Evidence-based management of ARDS

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AAGBI

CORE TOPICS, NOTTINGHAM

Acute Respiratory Distress Syndrome

"A spectrum of lung diseases characterised by a severe inflammatory process causing diffuse alveolar damage and resulting in a variable degree of ventilation perfusion mismatch, severe hypoxaemia and poor lung compliance"

Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

2013

	Acute Respiratory Distress Syndrome
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mm Hg $<$ $Pa_{O_2}/F_{I_{O_2}} \leq$ 300 mm Hg with PEEP or CPAP $\geq$5 cm H_2O[c]
Moderate	100 mm Hg $<$ $Pa_{O_2}/F_{I_{O_2}} \leq$ 200 mm Hg with PEEP $\geq$5 cm H_2O
Severe	$Pa_{O_2}/F_{I_{O_2}} \leq$ 100 mm Hg with PEEP $\geq$5 cm H_2O

Abbreviations: CPAP, continuous positive airway pressure; $F_{I_{O_2}}$, fraction of inspired oxygen; Pa_{O_2}, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.

[a] Chest radiograph or computed tomography scan.

[b] If altitude is higher than 1000 m, the correction factor should be calculated as follows: [$Pa_{O_2}/F_{I_{O_2}} \times$ (barometric pressure/760)].

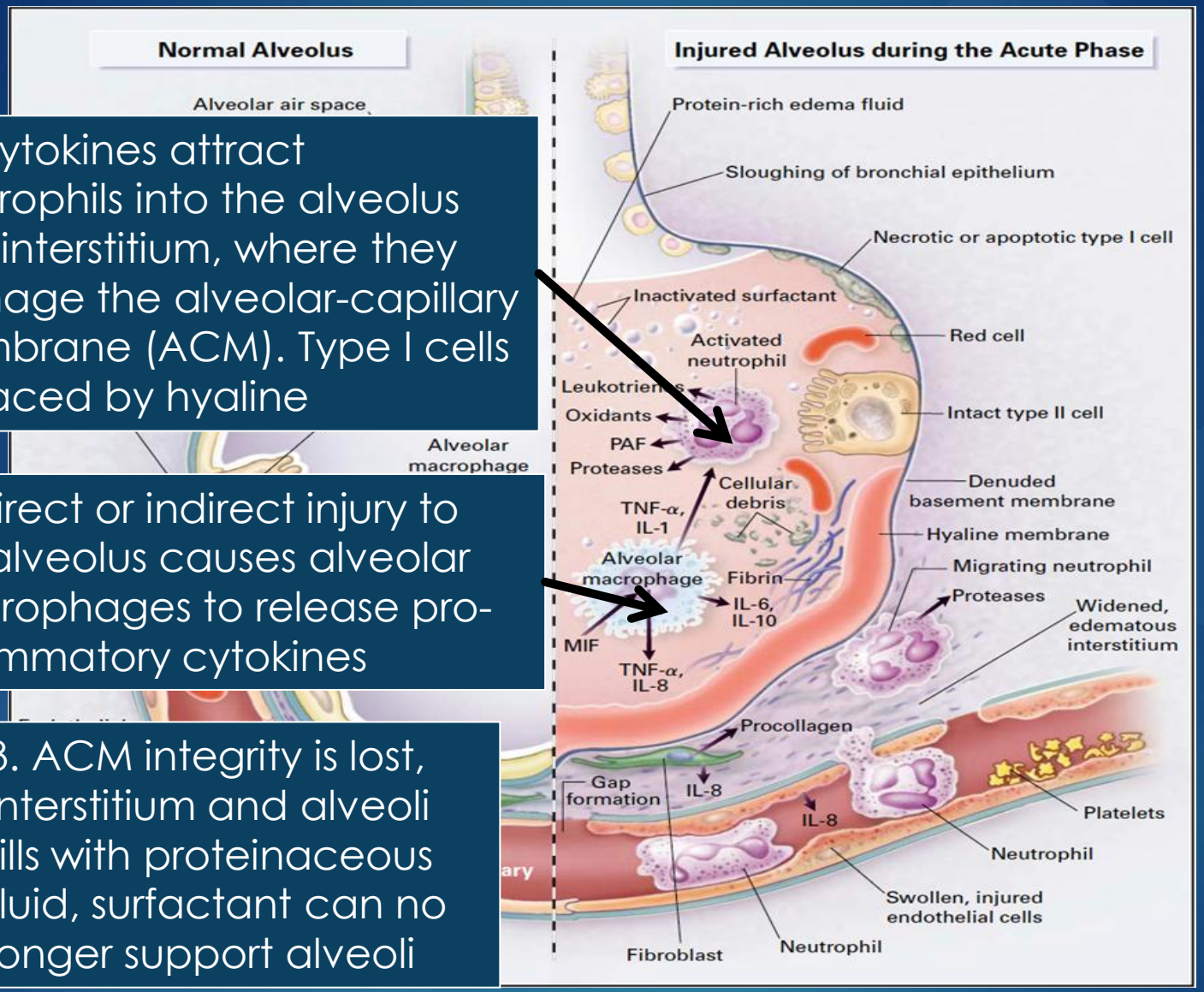
[c] This may be delivered noninvasively in the mild acute respiratory distress syndrome group.

ARDS definitions

2. Cytokines attract neutrophils into the alveolus and interstitium, where they damage the alveolar-capillary membrane (ACM). Type I cells replaced by hyaline

1. Direct or indirect injury to the alveolus causes alveolar macrophages to release pro-inflammatory cytokines

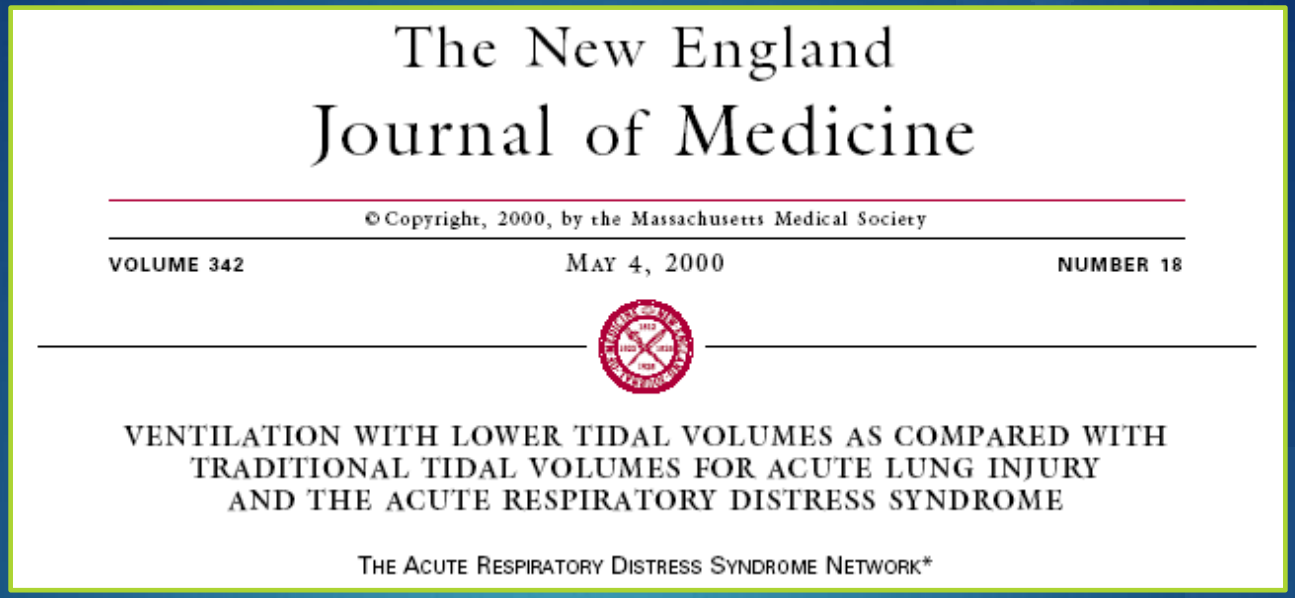
3. ACM integrity is lost, interstitium and alveoli fills with proteinaceous fluid, surfactant can no longer support alveoli



Acute/Exudative stage

(My) management principles

- Treat the underlying cause
- Levels of PaO_2 and $PaCO_2$ 'compatible with life'
- Minimise further damage
  - Avoid VALI/VILI
  - Avoid further infections
  - Rehab as early as possible
- Lung protective ventilation + sensible amount of PEEP
- Prone
- Keep them crispy dry
- Probably paralyse, maybe steroids
- APRV (in selected cases)
- ECMO (if failing despite the above)



The New England
Journal of Medicine

VOLUME 342 MAY 4, 2000 NUMBER 18

VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

In patients with ALI, ventilation with smaller tidal volumes (6 mL/kg) will result in better clinical outcomes than traditional tidal volumes (12 mL/kg)

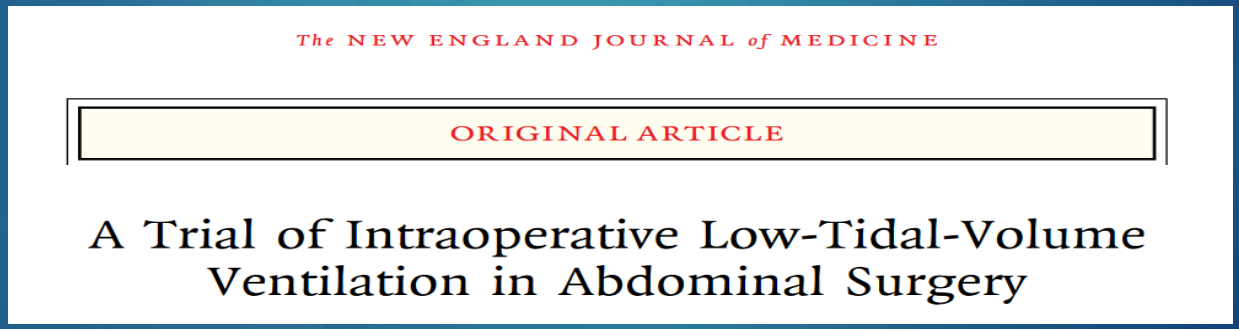
- Multicentre RCT, 860 pts, stopped early
22% reduction in mortality (40% to 31%) if ventilated with Vt 6mls/kg and plateau pressure < 35, compared to 12mls/kg and plateau pressure < 50

Lung-protective ventilation

ARDS is heterogeneous

Lung-protective ventilation

- 2nd ARDSnet study *NEJM 2004;351:327-336*
  - 550 pts. Similar results
- Sakr et al *Chest 2005; 128:3098-310*
  - 198 European ICUs, 393 patients with ALI/ARDS. High tidal volumes = risk factor for ↑mortality
- Do we actually do it?
- Should it be lower?



Aim

- Maximise recruitment of alveoli
- Decrease biotrauma from alveolar collapse
- Minimise cyclic atelectasis and atelectotrauma
- Allow lower FiO2

Disadvantages

- Impaired CO2 clearance
- ↓RV preload ↑RV afterload ↓LV preload & compliance
- Barotrauma
- ↑ICP ↓CO
- Worsen R to L shunt (↑PVR)
- Worsen airleaks
- ↓Splanchnic blood flow (esp if ≥ 20cmH20)

"Open Lung Approach" - PEEP, Recruitment & APRV

JAMA The Journal of the American Medical Association

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

Meade, M et al, JAMA. 2008; 299(6):637-645

Positive End-Expiratory Pressure Setting in Adults With Acute Lung Injury and Acute Respiratory Distress Syndrome

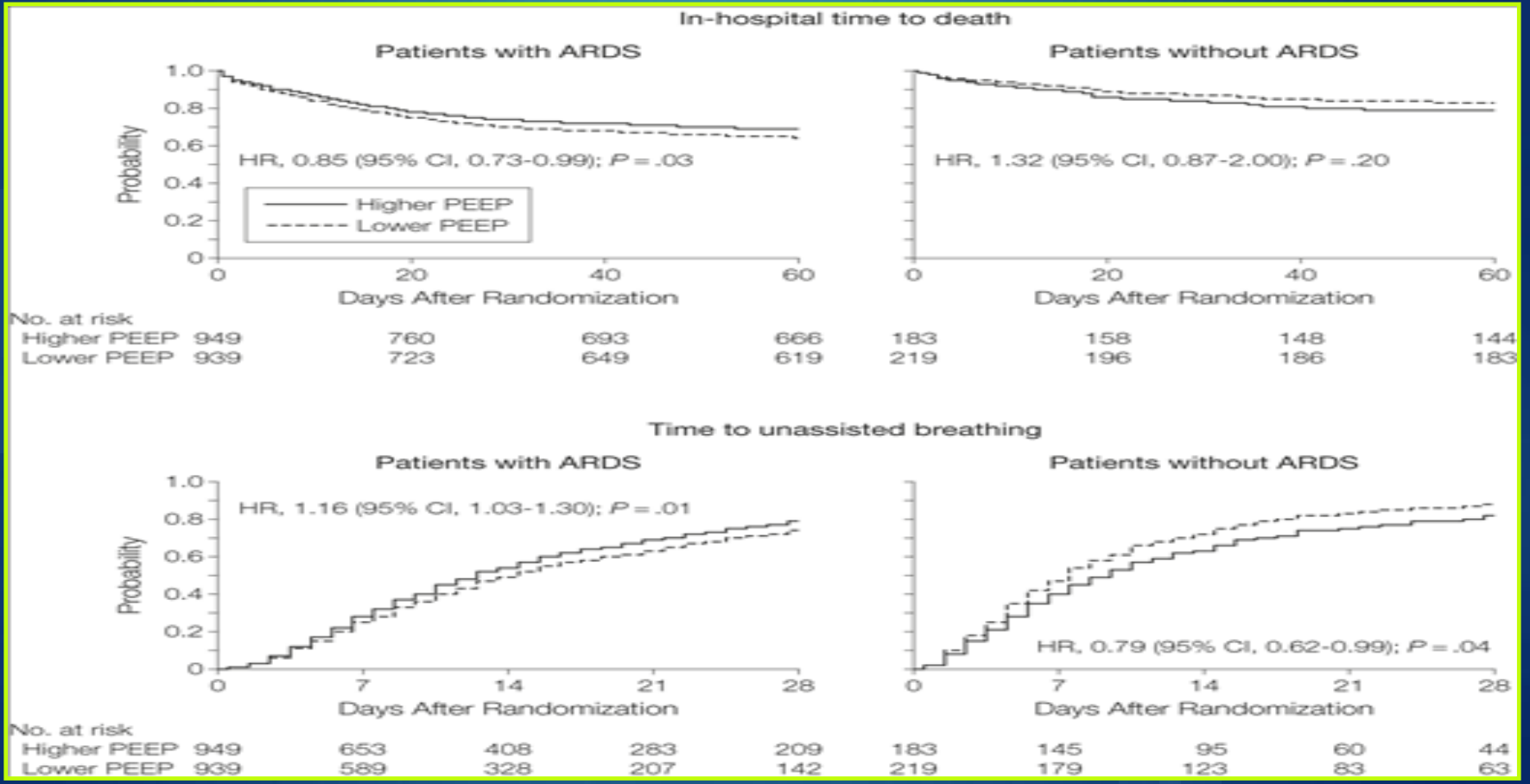
A Randomized Controlled Trial

Mercatt, M, et al. JAMA. 2008; 299(6):646-655.

PEEP – how much?

Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome

Systematic Review and Meta-analysis



- > Upper/lower infection point on PV loop?
- Stepwise recruitment?
- Maximise static compliance (TV/Pplat-PEEP)?
- Guided by oesophageal pressures?
- Adjust to FiO2?

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

Ideal PEEP?

ART trial 2017…

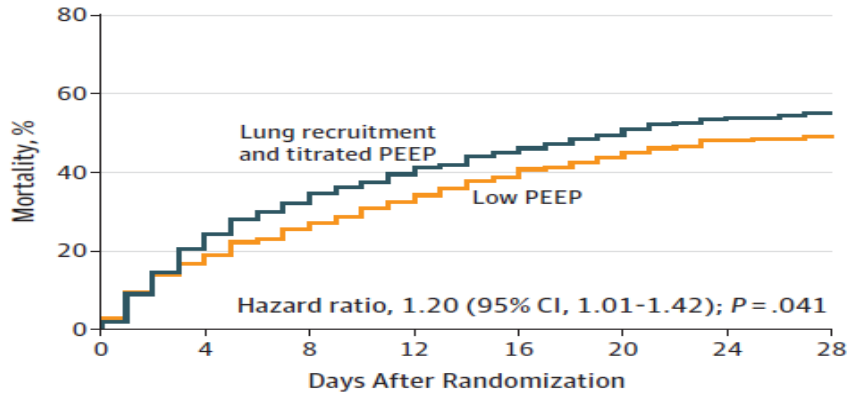
Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome A Randomized Clinical Trial

Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators

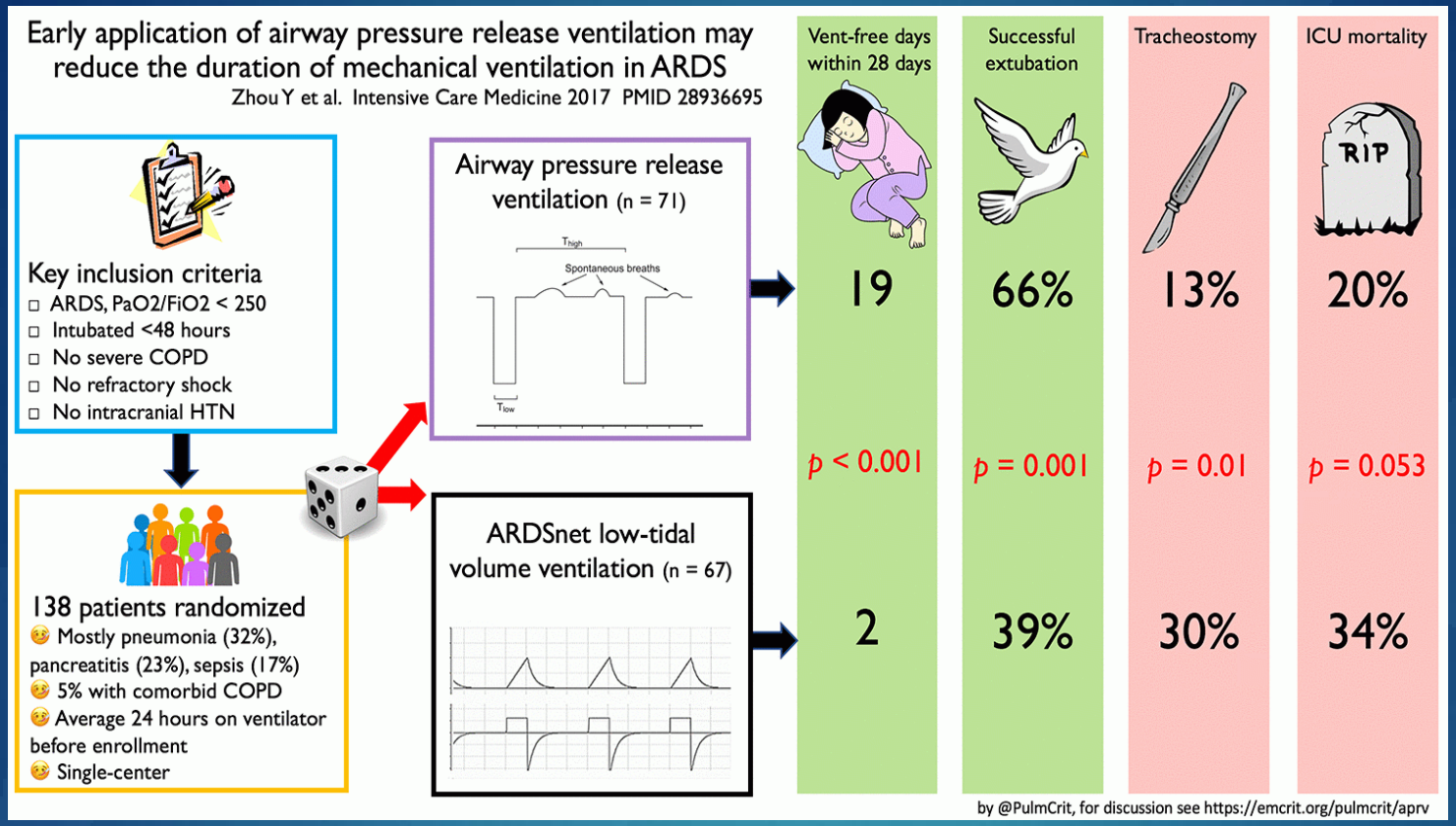
Figure 2. 28-Day Mortality in the Lung Recruitment Maneuver With Titrated PEEP Group vs the Low-PEEP Group



No. at risk								
Lung recruitment and titrated PEEP	501	397	340	303	276	254	233	225
Low PEEP	509	423	378	343	312	286	264	260

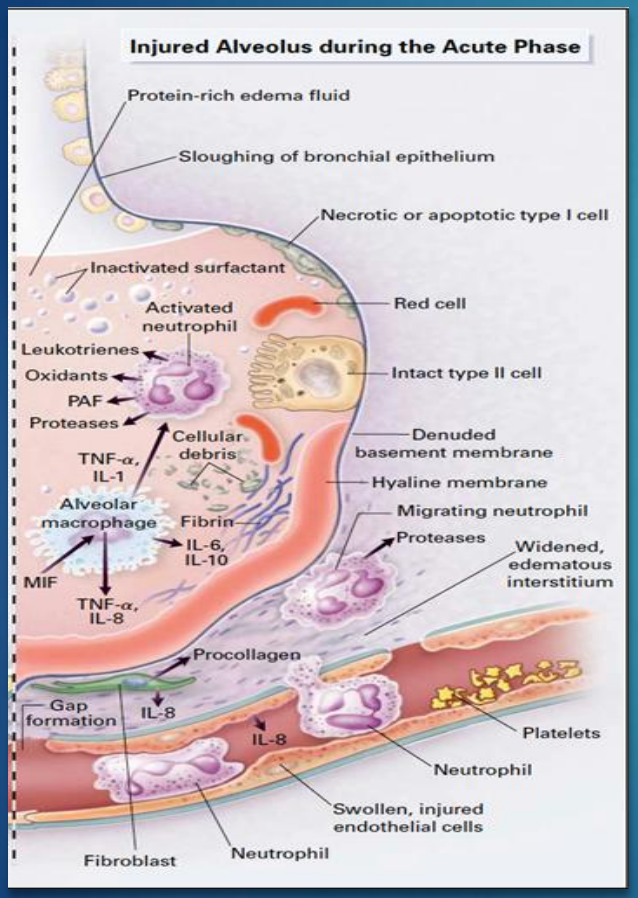
Airway Pressure Release Ventilation

- CPAP to open lung with short cyclic releases to facilitate ventilation
- Patient can breathe throughout respiratory cycle (works better if they do!)
- Reduce sedation to encourage breathing
- I use in:-
  - Obese
  - To recruit
  - Unable to prone



Zhou et al (2017)

Fluid Management



- Increased lung water is the underlying cause of many of the clinical abnormalities in ARDS (decreased compliance, poor gas exchange, atelectasis)
- After resolution of shock, effort should be made to attempt diuresis
- Frusemide – bolus vs infusion +/- spironolactone
- Renal Replacement Therapy (CVVH/CVVHDF) if needed

The NEW ENGLAND JOURNAL of MEDICINE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

FACTT Study – ARDS Network, NEJM, 2006;354:2564-2575

- 1001 pts
- Mean fluid in first 7d: -137ml vs +6992ml
- No difference in mortality but improved lung function and shortened the duration of mechanical ventilation and intensive care
- No increased shock/dialysis "non-pulmonary organ failure"
- **BUT…**

The Adult Respiratory Distress Syndrome Cognitive Outcomes Study

Long-Term Neuropsychological Function in Survivors of Acute Lung Injury

Fluid management

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 6, 2013 VOL. 368 NO. 23

Prone Positioning in Severe Acute Respiratory Distress Syndrome

Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D., Jean-Christophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D., Thierry Boulain, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D., Alain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D., Delphine Chatellier, M.D., Samir Jaber, M.D., Ph.D., Sylvène Rosselli, M.D., Jordi Mancebo, M.D., Ph.D., Michel Sirodot, M.D., Gilles Hilbert, M.D., Ph.D., Christian Bengler, M.D., Jack Richecoeur, M.D., Marc Gainnier, M.D., Ph.D., Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D., Raphaele Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D., for the PROSEVA Study Group*

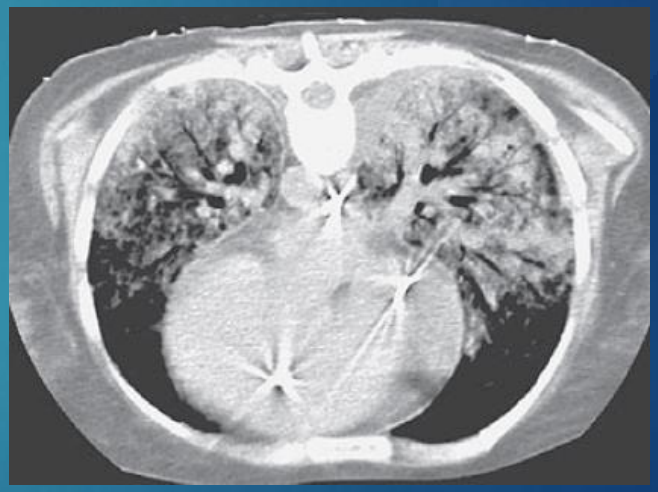
Hypothesis: Early application of prone positioning (16h) would improve survival in patients with severe ARDS.

Conclusion: Early application of prolonged prone positioning significantly decreased 28 day (16% prone vs 32.8% supine) and 90 mortality in patients with severe ARDS.

Proning

Proning - Why?

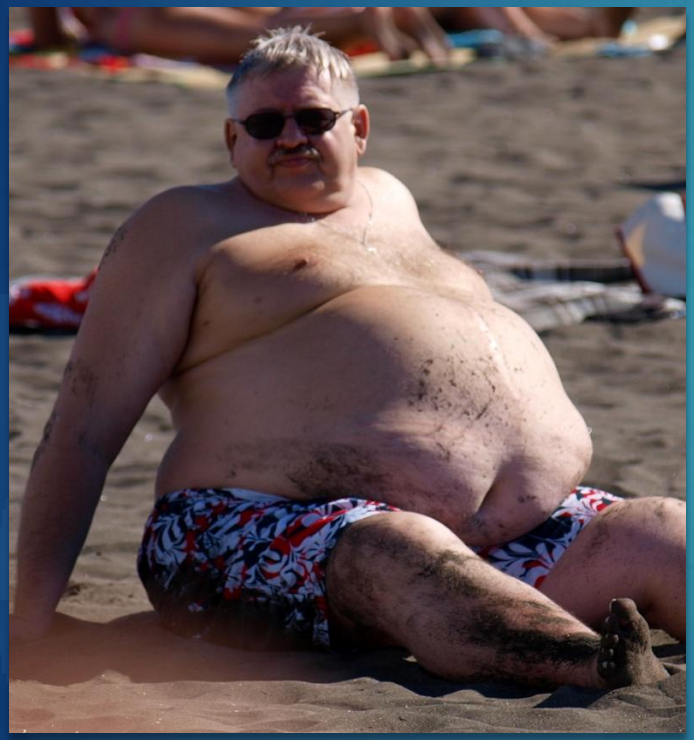
- Improvement in oxygenation in 50-75% of ARDS patients when turned prone
- Probable mechanisms:
  - VQ matching improved
  - "Cardiac weight"
  - Improvement in thoraco-abdominal compliance
  - Facilitates secretion drainage
  - Recruitment
- Improvement in gas exchange often persists even when patients turned supine



Proning: Why not?

- ETT / chest drain /invasive lines: obstruction / dislodgement
- ↑ICP
- Difficult to perform procedures / reintubate / CPR
- Decreased enteral nutrition
- Difficulty monitoring (e.g. ECG lead placement, CXR etc)
- Labour intensive – required at least 5 staff to turn
- May increase intra-abdo pressure / reduce hepatic perfusion
- Facial oedema
- Pressure trauma:
  - Eyes
  - Bridge of nose
  - Chin
  - Breasts / genitals
  - Shins / knees

Proning - Who?

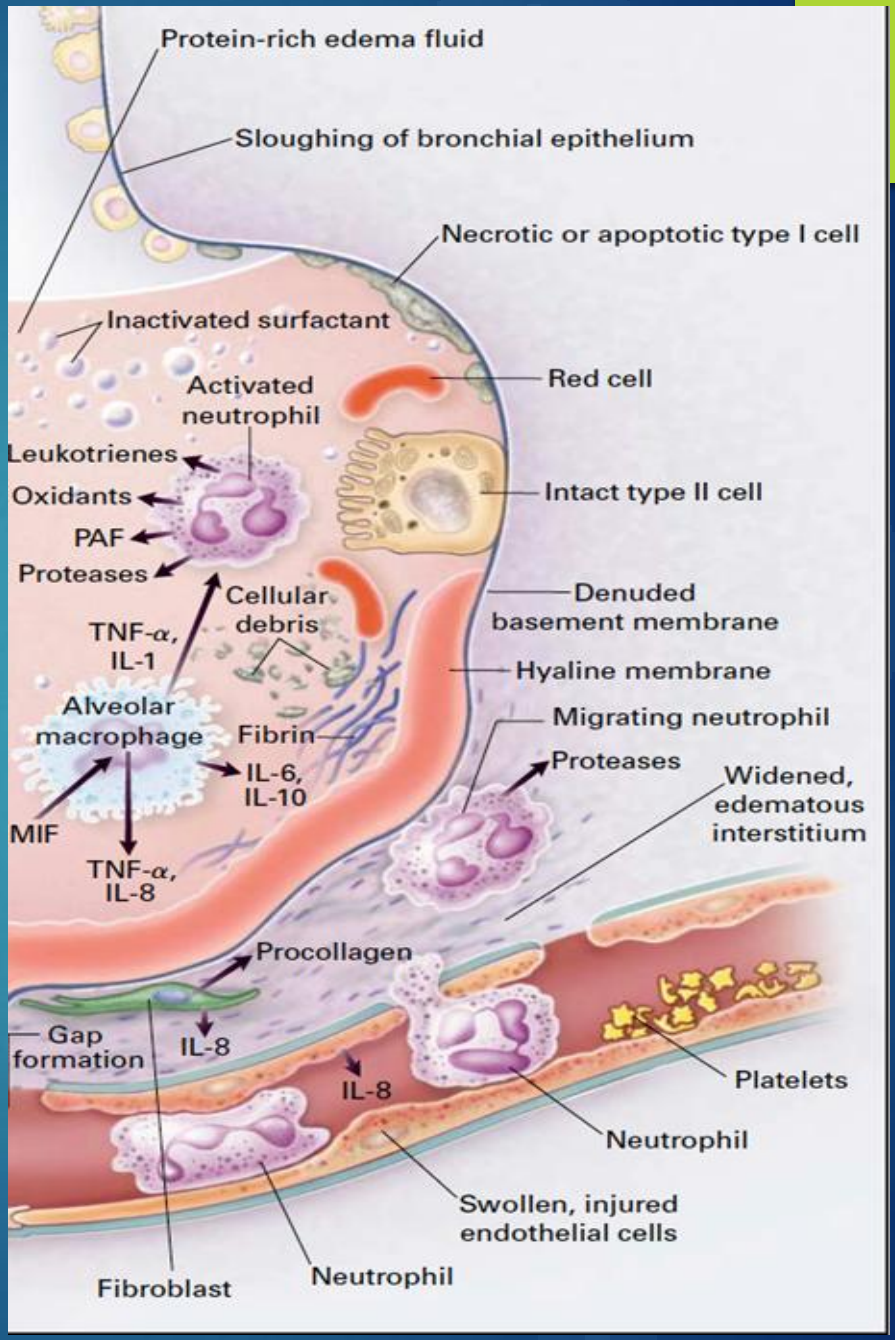


- Anyone requiring FiO_2 > 60% to achieve PaO_2 > 8kPa
- Absolute CI
  - Unstable Cx spines
  - Open chest or abdomens
- Relative CI
  - Eye / face / head injury
  - Thoraco-lumbar spinal injury / pelvic #
  - Recent abdominal surgery
  - Gross ascites / 3rd trimester pregnancy / super morbid obesity
- Think carefully about
  - Significant CVS stability (multiple inotropes and vasopressors) / IABP
  - Predominantly CO_2 clearance issues / asthmatics

Paralyse?

- Improve patient – ventilator synchrony
- Associated with critical illness polyneuromyopathy → longer weaning, longer LOS & higher mortality
- ?Reduce deleterious "PI-VILI"
- **ACURASYS: Papazian et al, N Engl J Med 2010;363:1107-1116**
  - 340 pts, 20 French ICU, PF < 150
  - 48 h Cis-Atracurium increased survival & ventilator free days without increase in neuromuscular weakness
- **ROSE**
  - 1006 pts, 48US ICUs
  - No difference in mortality
  - Higher rate of adverse events

Steroids??


Protein-rich edema fluid
Sloughing of bronchial epithelium
Necrotic or apoptotic type I cell
Inactivated surfactant
Red cell
Activated neutrophil
Leukotrienes
Oxidants
PAF
Proteases
Intact type II cell
Cellular debris
TNF-α, IL-1
Denuded basement membrane
Hyaline membrane
Alveolar macrophage
Fibrin
Migrating neutrophil
Proteases
IL-6, IL-10
MIF
TNF-α, IL-8
Widened, edematous interstitium
Procollagen
Gap formation
IL-8
IL-8
Platelets
Neutrophil
Swollen, injured endothelial cells
Fibroblast
Neutrophil

Steroids

- **Effect of Prolonged Methylprednisolone therapy in Unresolving ARDS**
  - *Meduri et al JAMA 1998; 280(2):159-165*
  - 24 patients (originally powered for 100, but cut short by the supervisory committee)
  - demonstrated statistically significant improvement in outcomes, (lung injury scores and mortality)

Intensive Care Medicine
May 2016, Volume 42, Issue 5, pp 829–840 | Cite as

Prolonged glucocorticoid treatment is associated with improved ARDS outcomes: analysis of individual patients' data from four randomized trials and trial-level meta-analysis of the updated literature

Authors | Authors and affiliations

G. Umberto Meduri, Lisa Bridges, Mei-Chiung Shih, Paul E. Marik, Reed A. C. Siemieniuk, Mehmet Kocak

ventilatory free days

  - BUT – small study, groups not matched, placebo group more catecholamine dependent shock

Others

- HFOV
- Pulmonary vasodilators
  - NO
  - Inhaled prostanoids
- β2 agonists
- Surfactant (calfactant)
- Ketoconazole
- Phosphodiesterase inhibitors
- Neutrophil elastase inhibitors – Sivelestat
- Antioxidants – Glutathione, N-Acetylcysteine
- The future? Stem cell therapy, liquid ventilation ...

In Summary …

- Treat the underlying cause
- Levels of PaO_2 and $PaCO_2$ 'compatible with life'
- Minimise further damage
- Use lung protective ventilation & 'sensible' PEEP
- Keep them crispy dry
- Consider APRV (if recruitable)
- Prone (and keep proning)
- Probably paralyse, maybe steroids
- Consider referral to an ECMO centre (if failing despite the above)

ECMO
HEARTLINK ECMO CENTRE
Glenfield Hospital
Leicester


so does anyone have any questions?
©hugh