Aprv IN ARDS

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APRV in ARDS

Disclosure

I have nothing to disclose

APRV in ARDS

Agenda

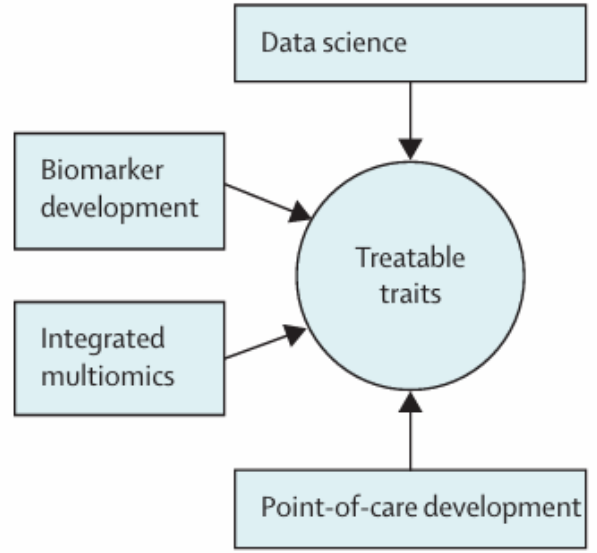
-review ARDS

-review evidence-based treatment options

-review APRV

-discuss how APRV fits into ARDS treatment options

	Previous criteria AECC	Current criteria Berlin	Short-term possible revisions	Future areas of research
	1994	2012	2022+	Onwards
Timing	Acute, not specified	New or worsening within 7 days		
Chest imaging	Bilateral infiltrates on chest radiograph	Bilateral infiltrates on chest radiograph (or CT)	Ultrasound	
Oxygenation	PaO_2/FiO_2 Acute lung injury <300 mm Hg ARDS <200 mm Hg	PaO_2/FiO_2 Mild >200 mm Hg to ≤300 mm Hg Moderate >100 mm Hg to ≤200 mm Hg Severe ≤100 mm Hg	SpO_2/FiO_2 ratio	
PEEP	Not specfied	Minimum PEEP 5 cm H_2O (continuous positive airway pressure in mild ARDS)	High-flow nasal oxygen, no requirement for minimum PEEP	
Origin of oedema	Pulmonary artery wedge pressure ≤17 mm Hg	Not fully explained by cardiac failure		
Biological markers	None	None		



Berlin criteria

Current diagnostic criteria established in 2012. Revision is likely in the near future

Gorman et al. Lancet 2022; 400: 1157–70

Pathophysiology

Dysregulated inflammatory injury to the alveolar-capillary barrier:

-increased permeability → pulmonary edema

-surfactant dysfunction

-impaired gas exchange

Direct (pulmonary) insult:

-pneumonia, aspiration, inhalational injuries

Indirect(extrapulmonary) insult :

-sepsis, pancreatitis, trauma, transfusion

Consequences

-alveolar flooding → V/Q mismatch and shunting

-surfactant dysfunction → atelectasis, lung collapse, decreased lung compliance

-microvasculature thrombi → increase dead space

-pulmonary arterial hypertension → RV dysfunction

HYPOXEMIA AND HYPERCARBIA

PATHOPHYSIOLOGY:

- Ventilator-Induced Lung Injury
- Mechanical ventilation is essential to the care of a patient with ARDS but it can also incite or perpetuate the cycle of injury and inflammation

- Volutrauma/barotrauma

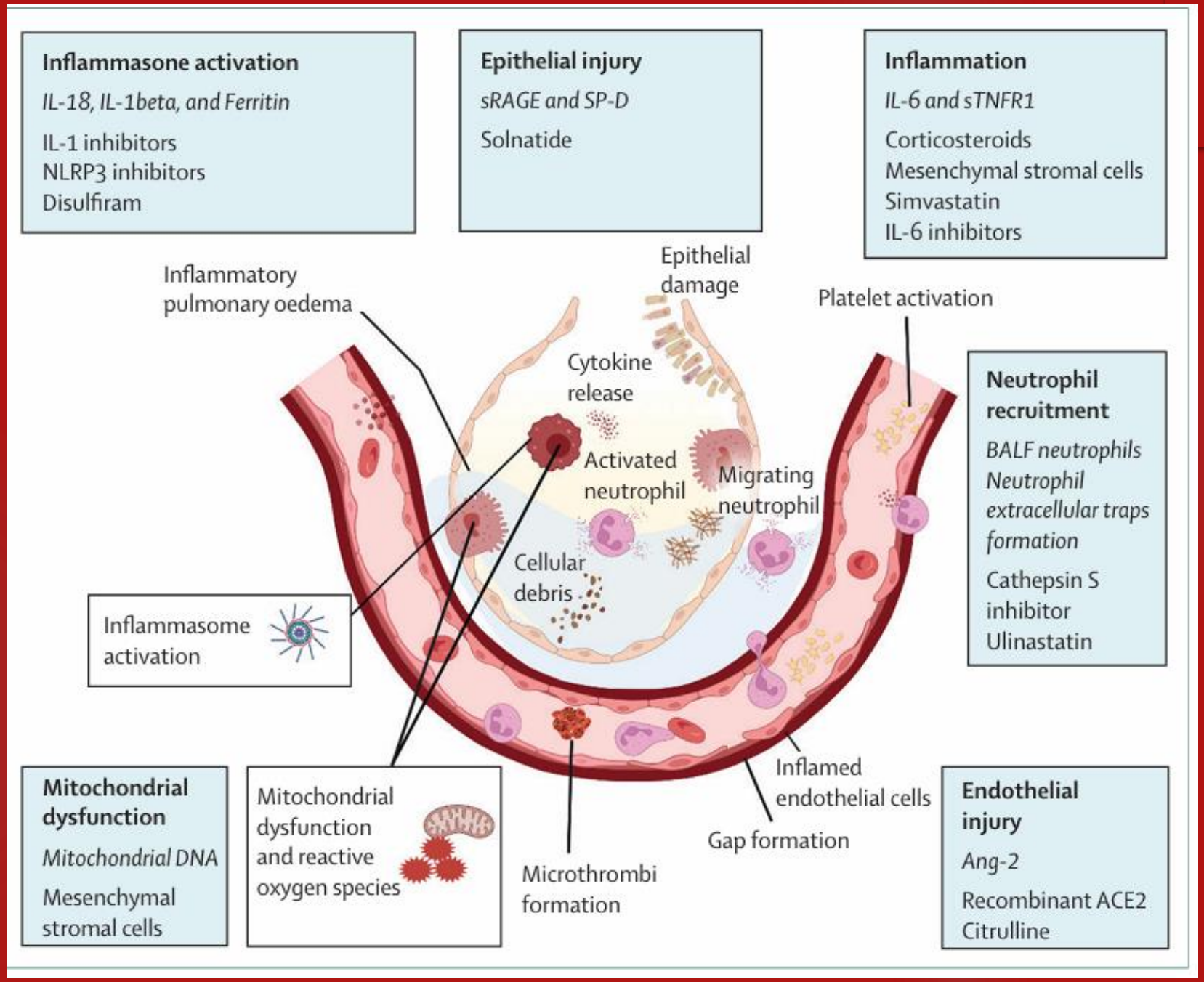
  -overdistention of the remaining aerated lung

- Atelectrauma

  -repetitive opening and closing of collapsed alveoli causing shearing stress

- Biotrauma

  -cyclic stretching activate proinflammatory pathways releasing cytokines


Inflammasone activation
IL-18, IL-1beta, and Ferritin
IL-1 inhibitors
NLRP3 inhibitors
Disulfiram
Epithelial injury
sRAGE and SP-D
Solnatide
Inflammation
IL-6 and sTNFR1
Corticosteroids
Mesenchymal stromal cells
Simvastatin
IL-6 inhibitors
Inflammatory pulmonary oedema
Epithelial damage
Platelet activation
Cytokine release
Activated neutrophil
Migrating neutrophil
Cellular debris
Neutrophil recruitment
BALF neutrophils
Neutrophil extracellular traps formation
Cathepsin S inhibitor
Ulinastatin
Inflammasome activation
Mitochondrial dysfunction
Mitochondrial DNA
Mesenchymal stromal cells
Mitochondrial dysfunction and reactive oxygen species
Microthrombi formation
Gap formation
Inflamed endothelial cells
Endothelial injury
Ang-2
Recombinant ACE2
Citrulline

Pathophysiology

Patient self-inflicted lung injury can also occur during spontaneous breathing

Vigorous inspiratory efforts can produce large transpulmonary pressure swings

Lung protective ventilation (ATS/ESICM/SCCM)

- Low tidal volume (6 to 8 mL/kg ideal body weight) with plateau pressure of less than 30 cm of water
  - Start at 6 mL/kg, can reduce to as low as 4 mL/kg to keep plateau < 30 cm of water
  - RR can be increased maximum of 35 breaths/min with permissive hypercapnia in absence of contra-indications (e.g. raised ICP) (ARDSnet trial 2000)
- Prone positioning for > 12 hours/day
  - (PaO2/FiO2 < 150 mmHg) moderate to severe ARDS. (PROVESA trial 2013)
- Higher PEEP, reserve for moderate to severe ARDS, without recruitment maneuver
- Neuromuscular blockade, not for all patients but remains appropriate for managing refractory ventilator dyssynchrony or severe hypoxemia when sedation alone is not adequate
- VV-ECMO for severe refractory ARDS (PaO2/FiO2 less than 80 mmHg or pH < 7.25 with PaCO2 >/= 60 mmHg) despite optimal treatment, at experienced ECMO centers (CESAR trial 2009, EOLIA trial 2018, ATS guideline 2024)

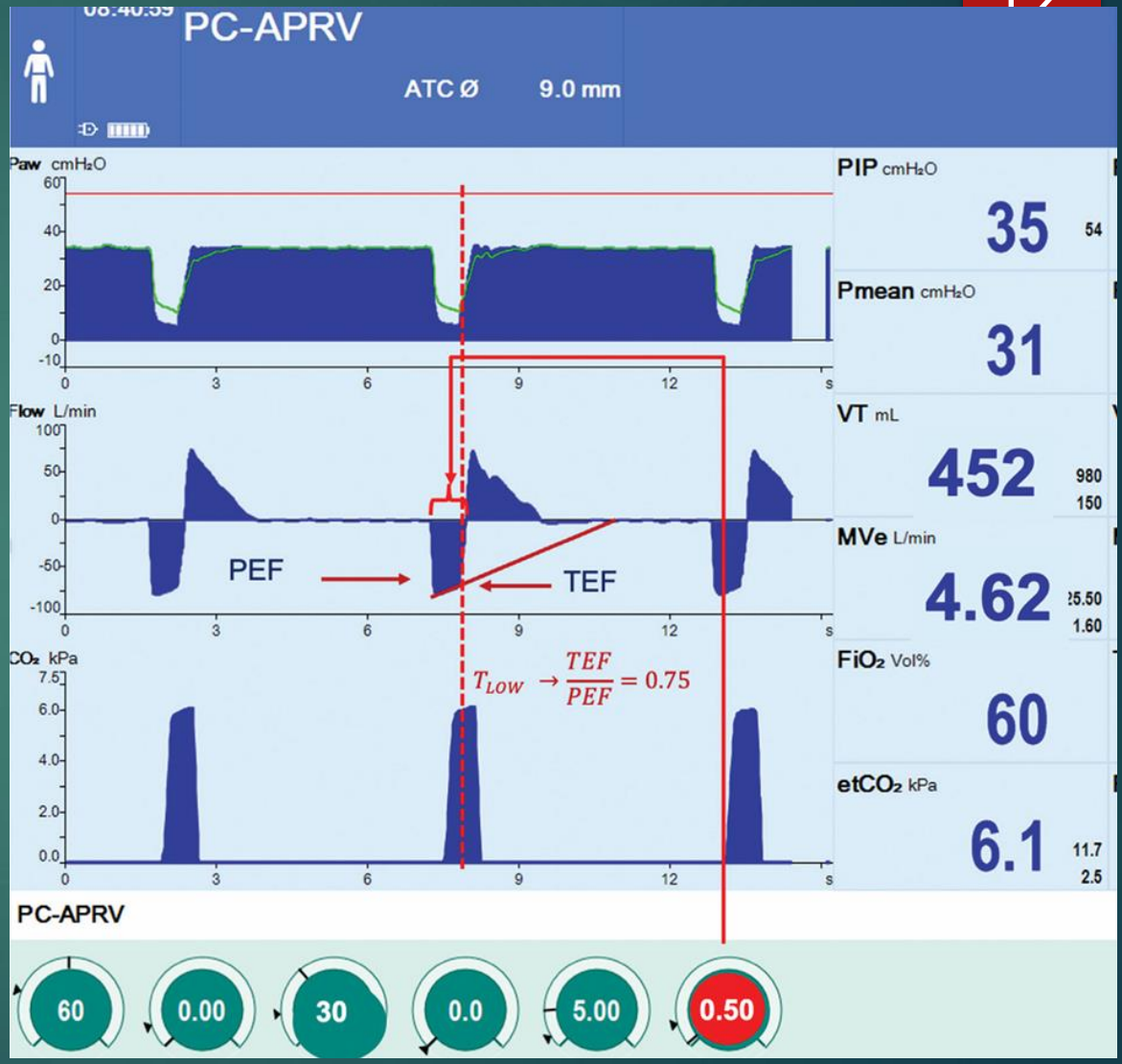
Airway pressure release ventilation

- APRV is a pressure-controlled mode that delivers a prolonged high airway pressure (P high) to maintain alveolar recruitment with brief intermittent time-cycled releases to a low pressure (P low) that allow CO2 clearance.
- Spontaneous breathing is encouraged
- Pressure is held at the P high for a longer inspiratory time (T high) than conventional mode of ventilation.
- Because of this long T high at P high (usually set at previously obtained P plateau), the mean airway pressure is increased.
- Higher mean airway pressure allow for "open lung" ventilation
- Minimize de-recruitment, maximize alveolar recruitment (using pressure as well time to open collapsed alveoli)
- APRV reduces dynamic stress by reducing the cyclical opening and collapse of atelectatic alveoli and therefore minimize lung injury
- Prolonged inspiratory time improves oxygenation.

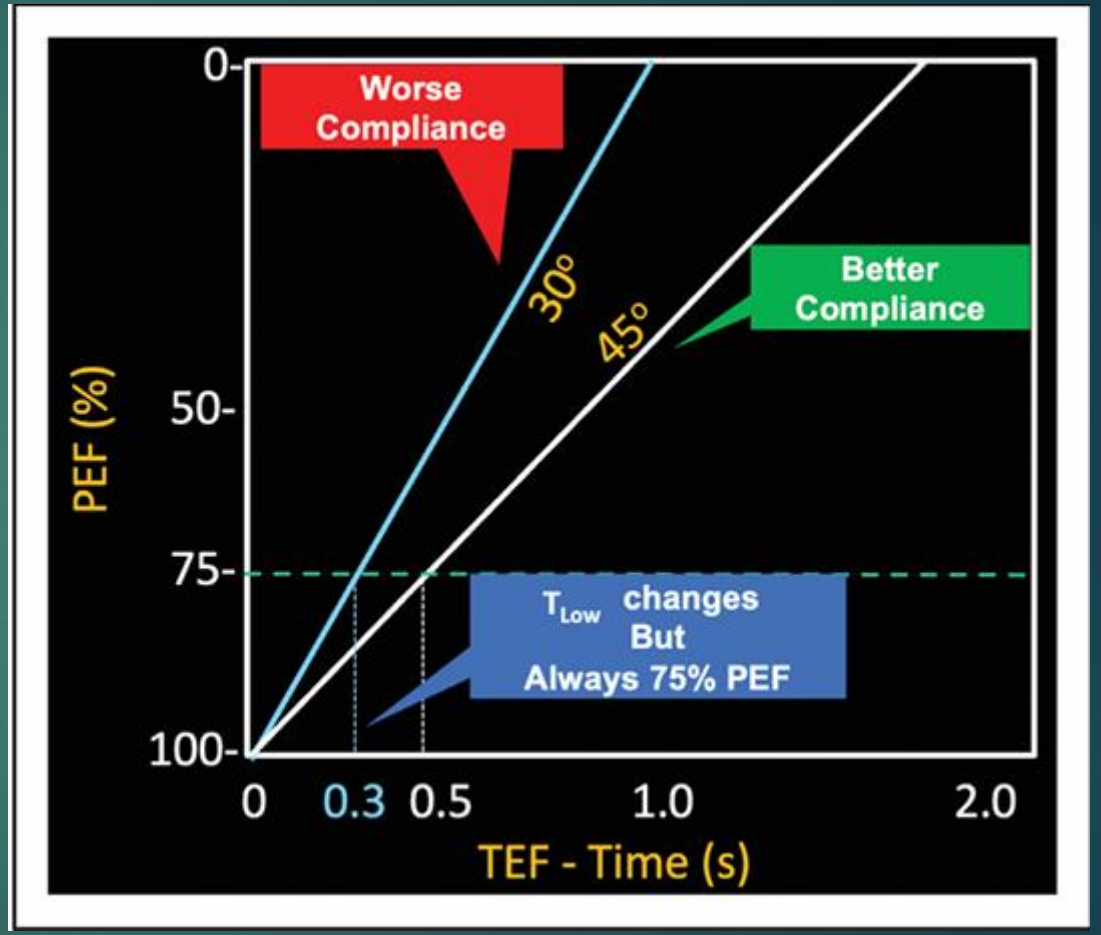
APRV and time controlled adaptive ventilation

- APRV settings
- Four main parameters to set
- P high
  - Usually set near prior plateau pressure, typically less than 30 cm of water
- T high
  - T high = (60/RR – T low), typically 3 to 9 seconds
- P low
  - Typically at zero. Due to long time spent and P high and short T low, typically, there is intrinsic PEEP.
- T low is set to achieve a termination of expiratory flow (Tef) of 75% of peak expiratory flow.
  - For example, if peak expiratory flow rate was 80 L/min, then T low should be set to achieve Tef of 60 L/min (80 x .75 = 60)
  - T low that is too long will lead to low end-expiratory pressure leading to de-recruitment and atelectrauma. A T low that is too brief will lead to hyperinflation and volutrauma.

APRV with Tcav



Aprv with TCAV



APRV

To improve oxygenation	To improve carbon dioxide clearance
• Increase FiO2	Shorten T high
• Increase P high carefully (1 to 2 cm of water at a time)	Lenghen T low if appropriate Ensure changes do not cause de-recruitment or excessive TV
• Lengthen T high • Optimize release termination to preserve recruitment	Evaluate spontaneous breathing contribution

APRV in ARDS

- Why APRV generates Interest
- Theoretical reduction in cyclic atelectrauma
- Potential reduction in sedation/paralysis requirement
- Improved oxygenation in some studies

APRV in ARDS

Roy et al, Shock 39(1); page 28-38, Jan 2013

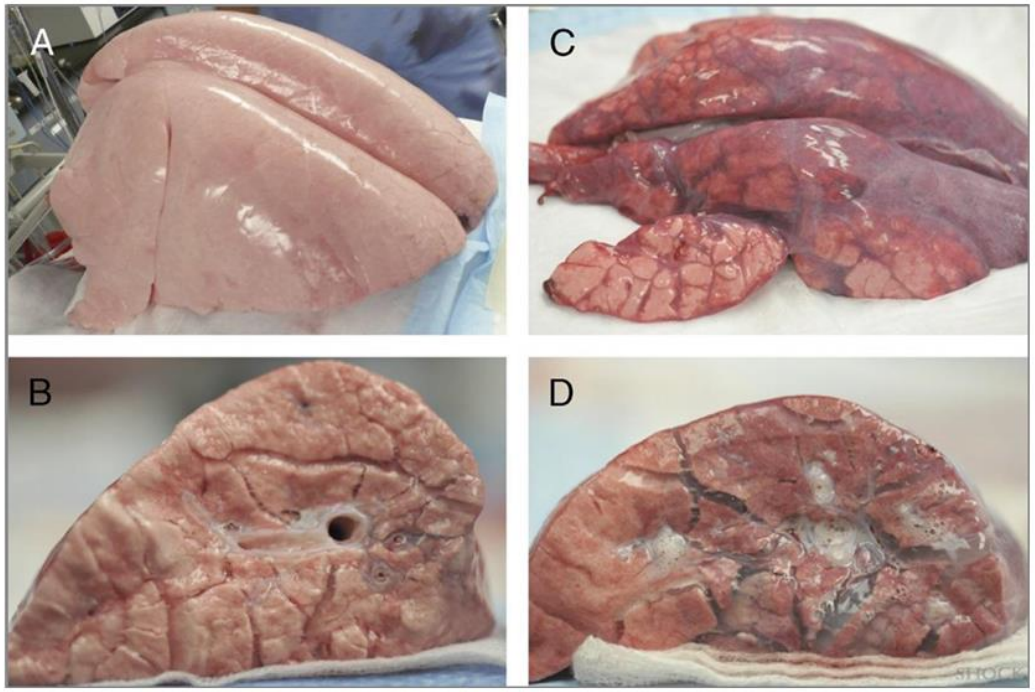


Fig 2 Macroscopic histological changes in a porcine model of airway pressure release ventilation (APRV) vs low tidal volume ventilation (LTV). This figure has been reproduced with permission from *Shock*. Gross pathology: (A) APRV whole lung – normal pink, homogenously inflated lung tissue with no evidence of inflammation or atelectasis. (B) APRV cut surface – no bronchial or septal oedema. (C) LTV whole lung – predominantly atelectatic with heterogenous parenchymal inflammation. (D) LTV cut surface – gel-like oedema seen filling the interlobular septae with airway oedema in the bronchial openings.

APRV

- Maxwell RA, Green JM, Waldrop J, Dart BW, Smith PW, Brooks D, et al. A randomized prospective trial of airway pressure release ventilation and low tidal volume ventilation in adult trauma patients with acute respiratory failure. J Trauma 2010;69(3):501-510;

- Adult trauma patients in acute respiratory failure, APRV (short Tlow) vs Low tidal volume approach using SIMV and PS (31 patients in APRV and 32 patients in conventional ventilation group)
- Significantly higher mean airway pressure in APRV group(18-20 cm of water vs 13 to 16 cm of water) compared to conventional ventilation group
- No difference in mortality, trend toward longer duration of ventilation and ICU stay in APRV group
- 8/31 in APRV had ARDS, 6 had ALI; 9/32 in control had ARDS and 2 had ALI

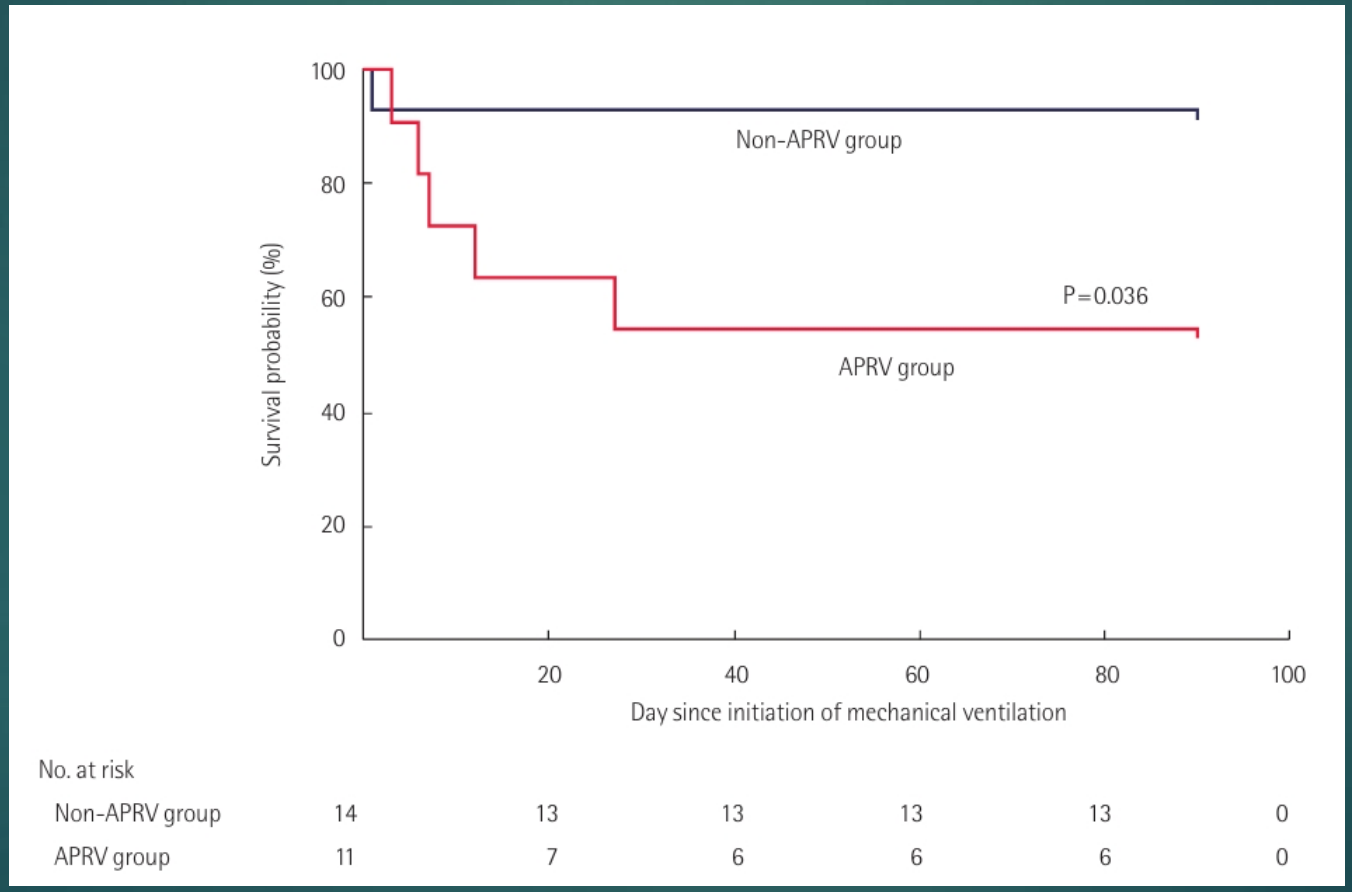
Physiologic Comparison of Airway Pressure Release Ventilation and Low Tidal Volume Ventilation in ARDS: A Randomized Controlled Trial

- Zou et al, Chest. 2025 Feb;167(2):453-465
- 40 patients randomized to get APRV vs LVT ventilation
- Electrical impedance tomography (EIT) used to assess ventilation and perfusion
- APRV, as compared with LTV ventilation, could recruit dorsal region, reduce dorsal shunt, increase dorsal $\dot{V}/\dot{Q}$ matching, and improve ventilation homogeneity of the lungs, leading to better gas exchange and respiratory system static compliance in patients with moderate to severe ARDS.

Airway pressure release ventilation in mechanically ventilated patients with COVID-19: a multicenter observational study

- Zorbas et al, Acute and Critical Care 2021 May 36(2):143-150
- A total of 25 patients with COVID-19 pneumonitis, 11 received APRV 14 received "any other mode" of mechanical ventilation

Airway pressure release ventilation in mechanically ventilated patients with COVID-19: a multicenter observational study



No. at risk						
Non-APRV group	14	13	13	13	13	0
APRV group	11	7	6	6	6	0

APRV in ARDS

- The AAST/ACS Committee on Trauma (2023) acknowledges that APRV has shown improved oxygenation, a possible mortality benefit, and increased ventilator-free days in meta-analyses of RCTs, but characterizes the evidence as **low quality** given small sample sizes and moderate heterogeneity.
- while early meta-analytic data are suggestive, studies to date have had methodological limitations and a robust multicenter trial is needed.

Questions and answers