. 2015;372(8):747-755.**
- Guérin et al. showed **a similar relationship between driving pressure and mortality** of two other trials. Schmidt et al
- **. Guérin C, Papazian L, Reignier J, et al. Effect of driving pressure on mortality in ARDS patients during lung protective mechanical ventilation in two randomized controlled trials. Crit Care. 2016;20(1):384**
- **Schmidt MFS, Amaral ACKB, Fan E, Rubenfeld GD. Driving pressure and hospital mortality in patients without ARDS: a cohort study. Chest. 2018;153(1):46-54**
- It is important to note that all these studies were observational and **no interventional trials of ventilation adjusted to driving pressure have yet been performed.**

PRONE POSITIONING

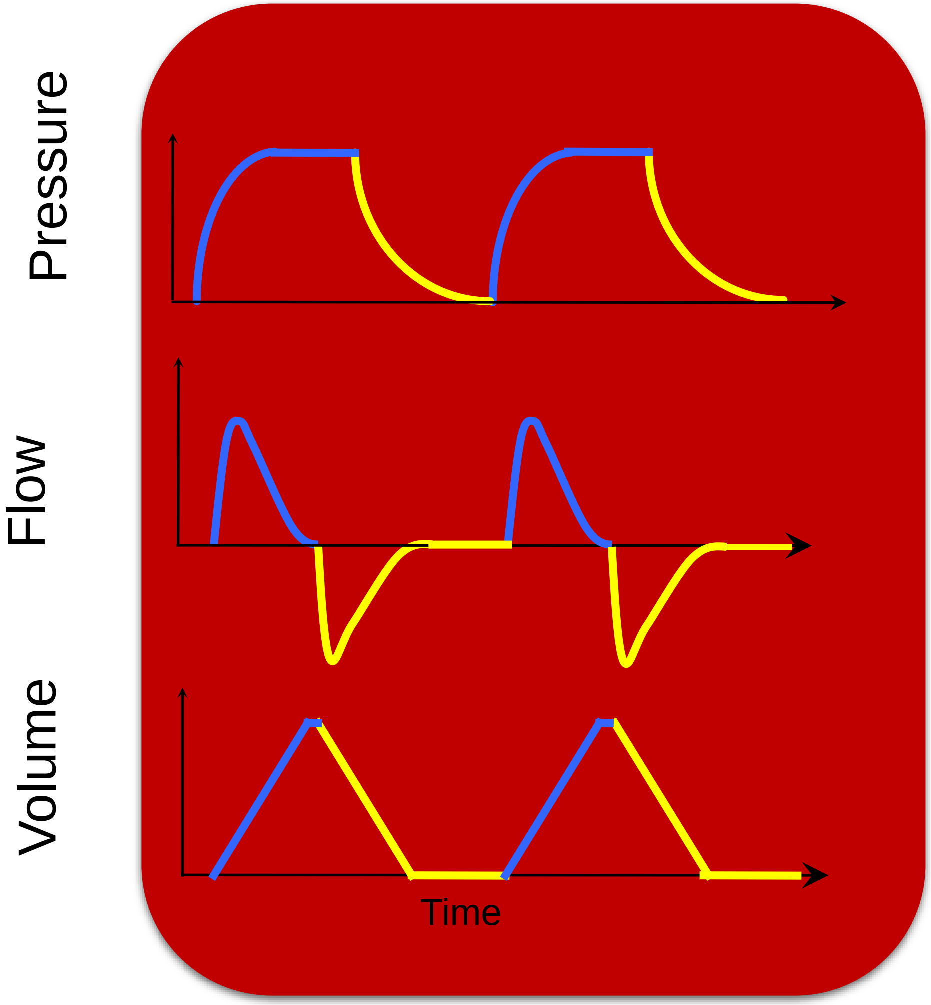
- In a supine patient, positive pressure from the ventilator lifts the ventral chest wall, but has minimal effect on the dorsal chest wall. When in prone position, the positive pressure lifts the dorsal chest wall .
- Gravity also causes dorsal lung compression when a patient is supine. The heart combined with the heavy edematous lungs in ARDS, increase the ventral–dorsal pleural pressure gradient and cause dorsal lung collapse, which can be reduced by prone positioning.
- Because the dorsal lung is larger than the ventral lung, dorsal recruitment exceeds ventral derecruitment, improving overall aeration and increasing lung compliance.
- As pulmonary blood flow is largely unchanged in the prone position, improved dorsal lung aeration also improves ventilation–perfusion matching.

PRONE POSITIONING(contin.)

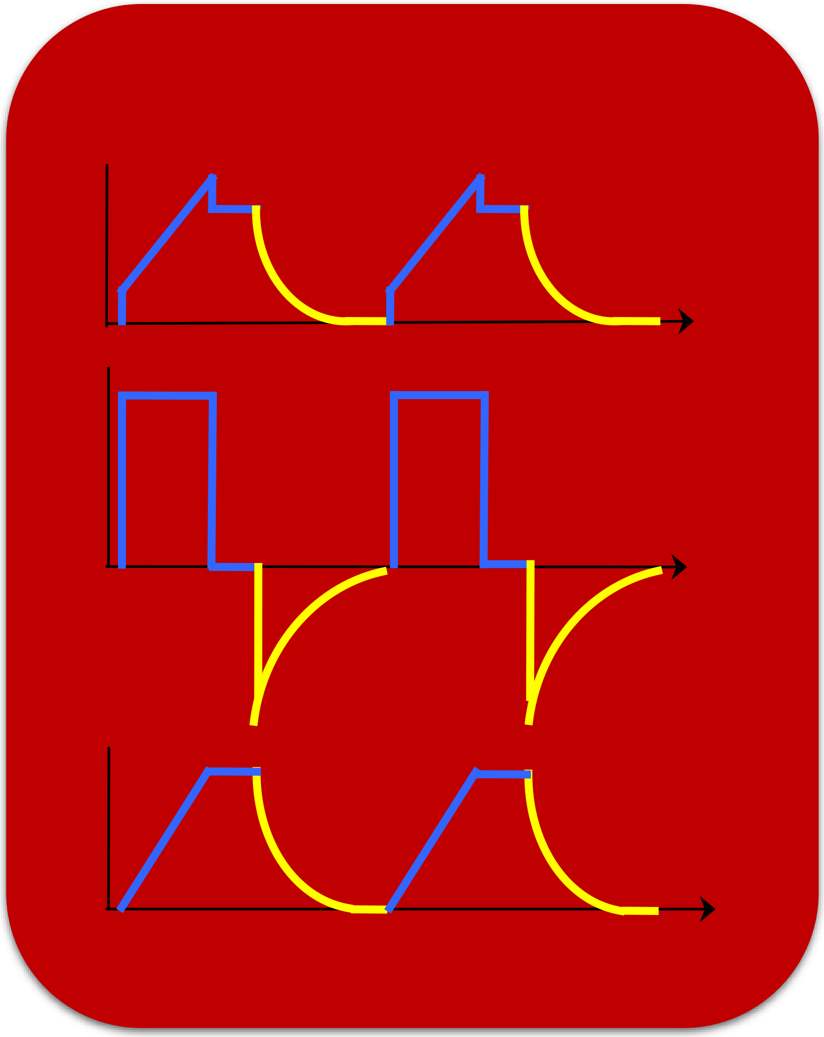
- Improved aeration during prone positioning leads to more uniform distribution of tidal volumes, more even transpulmonary pressures, and can facilitate sustained recruitment with the application of PEEP.
- The more homogeneous aeration also reduces regional hyperinflation and reduces the area of interface between open and closed lung units, collectively decreasing barotrauma and atelectrauma.
- Two recent meta-analyses of prone positioning trials found no overall mortality benefit associated with prone positioning but did report that the intervention is associated with lower mortality when applied for more than 12 hours per day in patients with moderate-to-severe ARDS with PaO_2/FiO_2 ratio ≤200 mm Hg.
- Munshi L, Del Sorbo L, Adhikari NKJ, et al. Prone position for acute respiratory distress syndrome. a systematic review and meta-analysis. Ann Am Thorac Soc. 2017;14(Suppl. 4):S280-S288

MODES OF VENTILATION

Pressure Modes



Volume Modes



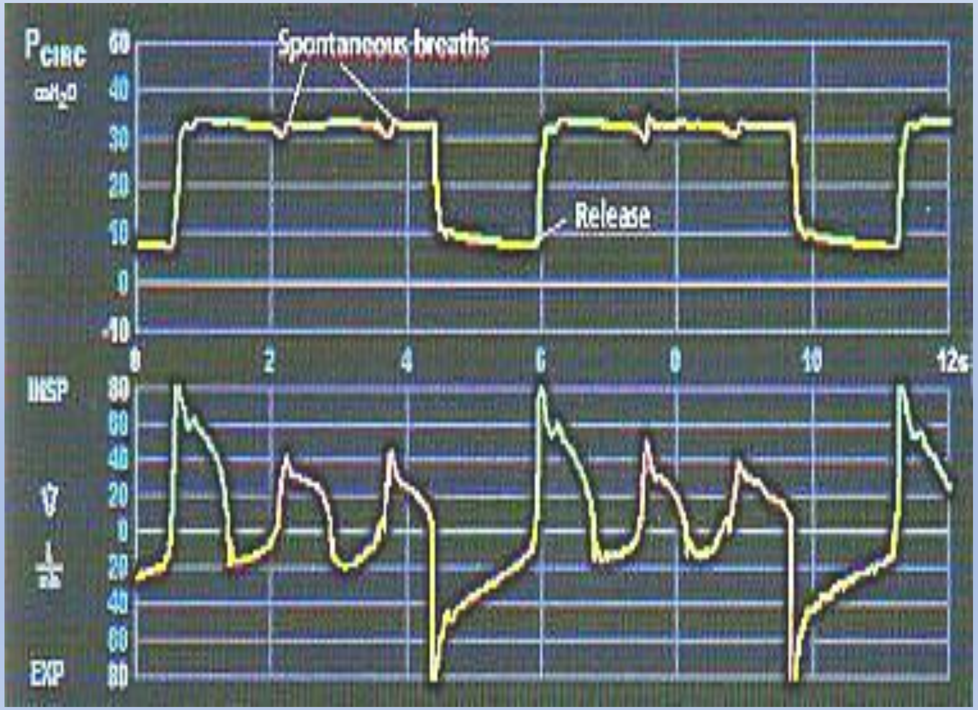
MODES OF VENTILATION

- **Volume-Targeted vs. Pressure-Targeted Ventilation**

- Considering the available evidence, it is unclear if either volume-targeted or pressure-targeted modes are superior for ventilation of patients with ARDS.

The role for assisted spontaneous ventilation in ARDS ventilation

AIRWAY PRESSURE RELEASE VENT(APRV)



- Putensen et al. showed that patients allowed to breath spontaneously with airway pressure release ventilation (APRV) had more ventilator-free days and shorter ICU stays compared with patients undergoing pressure control ventilation with neuromuscular blockade.
- Putensen C, Zech S, Wrigge H, et al. Long-term effects of spontaneous breathing during ventilatory support in patients with acute lung injury. Am J Respir Crit Care Med. 2001; 164(1):43-49.

The role for assisted spontaneous ventilation in ARDS ventilation(contin)

- Patients enrolled in these studies had mild-to-moderate ARDS.
- Spontaneous respirations can improve ventilation–perfusion matching through lung recruitment whereas diaphragmatic contraction during spontaneous ventilation improves aeration in the usually well-perfused dependent segments of the lung, decreasing intrapulmonary shunting and improving oxygenation.
- in severe ARDS spontaneous breathing can lead to **pendelluft**, which can cause VILI
- Therefore, the advantages associated with assisted spontaneous breathing **are likely to be limited to patients with mild to-moderate disease, and may actually be harmful in severe ARDS**.

NEUROMUSCULAR BLOCKING AGENTS

- Neuromuscular blocking agents (NMBAs) have been used for decades for refractory hypoxemia, ventilator desynchrony, and decreased respiratory system compliance(**early adoption of NMB)**
- Reevaluation **of Systemic Early Neuromuscular** Blockade (ROSE) trial.1, this trial included patients with ARDS with PaO_2/FiO_2 ratio<150 mm Hg

NEUROMUSCULAR BLOCKING AGENTS(contin.)

- Patients in the treatment arm were deeply sedated and received NMBA as a bolus and then 48 hours infusion, whereas patients in the control arm were lightly sedated with no NMBA.
- At 90 days, there was no mortality difference between the NMB group vs. the control group (42.5% vs. 42.8% 95% confidence interval, 26.4 to 5.9; P 5 0.93).
- These data suggest that **early adoption of NMB** in moderate to severe ARDS may not be beneficial
- Huang DT, Angus DC, Moss M, et al. Design and rationale of the reevaluation of systemic early neuromuscular blockade trial for acute respiratory distress syndrome. Ann Am Thorac Soc. 2017;14(1):124-133

High-Frequency Oscillatory Ventilation(HFOV)

- Theoretically, this should be an ideal approach to minimize VILI
- The small tidal volumes(1–3 mL/kg) can prevent volutrauma,
- The high mean airway pressure(**high mean airway pressure is applied to the lungs e delivered by an oscillating diaphragm at rates of 3–15 Hz, or 180–900 breaths per minute**) can recruit collapsed lung and prevent atelectrauma and the avoidance of high inspiratory pressure swings can prevent barotrauma.

High-Frequency Oscillatory Ventilation(HFOV)

- In 2013, Ferguson et al.92 reported the results of the Oscillation for ARDS Treated Early (OSCILLATE) trial that compared HFOV with lung-protective ventilation with 6 mL/kg PBW tidal volumes, Pplat ≤35 cm H2O, and high PEEP in patients with ARDS with PaO2/FiO2 ratio ≤200 mm Hg.
- The trial was stopped after 548 of the planned 1200 patients had been randomized **due to a signal of harm in the HFOV group**.
- In-hospital mortality was 47% in the HFOV group and 35% in the control group (absolute risk 12%; RR 1.33, 95% CI 1.12–1.79; P 5 .004).

LUNG-PROTECTIVE VENTILATION

Current evidence and clinical guidelines have shown that a lung-protective strategy including:

- low tidal volume (< 6–8 ml/kg of predicted body weight),
- and driving pressure (< 14 cmH_2O),
- and prone position for at least 12–16 h per day

may alleviate VILI and improve clinical outcome

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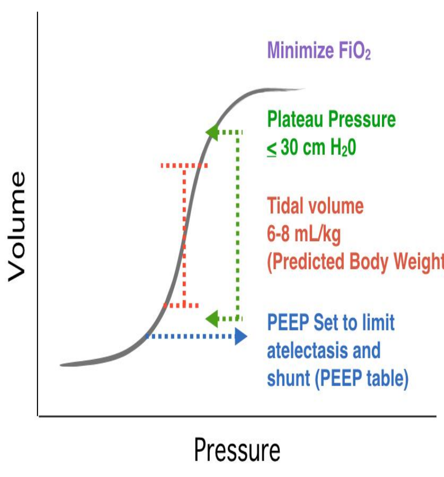

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You

Thank you

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