Acute Respiratory Distress Syndrome – The Past, Present and Future

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Agenda

- The ARDS Story
- Current state of management
  - ESICM 2023 Guideline
- What maybe coming up

The Story of ARDS

- World War I
  - Chlorine gas
  - Phosgene gas

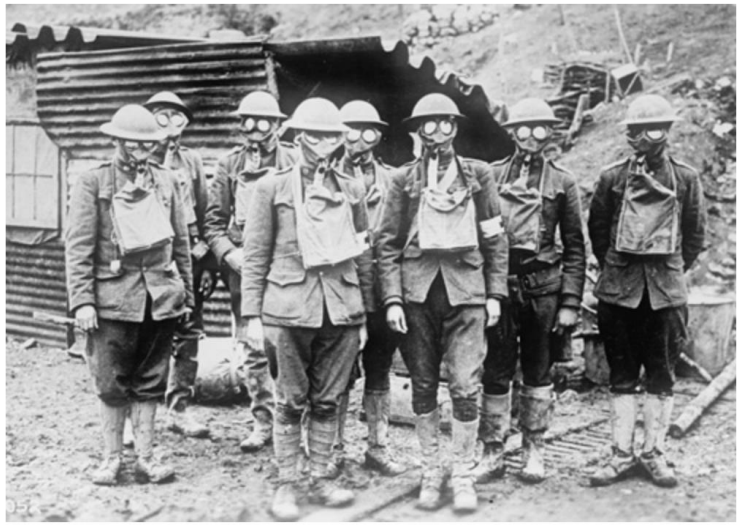
The New York Times

DEADLY LUNG AILMENT HAS BATTLEFIELD ORIGINS

Give this article

By Lawrence K. Altman, M.d.

April 9, 1985



The Vietnam War: 'Da Nang Lung'

Men of the 101st airborne call in helicopters to evacuate their wounded comrades. Medical evacuation from the battlefield reached its zenith in the Vietnam war with unexpected consequences.

Clin Transl Med. 2017; 6: 19. PMCID: PMC5457389
Published online 2017 Jun 2. doi: 10.1186/s40169-017-0149-2 PMID: 28577109

Phosgene-induced acute lung injury (ALI): differences from chlorine-induced ALI and attempts to translate toxicology to clinical medicine

Wenli Li[1] and Juergen Pauluhn[1,2]

The Story of ARDS

Shock Lung (Acute Respiratory Distress Syndrome): One Hundred Years on from the Great War
https://acadoodle.com/articles/17

ARDS

- 1967
  - 12 patients
  - Acute onset
    - Tachypnea
    - Hypoxemia
    - Loss of compliance
    - Cyanosis
    - Diffuse infiltrates
    - Does not respond to ordinary methods of respiratory therapy
- Mortality: 60%

The Adult Respiratory Distress Syndrome: Clinical Features, Factors Influencing Prognosis and Principles of Management*

THOMAS L. PETTY, M.D., F.C.C.P.

Associate Professor of Medicine and Head, Division of Pulmonary Diseases, University of Colorado Medical Center, Denver, Colorado

DAVID G. ASHBAUGH, M.D.

Associate Professor of Surgery, University of Colorado Medical Center, Denver, Colorado

Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. Lancet 1967;2:319-23

Story of ARDS

Research Article | Thomas L Petty Memorial Lecture

Thomas L Petty's Lessons for the Respiratory Care Clinician of Today

David J Pierson

Respiratory Care August 2014, 59 (8) 1287-1301; DOI: https://doi.org/10.4187/respcare.03495

TABLE 4.
MANAGEMENT PRINCIPLES IN ARDS

1. Prevent alveolar collapse and maintain oxygenation
   a. Tracheostomy
   b. Volume respirator
   c. Oxygen control
   d. Positive end-expiratory pressure (PEEP)
2. Prevent further injury
   a. Oxygen control
   b. Fluid restriction
   c. Antibiotics for specific infections
   d. Corticosteroid drugs

› Am J Respir Crit Care Med. 2001 Mar;163(3 Pt 1):602-3. doi: 10.1164/ajrccm.163.3.16331.

In the cards was ARDS: how we discovered the acute respiratory distress syndrome

T L Petty [1]

› Lancet Respir Med. 2017 Jun;5(6):474. doi: 10.1016/S2213-2600(17)30182-0. Epub 2017 May 26.

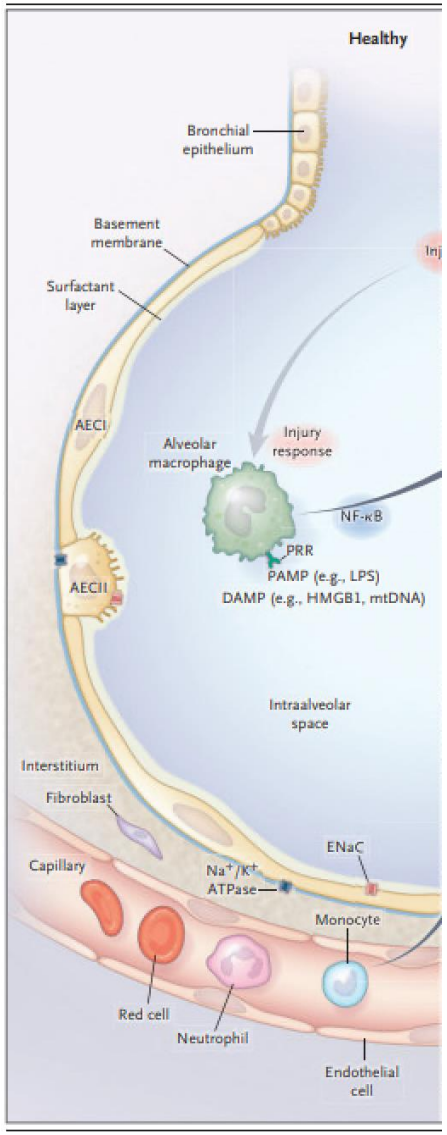
David Ashbaugh reminisces

David Ashbaugh

PMID: 28664849 DOI: 10.1016/S2213-2600(17)30182-0

Normal Lung

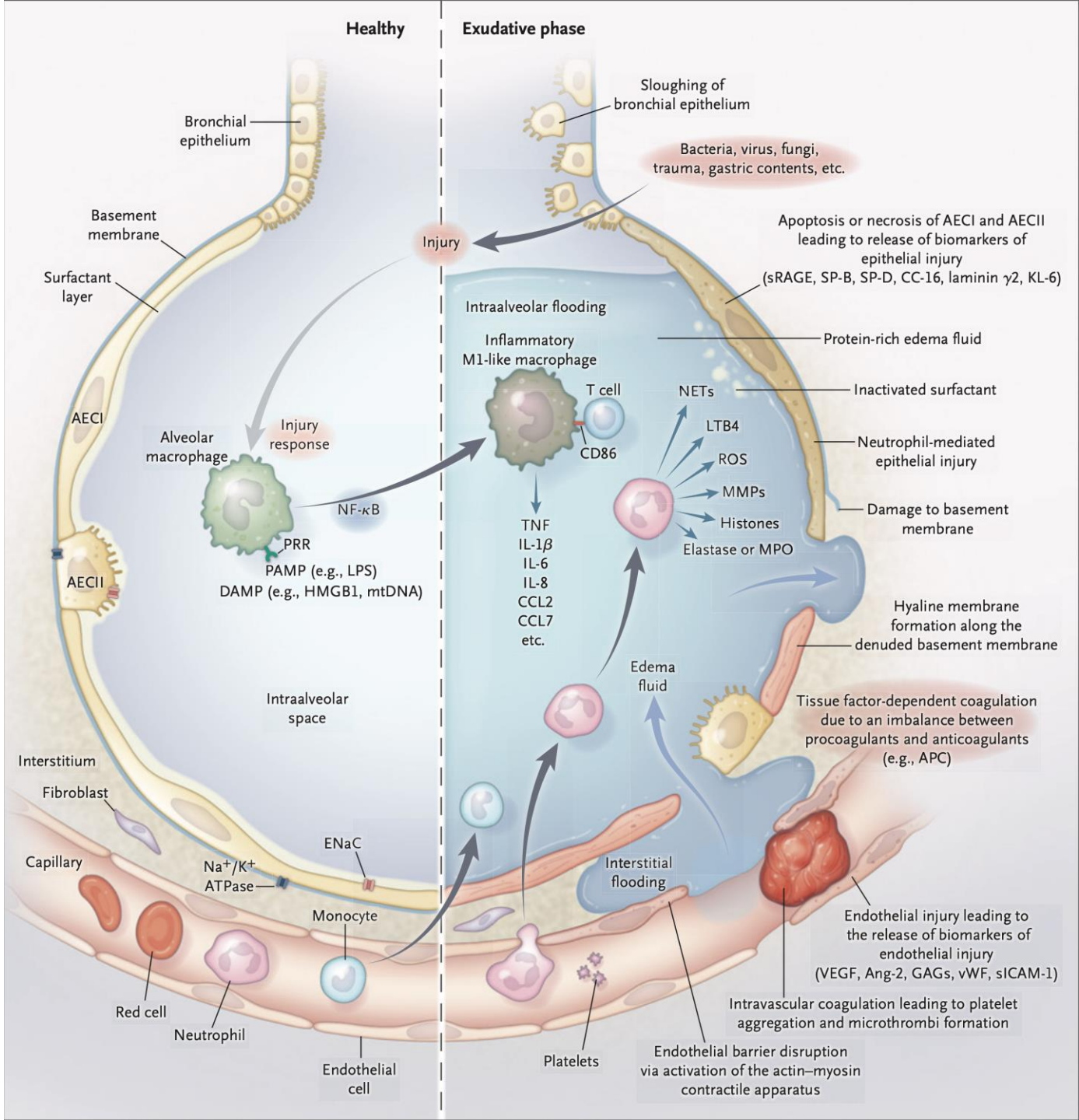
- Ventilation
- Oxygenation



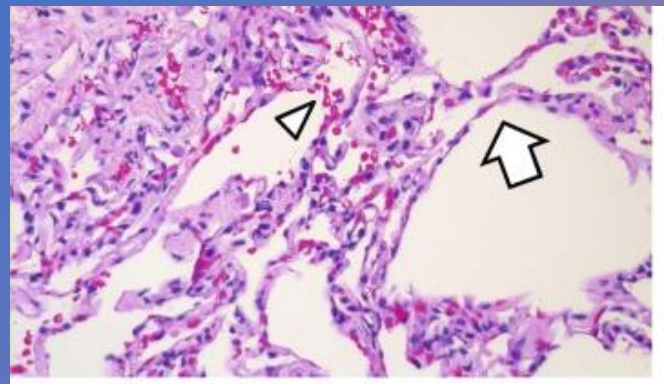
Thompson BT, Chambers RC, Liu KD. Acute Respiratory Distress Syndrome. N Engl J Med. 2017 Aug 10;377(6):562-572. doi: 10.1056/NEJMra1608077. PMID: 28792873

ARDS

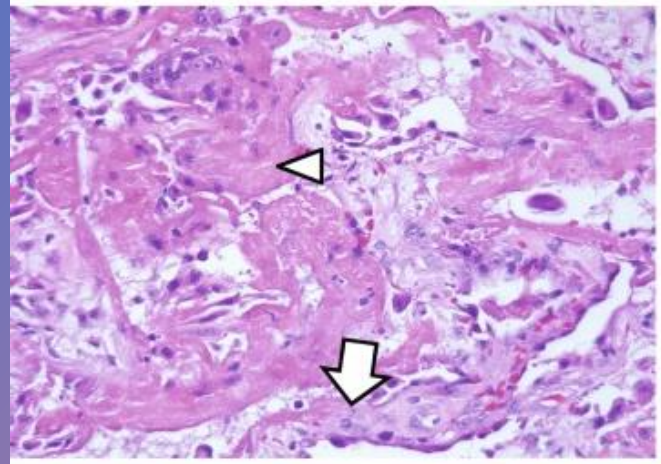
- Prevalence
  - 10% of ICU admits
  - 23% of mechanically ventilated patients
  - 46% mortality (in severe)



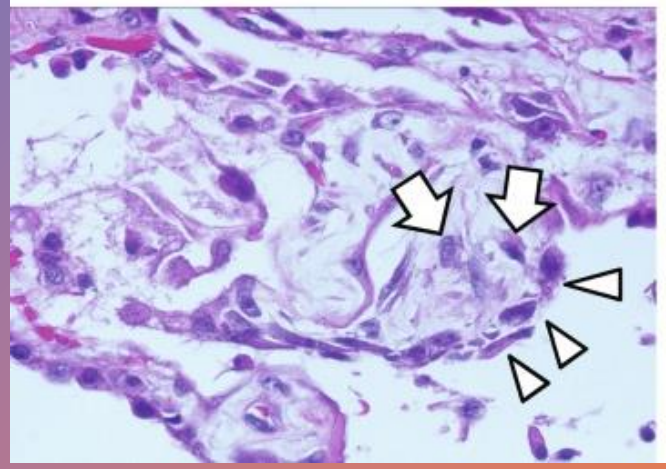
Thompson BT, Chambers RC, Liu KD. Acute Respiratory Distress Syndrome. N Engl J Med. 2017 Aug 10;377(6):562-572. doi: 10.1056/NEJMra1608077. PMID: 28792873



Normal human lung. Alveoli are aerated with thin septae (arrow); a mild amount of surgical (biopsy-induced) hemorrhage (arrowhead) is apparent



Exudative phase of human ARDS ('diffuse alveolar damage'). There is near-complete alveolar filling by an eosinophilic proteinaceous edema fluid ('hyaline membrane,' arrowhead). Thickening of the alveolar septae is noted (arrow)



Organizing (resolution) phase of human ARDS. Histology is notable for an organizing pattern, marked by thickened septae with embedded macrophages (arrows). Septae are lined by proliferating, reactive type II epithelial cells (arrowheads)

Where are we now

- 1988: Lung Injury Score
- 1994: American-European Consensus Conference
- 2012: Berlin Criteria
- 2017: ATS/ESICM Clinical Practice Guideline
- 2023: ESICM Guidelines on ARDS

Ann Intensive Care. 2014; 4: 4. PMCID: PMC3931496
Published online 2014 Feb 18. doi: 10.1186/2110-5820-4-4 PMID: 24533450

Is there still a role for the lung injury score in the era of the Berlin definition ARDS?

Kirsten Neudoerffer Kangelaris,[1] Carolyn S Calfee,[2,3] Addison K May,[4] Hanjing Zhuo,[3] Michael A Matthay,[2,3] and Lorraine B Ware[5]

Author information Article notes Copyright and License information Disclaimer

Definition – Berlin Criteria

"Mr. Justice, you will know it when you see it"

1. Why one week?
2. Non cardiogenic pulm edema vs opacities not full explained by cardiac failure?
3. Why the break down of Mild, Moderate, Severe at those cut offs?

https://www.mdcalc.com/calc/10294/berlin-criteria-acute-respiratory-distress-syndrome

Berlin Criteria for Acute Respiratory Distress Syndrome

Provides diagnostic criteria for acute respiratory distress syndrome (ARDS).

IMPORTANT
Launched during COVID-19 crisis.

When to Use

Required criteria Must have all three of the following:

- [x] Timing within 1 week of clinical insult or new/worsening respiratory symptoms
- [x] Chest XR shows bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules
- [x] Respiratory failure not fully explained by cardiac failure/fluid overload

Risk factor Select one of the following:

Risk factor

- (●) Risk factor for ARDS present (e.g. pneumonia, trauma, sepsis, pancreatitis)
- ( ) Objective assessment (Echo) excludes hydrostatic edema if no risk factor present
- ( ) None of the above

Severity Based on oxygenation, select one of the following:

Oxygenation

- ( ) Mild: PaO_2/FiO_2 >200 to ≤300 mmHg with PEEP OR CPAP ≥5 cm H_2O
- (●) Moderate: PaO_2/FiO_2 >100 to ≤200 mmHg with PEEP ≥5 cm H_2O
- ( ) Severe: PaO_2/FiO_2 ≤100 mmHg with PEEP ≥5 cm H_2O
- ( ) None of the above

Causes

- Common:
  - Pneumonia
  - Sepsis
  - Aspiration of gastric content
  - Shock
  - Trauma
  - High risk surgery
  - Drug overdose
  - Ischemic-reperfusion injury
- Less common
  - Smoke inhalation
  - Drowning
  - Vaping
  - Blood transfusions
  - Burns

Lancet. 2021 14-20 August; 398(10300): 622–637.

- My patient appears to have ARDS and meets the Berlin criteria. He is desaturating on low flow oxygen. What to do next?
  - HFNC?
  - BiPAP?
  - Invasive mechanical ventilation?

Conference Reports and Expert Panel | Open Access | Published: 16 June 2023

ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies

Giacomo Grasselli, Carolyn S. Calfee, Luigi Camporota, Daniele Poole, Marcelo B. P. Amato, Massimo Antonelli, Yaseen M. Arabi, Francesca Baroncelli, Jeremy R. Beitler, Giacomo Bellani, Geoff Bellingan, Bronagh Blackwood, Lieuwe D. J. Bos, Laurent Brochard, Daniel Brodie, Karen E. A. Burns, Alain Combes, Sonia D'Arrigo, Daniel De Backer, Alexandre Demoule, Sharon Einav, Eddy Fan, Niall D. Ferguson, Jean-Pierre Frat, the European Society of Intensive Care Medicine Taskforce on ARDS

+ Show authors

Intensive Care Medicine **49**, 727–759 (2023) | Cite this article

Grasselli, G., Calfee, C.S., Camporota, L. *et al.* ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Med* **49**, 727–759 (2023). https://doi.org/10.1007/s00134-023-07050-7

Definition update

- What about HFNC ?

- ESICM 2023:
  - Acute Hypoxemic Resp Failure (AHRF) not otherwise explained by preexisting lung disease or heart failure

Berlin Criteria for Acute Respiratory Distress Syndrome

Provides diagnostic criteria for acute respiratory distress syndrome (ARDS).

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Required criteria Must have all three of the following:

- [x] Timing within 1 week of clinical insult or new/worsening respiratory symptoms
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Risk factor Select one of the following:

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- (●) Moderate: PaO_2/FiO_2 >100 to ≤200 mmHg with PEEP ≥5 cm H_2O
- ( ) Severe: PaO_2/FiO_2 ≤100 mmHg with PEEP ≥5 cm H_2O
- ( ) None of the above

HFNC vs conventional O2

- Intubation risk:
  - lower
- Mortality:
  - unclear
- Verdict: use HFNC over conventional O2

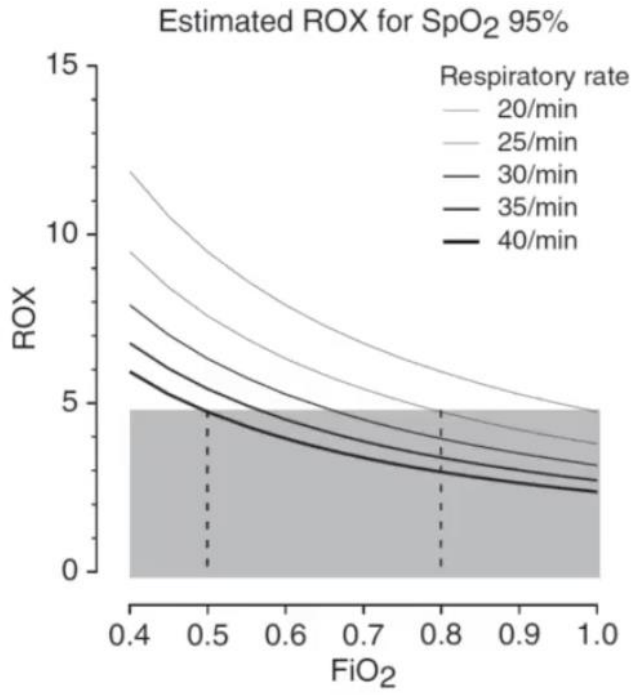
Recommendation 3.1
We **recommend** that non-mechanically ventilated patients with AHRF not due to cardiogenic pulmonary edema or acute exacerbation of COPD receive HFNO as compared to conventional oxygen therapy to reduce the risk of intubation *Strong recommendation; moderate level of evidence in favor*
We are **unable to make a recommendation** for or against the use of HFNO over conventional oxygen therapy to reduce mortality *No recommendation; high level of evidence of no effect* This recommendation applies also to AHRF from COVID-19 *Strong recommendation; low level of evidence in favor for intubation and no recommendation; moderate level of evidence of no effect for mortality, for indirectness.*

Grasselli, G., Calfee, C.S., Camporota, L. *et al.* ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Med* **49**, 727–759 (2023). https://doi.org/10.1007/s00134-023-07050-7

How to know if HFNC will work

- If you are breathing OK, you will be ok
- Watch work of breathing
- Tele ICU is bad is much worse in this case
- Bad specificity and sensitivity

Predicting HFNC Success: ROX Index



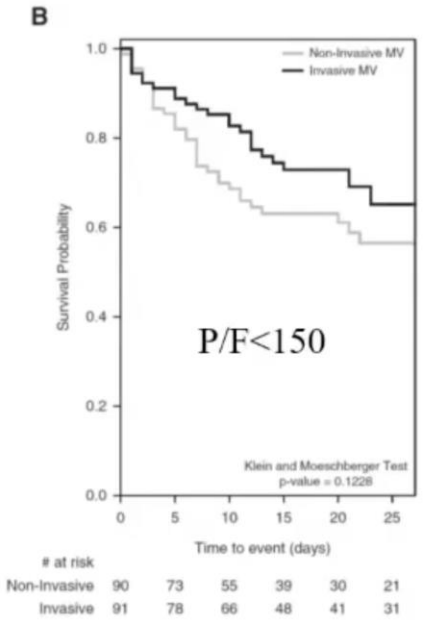
$$ROX = \frac{SpO_2/FiO_2\ (\%)}{\text{Respiratory rate}}$$

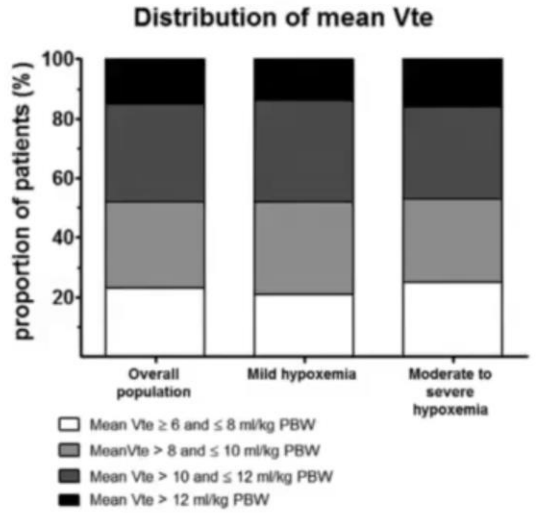
- ROC curve AUC = 0.75
- Sensitivity = 0.67
- Specificity = 0.72
- Better with C-19
- Cutoff >5 at 6 hours was best

AJRCCM 2019; 200:115
Resp Res 2022; 23:33

Should we use NIV

- Patient-self induced lung injury (P-SILI)





Exhaled Vt > 9.5 cc/kg predicted NIV failure

AJRCCM 2017; 195:67
Crit Care Med 2016; 44:282

HFNC vs NIV

- Intubation risk: unclear
- Mortality: unclear
- Consider CPAP/NIV over HFNC in COVID-19 (low quality)
  - If you use it, close monitoring
  - Patient comfort/values?

Recommendation 3.2
We are **unable to make a recommendation** for or against the use of HFNO compared to continuous positive airway pressure (CPAP)/NIV to reduce intubation or mortality in the treatment of unselected patients with acute hypoxemic respiratory failure not due to cardiogenic pulmonary edema or acute exacerbation of COPD. *No recommendation; moderate level of evidence for mortality, low level of evidence for intubation, not in favor nor against.*
We **suggest** that CPAP/NIV can be considered instead of HFNO for the treatment of AHRF due to COVID-19 to reduce the risk of intubation (*weak recommendation, high level of evidence*), but **no recommendation** can be made for whether CPAP/NIV can decrease mortality compared to HFNO in COVID-19. *No recommendation; high level of evidence of no effect.*

Grasselli, G., Calfee, C.S., Camporota, L. *et al.* ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Med* **49**, 727–759 (2023). https://doi.org/10.1007/s00134-023-07050-7

NIV vs conventional O2

- Would a patient benefit from using NIV earlier?
- Mortality: unclear
- Reducing intubation: unclear
  - COVID-19: maybe
- Verdict: clinician judgment needed

Recommendation 4.1
We are **unable to make a recommendation** for or against the use of CPAP/NIV compared to conventional oxygen therapy for the treatment of AHRF (not related to cardiogenic pulmonary edema or acute exacerbation of COPD) to reduce mortality or to prevent intubation. *No recommendation; high level of evidence for mortality, moderate level of evidence for intubation.*
We **suggest** the use of CPAP over conventional oxygen therapy to reduce the risk of intubation in patients with acute hypoxemic respiratory failure due to COVID-19. *Weak recommendation; low level of evidence in favor.*
In this population, we are **unable to make a recommendation** for or against the use of CPAP over conventional oxygen therapy to reduce mortality. *No recommendation; moderate level of evidence of no effect.*

Grasselli, G., Calfee, C.S., Camporota, L. *et al.* ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Med* **49**, 727–759 (2023). https://doi.org/10.1007/s00134-023-07050-7

NIV via Helmet vs face mask

- Not enough evidence to make a recommendation

Recommendation 4.2

We are **unable to make a recommendation** for or against the use of helmet interface for CPAP/NIV as compared to face mask to prevent intubation or reduce mortality in patients with acute hypoxemic respiratory failure.

No recommendation; very low level of evidence in favor.

Grasselli, G., Calfee, C.S., Camporota, L. *et al.* ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Med* **49**, 727–759 (2023). https://doi.org/10.1007/s00134-023-07050-7

CPAP vs BiPAP

- Pressure swings lower in CPAP
- Lower P-SILI?

- Not enough evidence to make a recommendation
  - No data

Recommendation 4.3

We are **unable to make a recommendation** for or against the use of NIV compared to CPAP for the treatment of AHRF.

No recommendation; no evidence.

Grasselli, G., Calfee, C.S., Camporota, L. *et al.* ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Med* **49**, 727–759 (2023). https://doi.org/10.1007/s00134-023-07050-7

Awake Proning

Recommendation 7.3
We **suggest** awake prone positioning as compared to supine positioning for non-intubated patients with COVID-19-related AHRF to reduce intubation. *Weak recommendation; low level of evidence in favor.*
We are **unable to make a recommendation** for or against APP for non-intubated patients with COVID-19-related AHRF to reduce mortality. *No recommendation; moderate level of evidence of no effect.*
We are **unable to make a recommendation** for or against APP for patients with AHRF not due to COVID-19. *No recommendation; no evidence.*

Summary for AHRF

- Conventional O2 vs HFNC: HFNC may lower intubation risk
- HFNC vs CPAP/NIV: unclear, CPAP/NIV seemed to help with COVID-19 – intubation risk
  - Monitor closely if used
- Conventional O2 vs CPAP/NIV: CPAP seemed to help in COVID-19 – intubation risk
  - Monitor closely if used
- CPAP vs NIV: no evidence yet
- Face mask vs Helmet: unable to make a recommendation
- Awake prone positioning vs suping: suggest awake proning

Mechanical ventilation

Tidal volume

- Resp acidosis is well tolerated if well oxygenated
- Overdistention feeds a positive feedback loop of VILI
- “Baby lung”

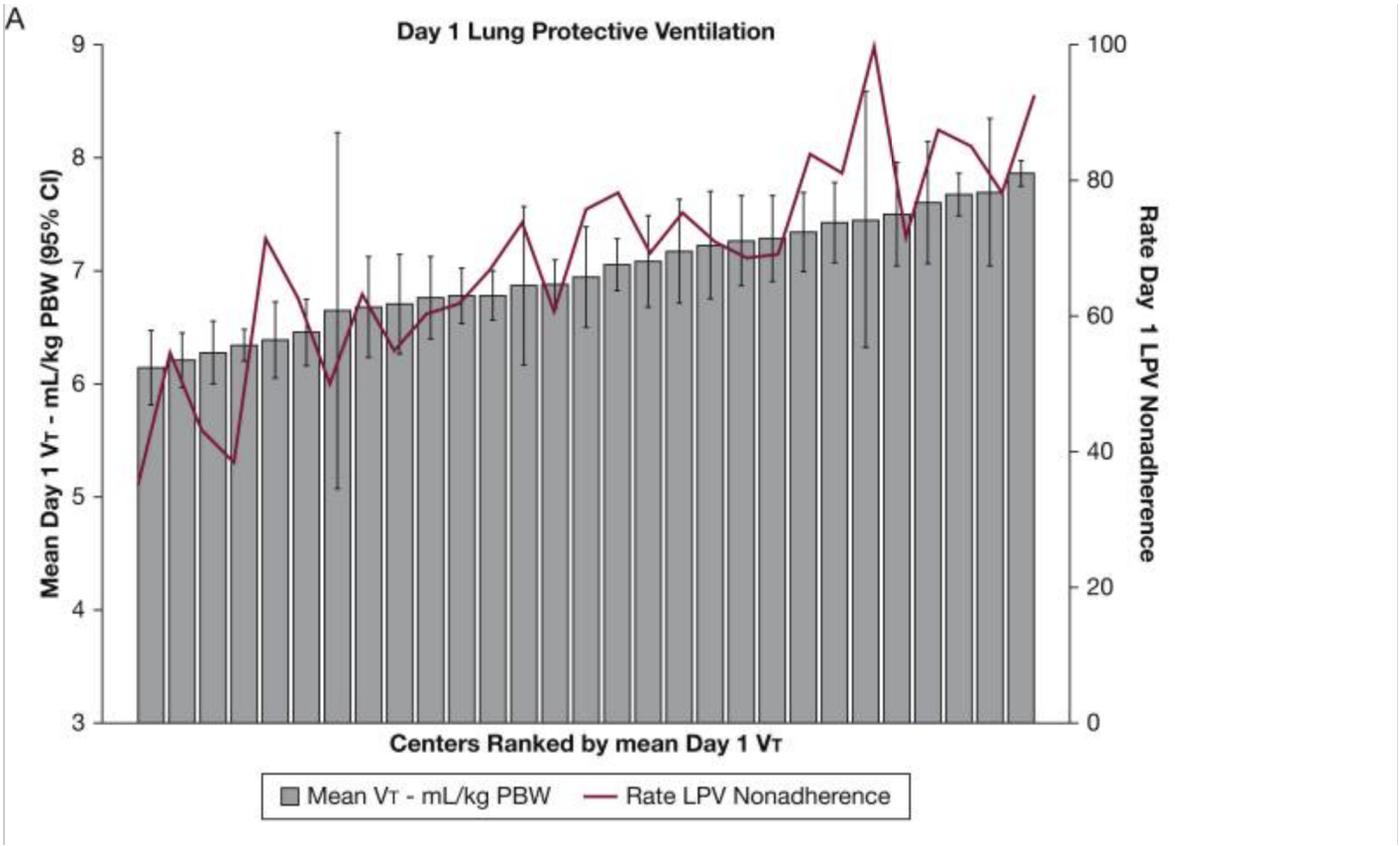
	Vt (ml/kg)		Paw Limit (cmH_2O)		Notes
	Interventional Arm	**Control Arm**	**Interventional Arm**	**Control Arm**	
Villar et al. [28]	5–8 PBW	9–11 PBW	PIP 35–40	PIP < 35–40	
Brochard et al. [95]	6–10 ABW	10–15 ABW	Pplat ≤ 25–30	PIP ≤ 60	
Amato et al. [96]	< 6 ABW	12 ABW	PIP < 40 and ΔP < 20	–	RM allowed – Explicit sedation protocol
Stewart et al. [97]	≤ 8 IBW	10–15 IBW	PIP ≤ 30	PIP ≤ 50	
Brower et al. [98]	5–8 PBW	10–12 PBW	Pplat < 30	Pplat < 45–55	
ARDS Net [99]	4–8 PBW	12 PBW	Pplat ≤ 30	Pplat ≤ 50	PP allowed – Explicit weaning protocol
Orme et al. [100]	4–8 PBW	10–15 PBW	Pplat < 40	Pplat < 70	Explicit sedation and weaning protocol

Tidal volume

Recommendation 5.1
We **recommend** the use of low tidal volume ventilation strategies (i.e., 4–8 ml/kg PBW), compared to larger tidal volumes (traditionally used to normalize blood gases), to reduce mortality in patients with ARDS not due to COVID-19. *Strong recommendation based on expert opinion despite lack of statistical significance; high level of evidence.*
This recommendation applies also to ARDS from COVID-19. *Strong recommendation; moderate level of evidence for indirectness.*

Grasselli, G., Calfee, C.S., Camporota, L. *et al.* ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensive Care Med* **49**, 727–759 (2023). https://doi.org/10.1007/s00134-023-07050-7

Lung Protective Ventilation (LPV): How are we doing?



- Multicenter observational cohort study across 29 centers

Chest . 2021 Oct;160(4):1304-1315.

CRITICAL CARE

What Is the Impact of Treatment Variability on Mortality in Patients With Moderate-to-Severe ARDS?

STUDY DESIGN

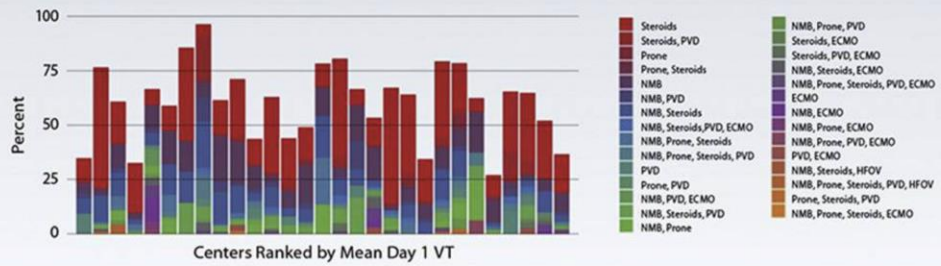
Multicenter, observational cohort study of 125 ICUs in 29 US centers between October 1, 2016, and April 30, 2017

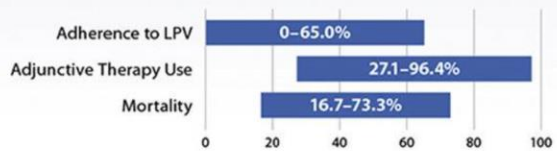
Included 2,466 mechanically ventilated adults with ARDS and Pao_2/FIO_2 < 150 on PEEP > 5 cm H_2O

Assessed adherence to lung protective strategies (LPV) and standardized mortality ratios (SMR)

RESULTS

Substantial center-to-center variability in ARDS management





Of the treatment-level factors explored, only center adherence to early (day 1) LPV correlated with SMR

Early adherence to LPV was associated with lower center mortality and may be a surrogate for overall quality of care processes.

Park P, et al. *CHEST* October 2021 | @journal_CHEST | https://doi.org/10.1016/j.chest.2021.05.047

Chest . 2021 Oct;160(4):1304-1315.

PEEP/FiO2

Clinical Trial > N Engl J Med. 2004 Jul 22;351(4):327-36. doi: 10.1056/NEJMoa032193.

Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome

Roy G Brower [1], Paul N Lanken, Neil MacIntyre, Michael A Matthay, Alan Morris, Marek Ancukiewicz, David Schoenfeld, B Taylor Thompson; National Heart, Lung, and Blood Institute ARDS Clinical Trials Network

Affiliations + expand

PMID: 15269312 DOI: 10.1056/NEJMoa032193

Free article

Randomized Controlled Trial > JAMA. 2008 Feb 13;299(6):646-55.

doi: 10.1001/jama.299.6.646.

Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial

Alain Mercat [1], Jean-Christophe M Richard, Bruno Vielle, Samir Jaber, David Osman, Jean-Luc Diehl, Jean-Yves Lefrant, Gwenaël Prat, Jack Richecoeur, Ania Nieszkowska, Claude Gervais, Jérôme Baudot, Lila Bouadma, Laurent Brochard; Expiratory Pressure (Express) Study Group

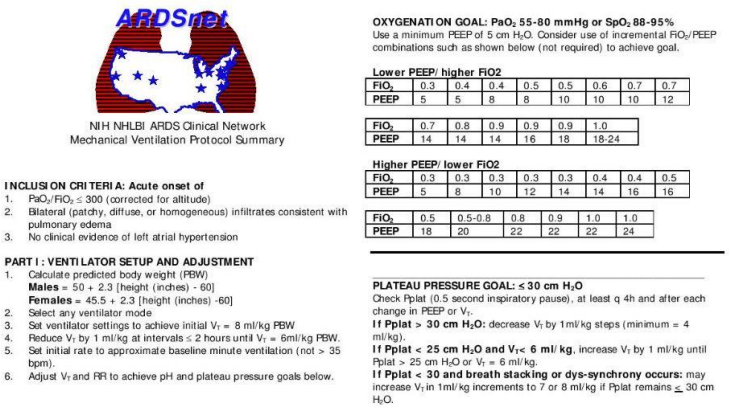
Randomized Controlled Trial > JAMA. 2008 Feb 13;299(6):637-45.

doi: 10.1001/jama.299.6.637.

Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial

Maureen O Meade [1], Deborah J Cook, Gordon H Guyatt, Arthur S Slutsky, Yaseen M Arabi, D James Cooper, Andrew R Davies, Lori E Hand, Qi Zhou, Lehana Thabane, Peggy Austin, Stephen Lapinsky, Alan Baxter, James Russell, Yoanna Skrobik, Juan J Ronco, Thomas E Stewart; Lung Open Ventilation Study Investigators

High vs Low PEEP



ARDSnet

NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of

1. $PaO_2/FiO_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT

1. Calculate predicted body weight (PBW)
   Males = 50 + 2.3 [height (inches) - 60]
   Females = 45.5 + 2.3 [height (inches) -60]
2. Select any ventilator mode
3. Set ventilator settings to achieve initial V_T = 8 ml/kg PBW
4. Reduce V_T by 1 ml/kg at intervals ≤ 2 hours until V_T = 6ml/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust V_T and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: PaO_2 55-80 mmHg or SpO_2 88-95%
Use a minimum PEEP of 5 cm H_2O. Consider use of incremental FiO_2/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/ higher FiO2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/ lower FiO2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

PLATEAU PRESSURE GOAL: ≤ 30 cm H_2O
Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T.
If Pplat > 30 cm H_2O: decrease V_T by 1ml/kg steps (minimum = 4 ml/kg).
If Pplat < 25 cm H_2O and V_T< 6 ml/kg, increase V_T by 1 ml/kg until Pplat > 25 cm H_2O or V_T = 6 ml/kg.
If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H_2O.

Recommendation 6.1
We are **unable to make a recommendation** for or against routine PEEP titration with a higher $PEEP/FiO_2$ strategy versus a lower $PEEP/FiO_2$ strategy to reduce mortality in patients with ARDS. *No recommendation; high level of evidence of no effect.*
This statement applies also to ARDS from COVID-19. *No recommendation; moderate level of evidence of no effect for indirectness.*

PEEP titration

- Pplat modulation
- Driving pressure
- Excessive PEEP

Recommendation 6.2
We are **unable to make a recommendation** for or against PEEP titration guided principally by respiratory mechanics, compared to PEEP titration based principally on PEEP/FiO_2 strategy, to reduce mortality in patients with ARDS. *No recommendation; high level of evidence of no effect.*
This statement applies also to ARDS from COVID-19. *No recommendation; moderate level of evidence for indirectness.*

Recruitment Maneuvers

- > 35 cmH20 for a min or more or less than a min
- Risks
- When to use it

Recommendation 6.3
We **recommend against** use of prolonged high-pressure recruitment maneuvers (defined as airway pressure maintained ≥ 35 cmH_2O for at least one minute) to reduce mortality of patients with ARDS. *Strong recommendation; moderate level of evidence against.*
This recommendation applies also to ARDS from COVID-19. *Strong recommendation; low level of evidence against for indirectness.*

Recommendation 6.4
We **suggest against** *routine* use of brief high-pressure recruitment maneuvers (defined as airway pressure maintained ≥ 35 cmH_2O for less than one minute) to reduce mortality in patients with ARDS. *Weak recommendation; high level of evidence of no effect.*
This suggestion applies also to ARDS from COVID-19. *Weak recommendation; moderate level of evidence of no effect for indirectness.*

Prone Position

- PROSEVA 2013
  - 28 day mortality benefit
  - 90 day mortality benefit

Recommendation 7.1
We **recommend** using prone position as compared to supine position for patients with moderate-severe ARDS (defined as $PaO_2/FiO_2 < 150$ mmHg and PEEP ≥ 5 cmH_2O, despite optimization of ventilation settings) to reduce mortality. *Strong recommendation, high level of evidence in favor.*
This recommendation applies also to ARDS from COVID-19. *Strong recommendation; moderate level of evidence in favor for indirectness.*

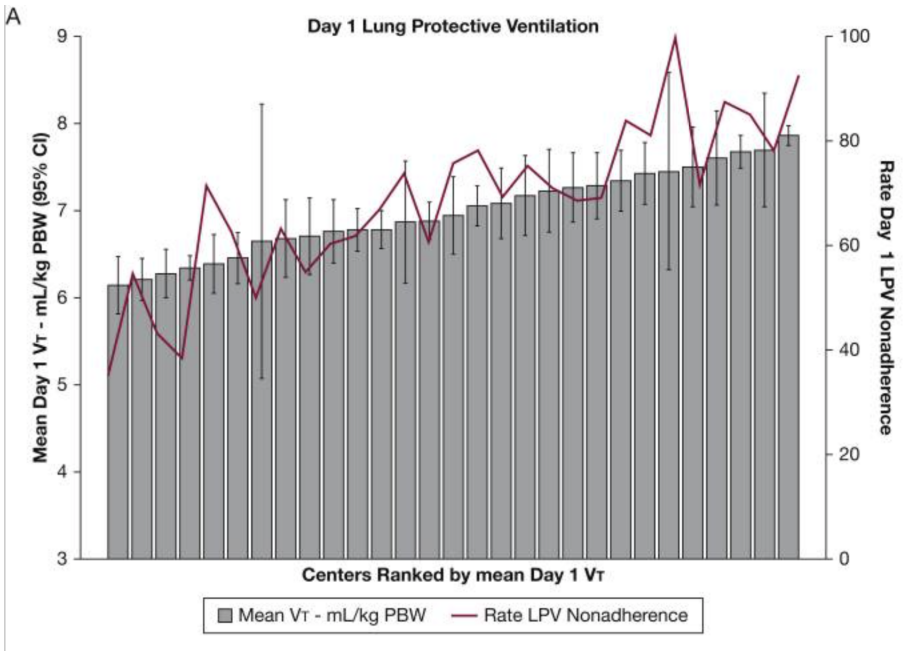
Recommendation 7.2
We **recommend** starting prone position in patients with ARDS receiving invasive mechanical ventilation early after intubation, after a period of stabilization during which low tidal volume is applied and PEEP adjusted and at the end of which the PaO_2/FiO_2 remains < 150 mmHg; and proning should be applied for prolonged sessions (16 consecutive hours or more) to reduce mortality. *Strong recommendation; high level of evidence in favor.*
This recommendation applies also to ARDS from COVID-19. *Strong recommendation; moderate level of evidence in favor for indirectness.*

Neuromuscular Blockade

- ACURASYS 2010
  - 48 hour NMB
  - Positive for mortality and VFD
  - Control group and deep sedation
- ROSE 2019
  - No mortality benefit seen
- A necessary evil

Recommendation 8.1
We **recommend against** the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate-to-severe ARDS not due to COVID-19. *Strong recommendation, moderate level of evidence.*
We are **unable to make a recommendation** for or against the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate-to-severe ARDS due to COVID-19. *No recommendation; no evidence.*

VV ECMO



Recommendation 9.1

We **recommend** that patients with severe ARDS not due to COVID-19 as defined by the EOLIA trial eligibility criteria, should be treated with ECMO in an ECMO center which meets defined organizational standards, adhering to a management strategy similar to that used in the EOLIA trial.

Strong recommendation, moderate level of evidence in favor

This recommendation applies also to patients with severe ARDS due to COVID-19.

Strong recommendation; low level of evidence in favor for indirectness.

Summary for IMV

- Low tidal volume ventilation vs high:
  - LTVV
- PEEP titration using high PEEP/FiO2 vs low PEEP/FiO2
  - Unable to make recommendation re mortality benefit
- PEEP titration guided by respiratory Mechanics
  - Unable to make recommendation re mortality benefit
- Prolonged RM
  - Recommend against, mortality
- Brief RM
  - Suggest against, mortality
  - De-recruiting events

Summary for IMV

- Prone position
  - Recommend proning, mortality benefit
  - After a stabilization period
- NMB
  - Recommend against routine use
  - PTX risk reduction
- VV ECMO
  - Recommend for ECMO eval and treatment in an ECMO center

What are we missing

- Non-intubated
  - Avoiding intubation
  - Mortality
- Intubated
  - Mortality
- Are there other important factors to consider?

The future

- ARDS is heterogenous
- How can we group patients and target the appropriate treatment ?
- Subphenotype classification in prospective studies likely requires: (1) on-site, real-time testing and rapid results, and (2) operator independence.
  - Based on biomarkers
    - Can that influence
      - Anti inflammatory use
      - PEEP use
      - Fluid strategy
      - Prognosis

Take Home

- COVID-19 highlighted the heterogeneity in response to therapy
  - Steroids
  - IMV
- HFNC seems to have a role in delaying intubation
- Mechanical ventilation is not a benign intervention
  - Do no harm
- Lung protective ventilation
  - LTVV
  - Pplat
  - Driving pressure
  - Liberate the TV if you are meeting your goals