ARDS:2019 UPDATE

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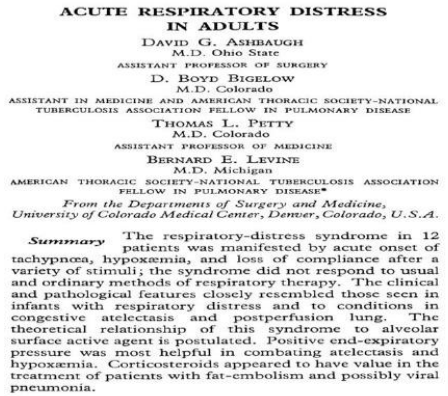
Acute Respiratory distress Syndrome (ARDS)



ACUTE RESPIRATORY DISTRESS
IN ADULTS

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Summary The respiratory-distress syndrome in 12 patients was manifested by acute onset of tachypnœa, hypoxæmia, and loss of compliance after a variety of stimuli; the syndrome did not respond to usual and ordinary methods of respiratory therapy. The clinical and pathological features closely resembled those seen in infants with respiratory distress and to conditions in congestive atelectasis and postperfusion lung. The theoretical relationship of this syndrome to alveolar surface active agent is postulated. Positive end-expiratory pressure was most helpful in combating atelectasis and hypoxæmia. Corticosteroids appeared to have value in the treatment of patients with fat-embolism and possibly viral pneumonia.

- First described as clinical syndrome in 1967 by Ashbaugh & Petty .

- Clinical terms synonymous with ARDS
- Acute respiratory failure
- Capillary leak syndrome
- Shock Lung
- Traumatic wet Lung
- Adult hyaline membrane disease

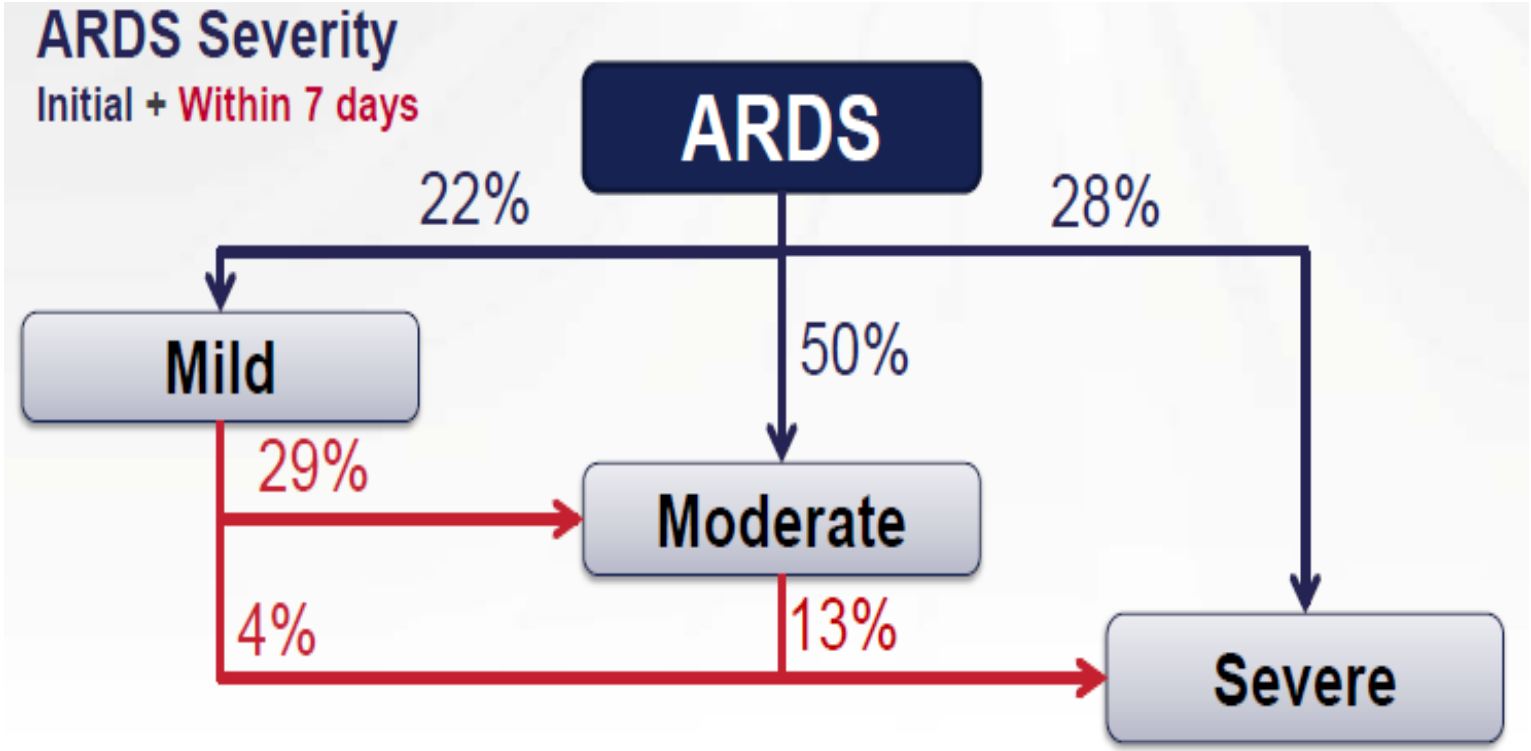
The American-European Consensus Conference Definition of Acute Lung Injury and ARDS, AECC(1994)

	Timing	Oxygenation (PaO_2/FiO_2)	Chest Radiograph	Pulmonary Artery Wedge pressure
ALI	Acute onset	≤ 300 mmHg (40 kPa) (regardless of PEEP)	Bilateral infiltrates	≤18 mmHg/no evidence of left atrial hypertension
ARDS	Acute onset	≤ 200 mmHg (26 kPa) regardless of PEEP	Bilateral infiltrates	≤ 18 mmHg or no evidence of left atrial hypertension

The current Berlin definition of ARDS (2012)

Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

	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 < PaO_2/FIO_2 ≤ 300 mm Hg with PEEP or CPAP ≥5 cm H_2O[c]
Moderate	100 mm Hg < PaO_2/FIO_2 ≤ 200 mm Hg with PEEP ≥5 cm H_2O
Severe	PaO_2/FIO_2 ≤ 100 mm Hg with PEEP ≥5 cm H_2O



	Mild	Moderate	Severe
Berlin Definition of ARDS PaO_2/FiO_2 (mmHg) PEEP (cm H_2O)	200 < P/F ≤ 300 (or CPAP) ≥ 5	100 < P/F ≤ 200 ≥ 5	P/F ≤ 100 ≥ 5
Mortality [95% CI]	**27%** [24-30]	**32%** [29-34]	**45%** [42-48]
Duration of MV [IQR]	**5 days** [2-11]	**7 days** [4-14]	**9 days** [5-17]

Commentary

The ARDS Kigali definition: do we need a new definition for low-income countries?

Gautam Rawal[1,*], Sankalp Yadav[2], Raj Kumar[3]

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*Corresponding Author

	Berlin criteria	Kigali modifications	Recent research (2015–2016) investigating the validity of the modifications
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms	Within 1 week of a known clinical insult or new or worsening respiratory symptoms	No modification
Oxygenation	$PaO_2/FiO_2 \leq 300$	$SpO_2/FiO_2 \leq 315$	Brown *et al.* [25▪▪]; Sanz *et al.* [26▪▪]; Chen *et al.* [27▪▪]; Khemani *et al.* [28]; Bass *et al.* [29]
PEEP requirement	Minimum 5 cm H_2O PEEP required by invasive mechanical ventilation (noninvasive acceptable for mild ARDS)	No PEEP requirement	Caironi *et al.* [30▪▪]
Chest imaging	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules by chest radiograph or CT	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules by chest radiograph or ultrasound	Ma *et al.* [31]; Lichtenstein [32▪]; Pesenti *et al.* [33]; Ye *et al.* [34▪▪]; Shah *et al.* [35▪]; Bass *et al.* [29]
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload [need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present]	Respiratory failure not fully explained by cardiac failure or fluid overload [need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present]	No modification

ARDS, acute respiratory distress syndrome; PEEP, positive end expiratory pressure.

Validation Study suggest good sensitivity but moderate specificity.

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Thorax. 2018 September ; 73(9): 840–846. doi:10.1136/thoraxjnl-2017-211280.

Severity Scoring of Lung Edema on the Chest Radiograph Is Associated with Clinical Outcomes in ARDS

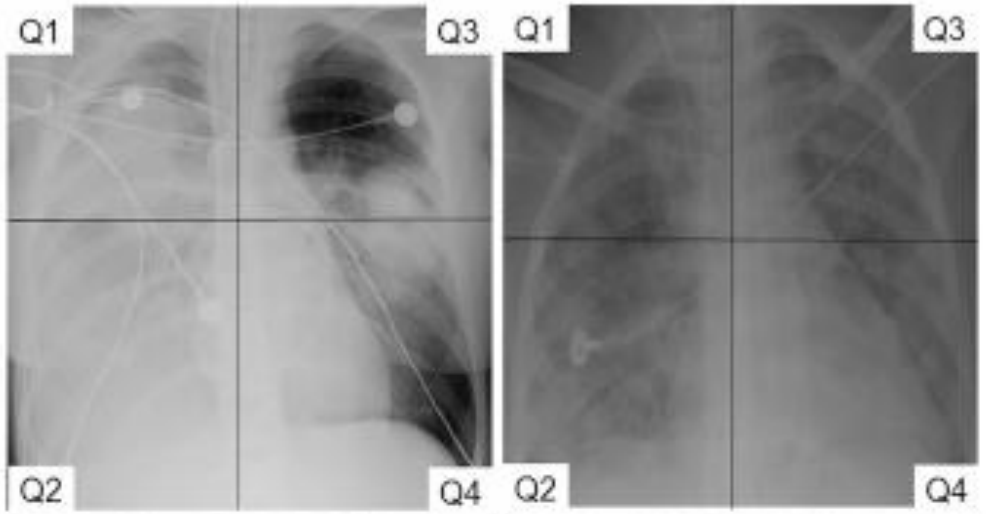
Radiographic Assessment of Lung Edema (RALE)

A

Consolidation[a]	
Consolidation Score	Extent of alveolar opacities
0	None
1	<25%
2	25-50%
3	50-75%
4	>75%
Density[b]	
Density Score	Density of alveolar opacities
1	Hazy
2	Moderate
3	Dense
Final RALE Score[c]	
Right Lung	Left Lung
Upper Quadrant Cons x Den = Q1 score	Upper Quadrant Cons x Den = Q3 score
Lower Quadrant Cons x Den = Q2 score	Lower Quadrant Cons x Den = Q4 score
Total RALE = Q1+ Q2 + Q3 + Q4	

[a]Consolidation is scored for each quadrant
[b]Density is scored for each quadrant that has a consolidation score ≥ 1
[c]If Quadrant consolidation score is = then Quadrant score is 0

B

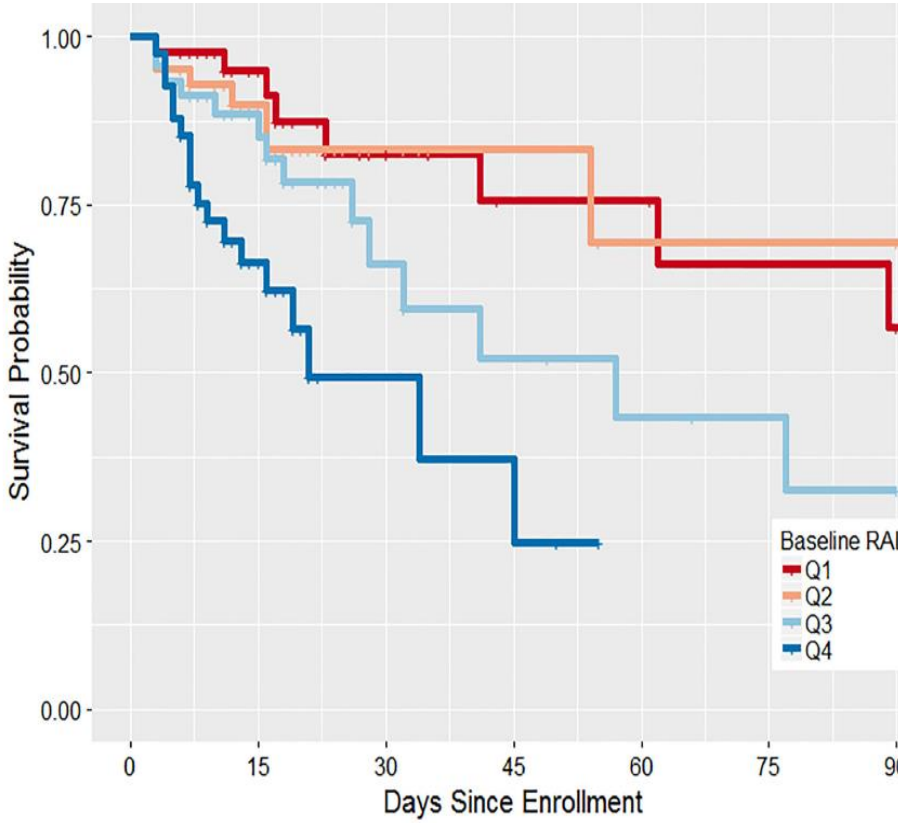


Calculation of the RALE Score for Left Radiograph					
Score	Q1	Q2	Q3	Q4	Total
Consolidation	4	4	1	2	
Density	3	3	3	3	
Quadrant Score	4 x 3 = 12	4 x 3 = 12	1 x 3 = 3	2 x 3 = 6	33

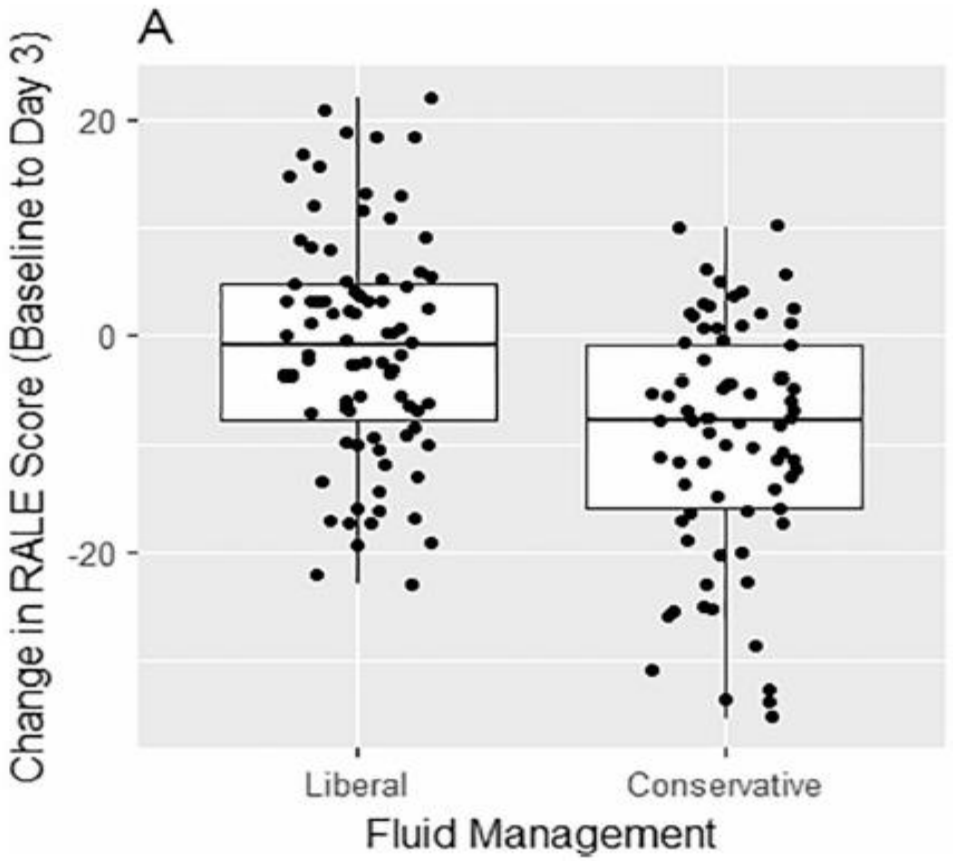
Calculation of the RALE Score for Right Radiograph					
Score	Q1	Q2	Q3	Q4	Total
Consolidation	4	4	4	4	
Density	1	2	1	2	
Quadrant Score	4 x 1 = 4	4 x 2 = 8	4 x 1 = 4	4 x 2 = 8	24

Results: Agreement between two independent reviewers for RALE score was excellent (intra-class correlation coefficient=0.93, 95% CI:0.91–0.95). In donors, pre-procurement RALE score correlated with height-adjusted total lung weight (ρ=0.59, $p<0.001$). In ARDS patients, higher RALE scores were independently associated with lower PaO_2/FiO_2 and worse survival. Conservative fluid management significantly decreased RALE score over 3 days compared to liberal fluid management.

- SURVIVAL OUTCOME



FLUID BALANCE



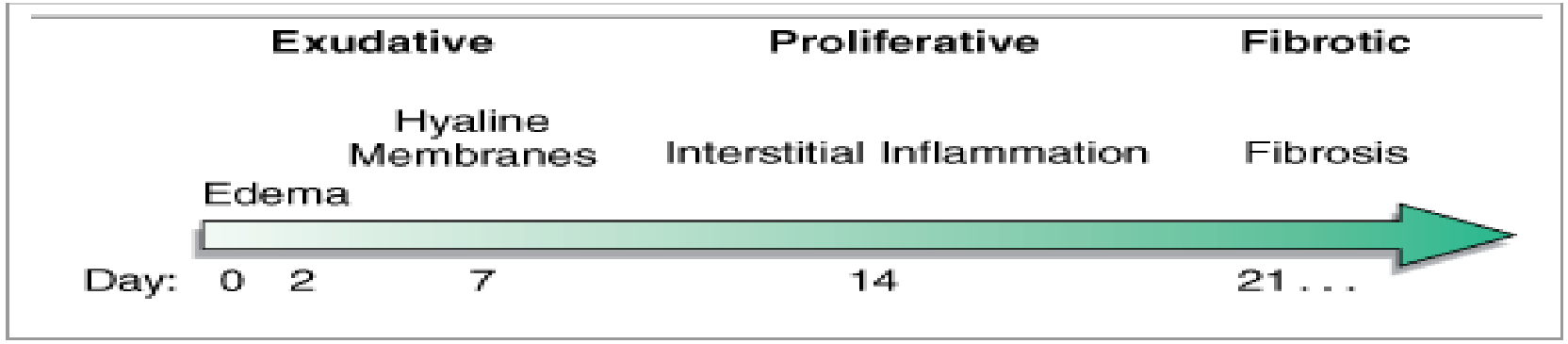
ERIES

Clinical Course and Pathophysiology

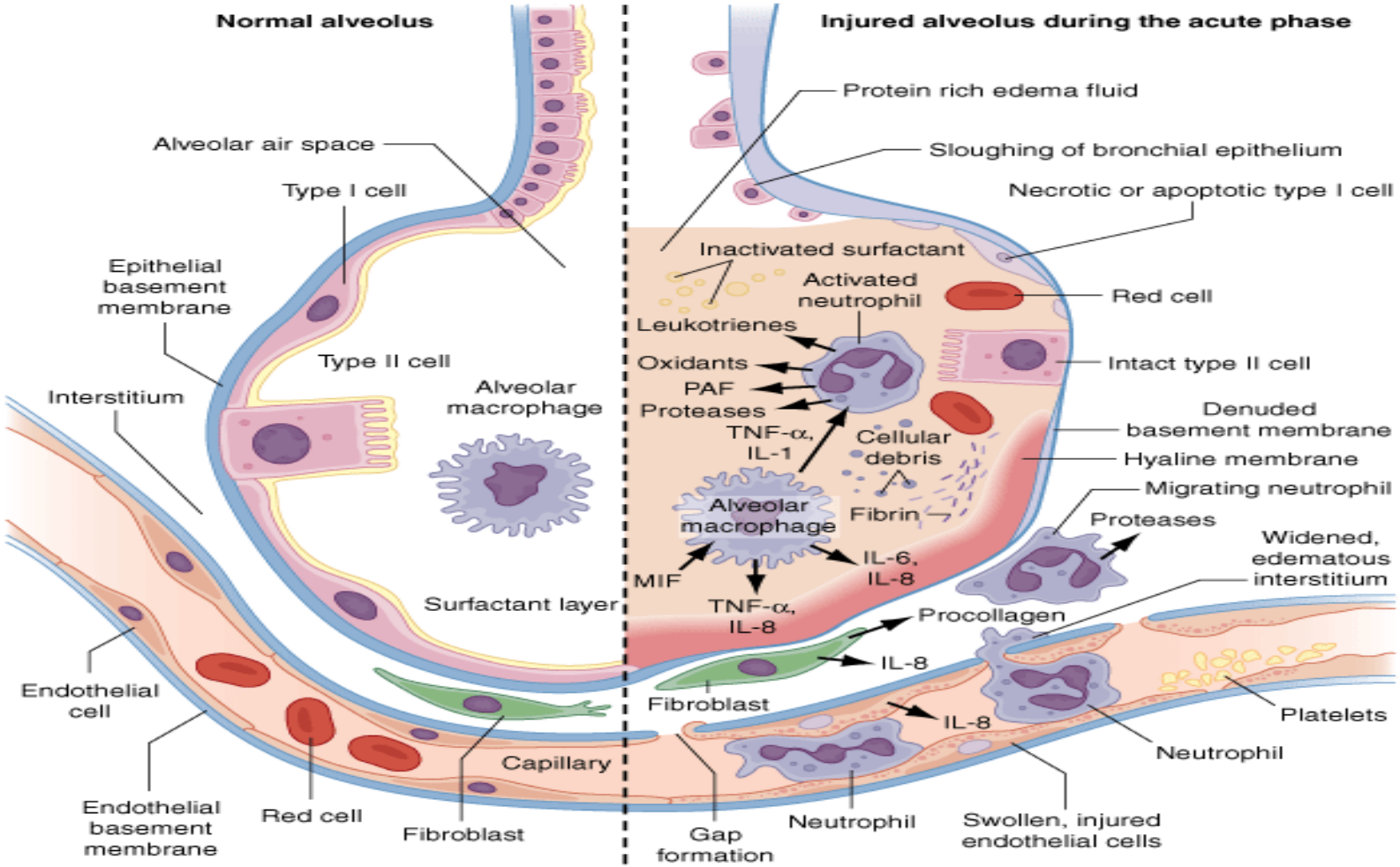
The natural history of ARDS is marked by three phases

1. Exudative,
2. Proliferative, and
3. Fibrotic

Each with characteristic clinical and pathologic features



Exudative phase



ENDOTYPES OR PHENOTYPES OF ARDS

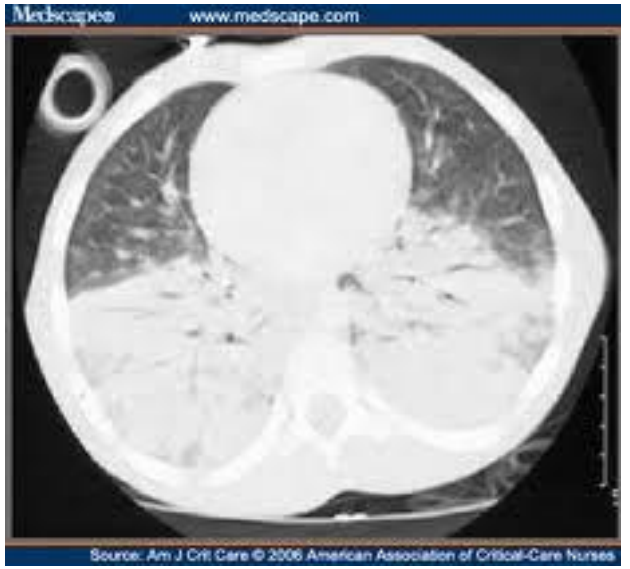
- Hyper inflammatory versus hypo inflammatory types
- Based on four biomarkers: interleukin-6, interferon gamma, angiopoietin 1/2, and plasminogen activator inhibitor-1
- Hyper inflammatory on day-0 :-
  - High PEEP improved outcomes
  - Liberal fluid management worsened mortality
  - Higher vasopressor use, lower serum bicarbonate
  - Higher prevalence of sepsis
  - Mortality, ventilator-free days, and organ failure-free days were all worse

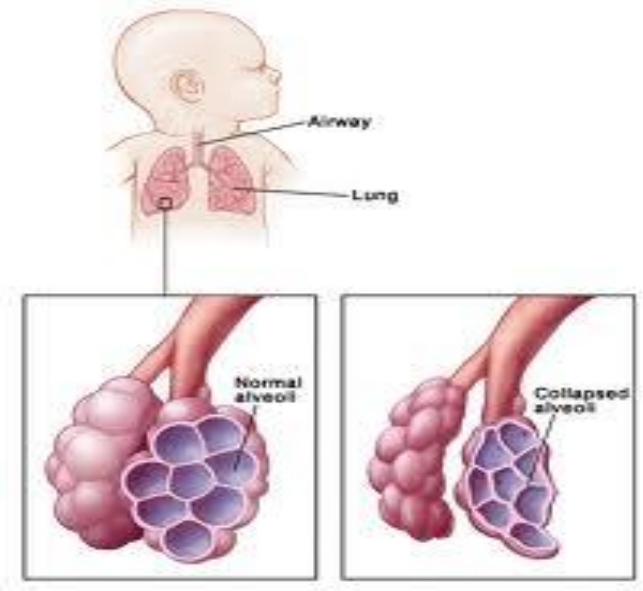
Conservative fluid management strategy was harmful in “hypo inflammatory” group

Thorax. 2018 May; 73(5):439-445.

Clinical impact of alveolar injury

- Plasma proteins with cellular debris and dysfunctional surfactant to ***form hyaline membrane whorls.***
- Alveolar edema in *dependent* portions, leading to ↓ aeration and atelectasis
- ↓ lung compliance in the dependent area.
- Consequently, intrapulmonary shunting and hypoxemia develop and ↑ work of breathing and dyspnea.



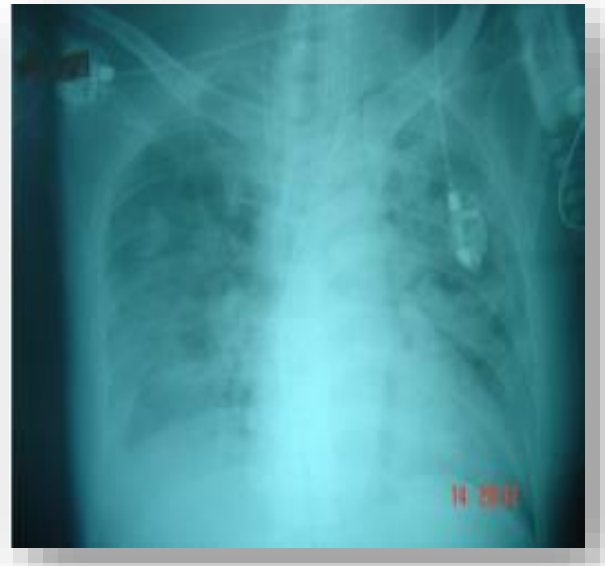


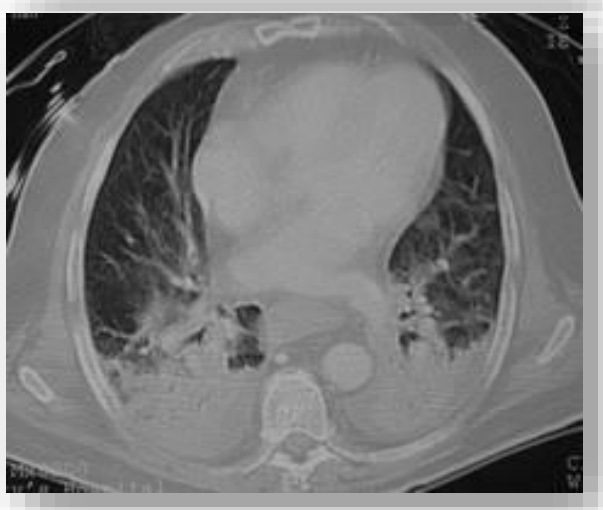
Investigations : Hints

- Generally nonspecific and primarily indicative of underlying clinical disorders.

- CXR - alveolar and interstitial opacities involving at least three-quarters of the lung fields

- CT scanning - in ARDS reveals extensive heterogeneity of lung involvement

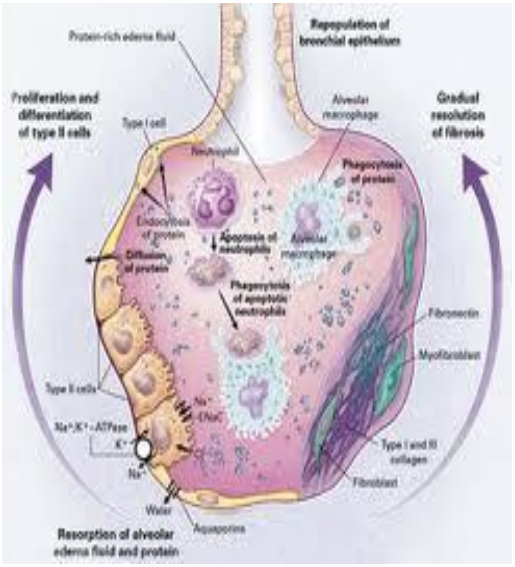




Proliferative Phase

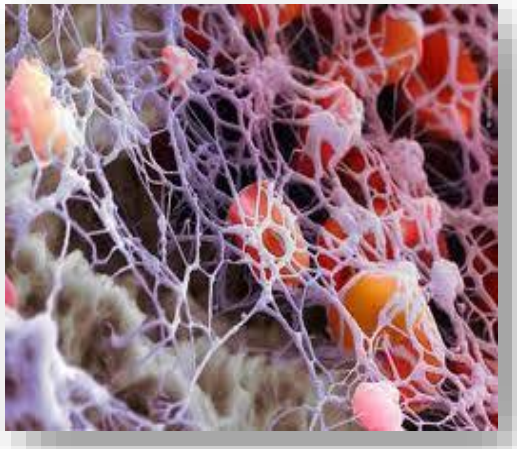
Usually lasts from day **7** to day **21**.

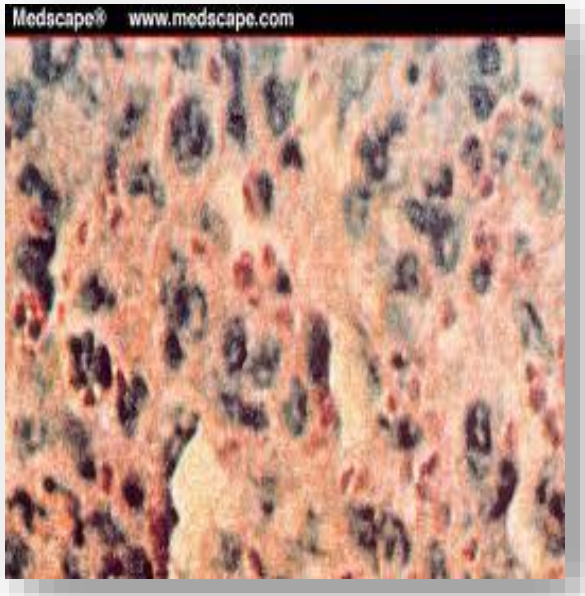
- Initiation of lung repair, organization of alveolar exudates, and a shift from a neutrophil → lymphocyte
- Type II pneumocytes synthesize new pulmonary surfactant and differentiate into type I pneumocytes
- Most recover rapidly and weaned off
- Some progress to fibrotic phase



Fibrotic Phase

- Seen after 3-4 weeks of the injury
- Histologically, there is extensive alveolar duct and interstitial fibrosis
- Require long-term support on MV and /or supplemental oxygen.
- Bad prognosis
- ↑Mortality.





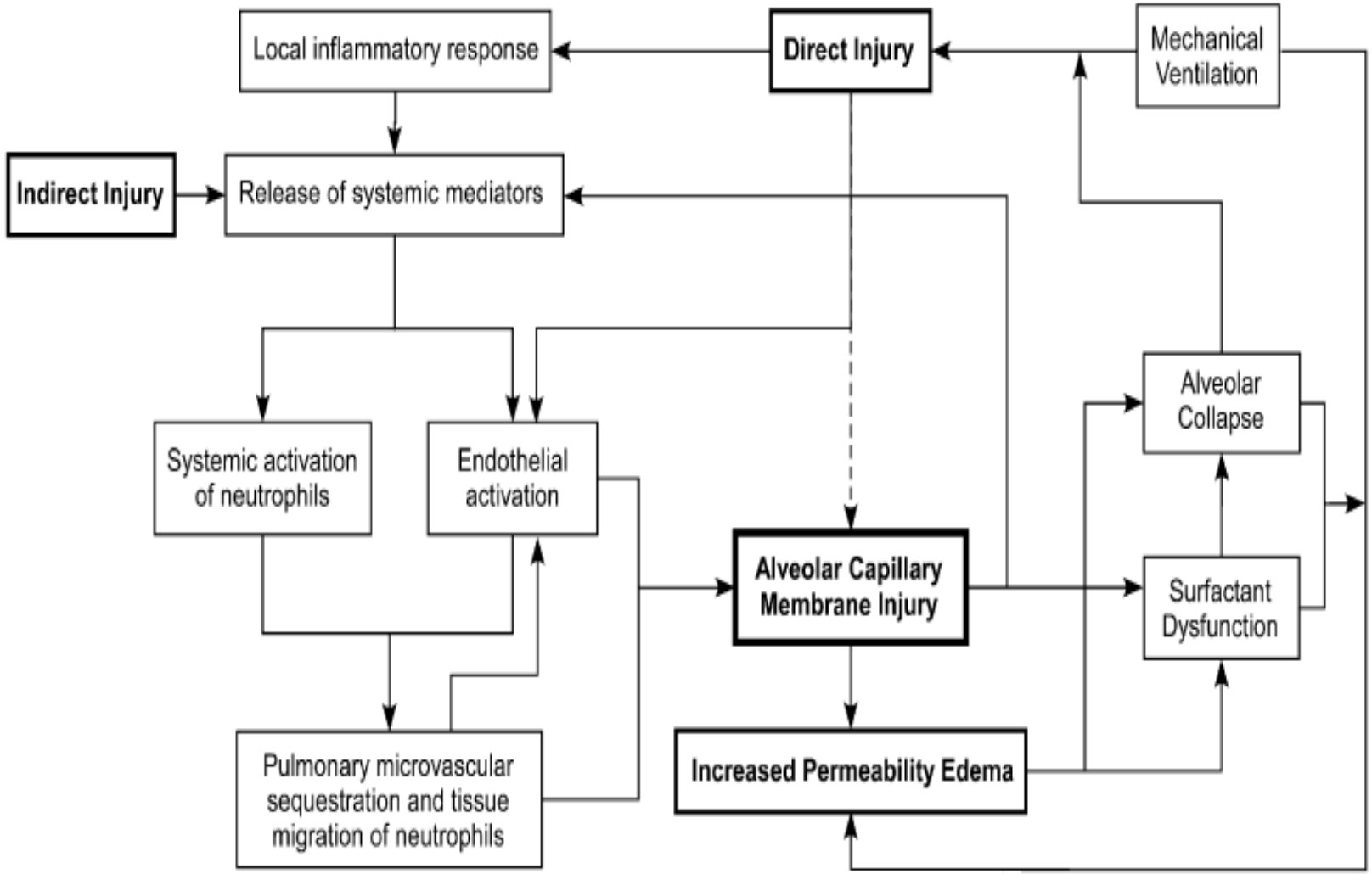
Bullae formation:

- Disrupted acinar architecture leading to emphysema-like changes
- Rupture leads to -Pneumothorax

Vascular occlusion:

- Intimal fibro - proliferation in the pulmonary microcirculation leads to pulmonary hypertension

Pathophysiology : Direct vs Indirect



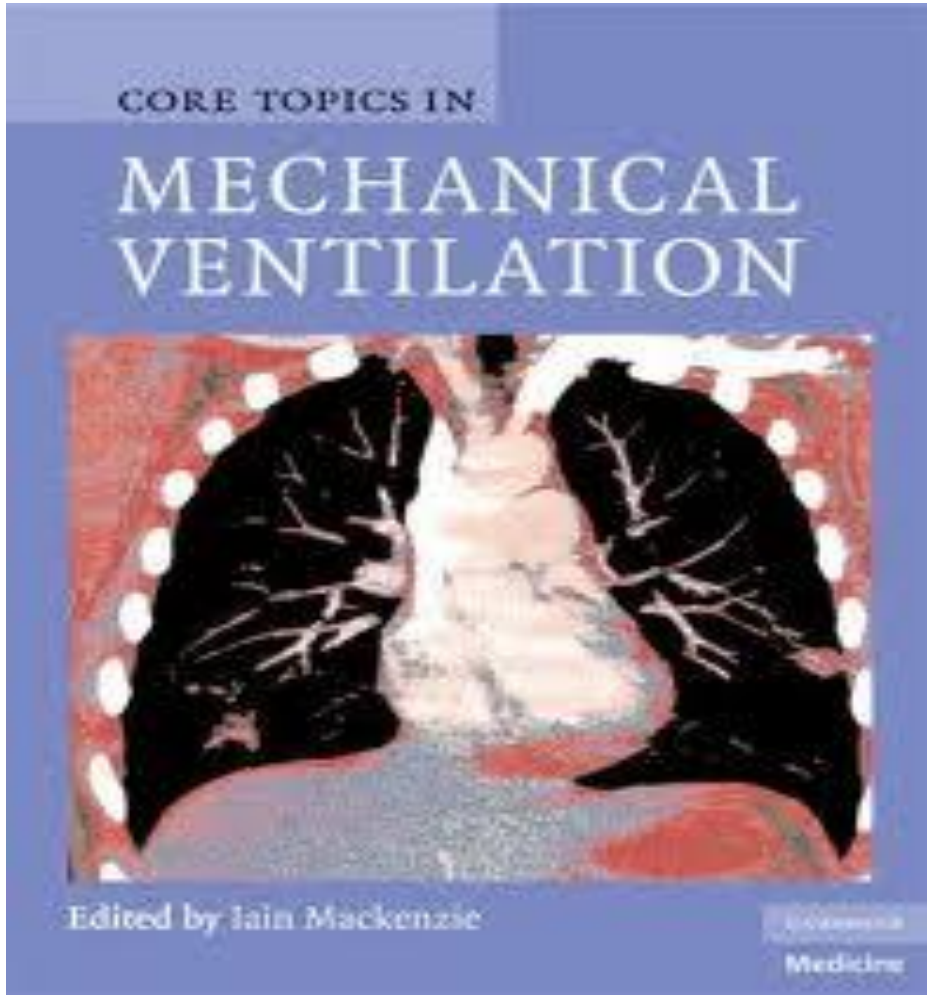
Management Strategies

- Identify and treat underlying causes
- Ventilatory support
  - Lung protective ventilatory support strategy
  - Application of PEEP
- Restore and maintain hemodynamic function
  - Conservative fluid replacement strategy
  - Vasopressors and inotropics support
- Prevent complications of critical illness
- Ensure adequate nutrition
- Avoid oversedation
- Using weaning protocol with spontaneous breathing trials

Ventilator -based Strategies in the Management of ARDS

- Only therapy that has been proven to be effective at reducing mortality is **a protective ventilatory strategy**

- ***Low volume ventilation***

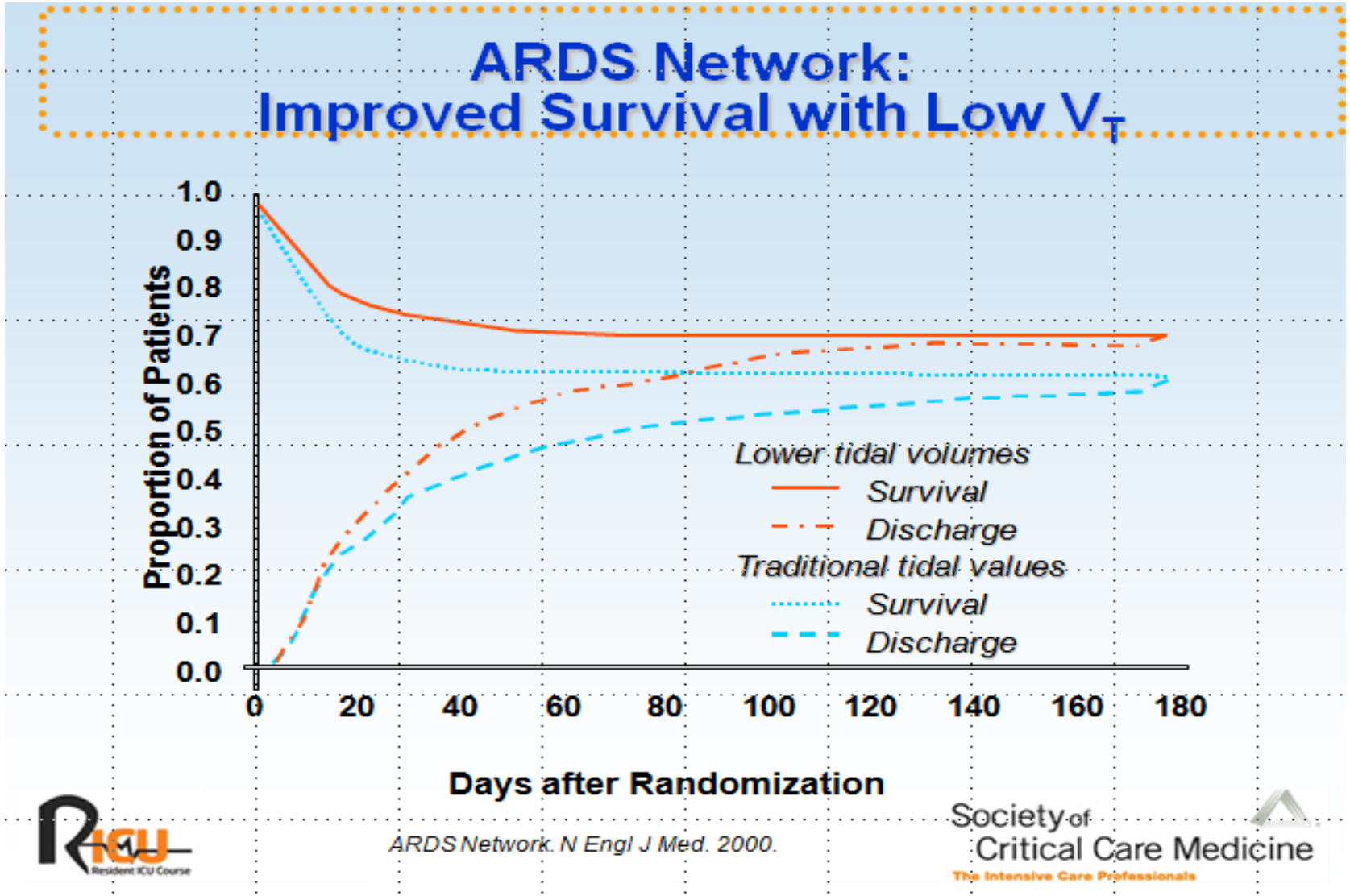


BABY LUNG CONCEPT

- CXR vs CT scan

- Uninvolved non dependent area is the functional portion of the lungs in ARDS.(***baby lungs)***

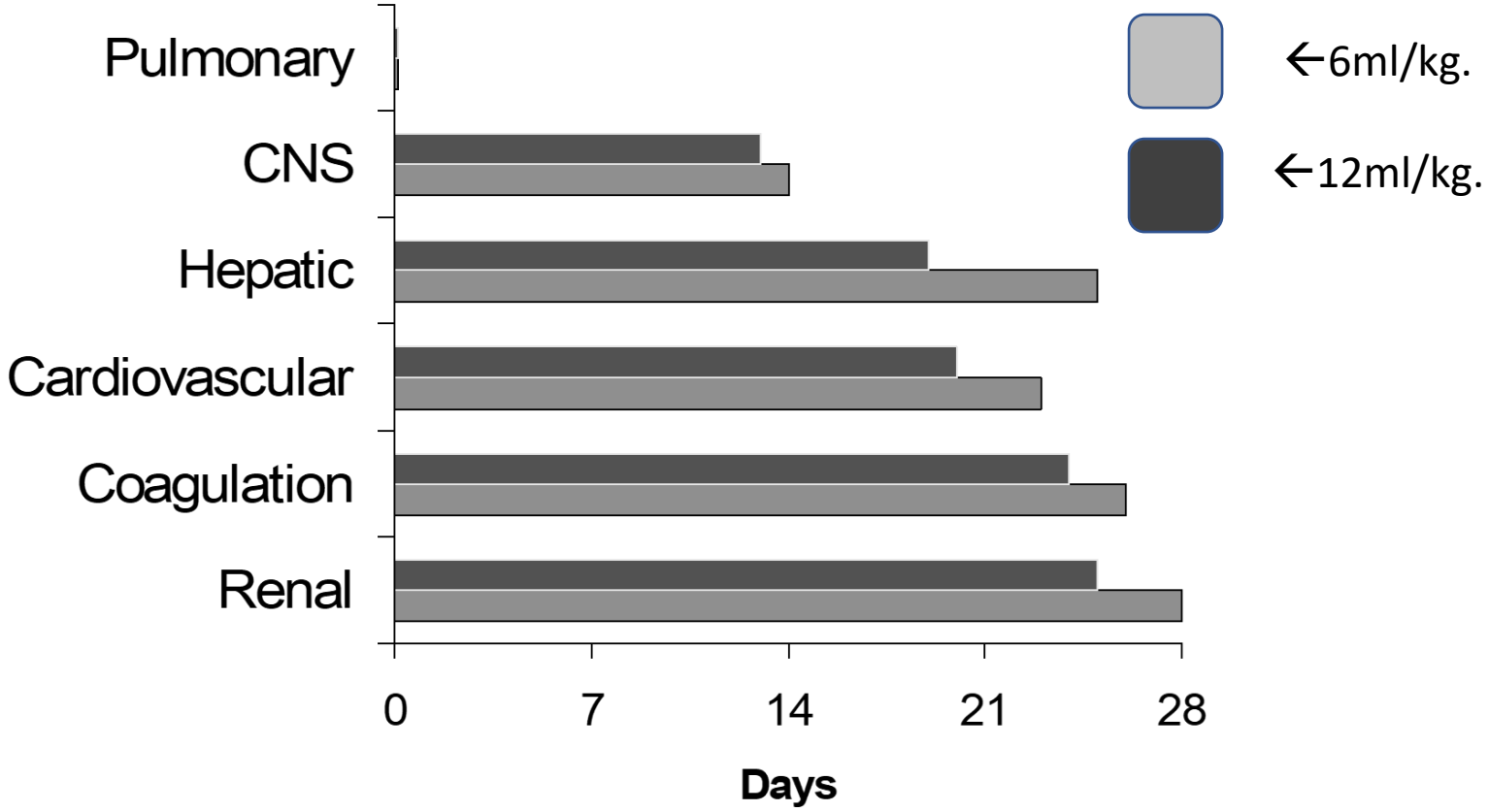
- The large inflation volumes cause overdistention and rupture of BABY LUNG→ ***Ventilator-induced lung injury.***


ARDS Network:
Improved Survival with Low V_T
Proportion of Patients
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
20
40
60
80
100
120
140
160
180
Days after Randomization
Lower tidal volumes
Survival
Discharge
Traditional tidal values
Survival
Discharge
ARDS Network. N Engl J Med. 2000.
Society of Critical Care Medicine
The Intensive Care Professionals

Low-Volume Ventilation-EVIDENCE

- 5 clinical trials compared MV with low TV (6 mL/kg) and conventional TV (12 mL/kg)
- The most successful was conducted by the ARDS Clinical Network –ARMA TRAIL
- Ventilation with low tidal volumes was associated with a ***9% (absolute) reduction*** in mortality when the end-inspiratory plateau pressure was <30 cm H2O.

Median Organ Failure Free Days



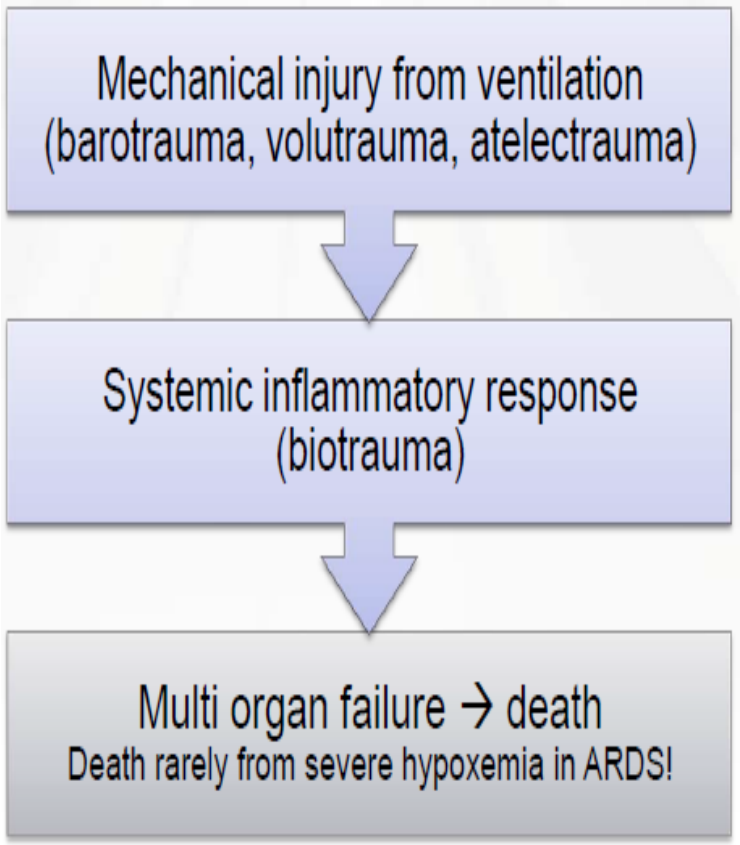
Ventilator-Induced Lung Injury

MECHANISM

- Excessive inflation volumes → stress fractures in the alveolar capillary interface → infiltration of inflammatory cells and proteinaceous material.

- VILI is strikingly similar to ARDS

- The organ injury from mechanical ventilation may not be confined to the lungs.



REVIEW Open Access

Close down the lungs and keep them resting to minimize ventilator-induced lung injury

Pelosi et al. Critical Care (2018) 22:72

Paolo Pelosi[1*], Patricia Rieken Macedo Rocco[2] and Marcelo Gama de Abreu[3]

‘permissive atelectasis’ to minimize VILI

- 1) a minimal PEEP to allow ‘permissive hypoxemia’ (SPO2> 88%) associated with
- 2) low VT or a VT able to ventilate only the aerated lung
- 3) the respiratory rate should be set to keep pH within physiologic ranges, or even to allow a certain degree of permissive hypercapnia.

Concept of driving pressure?

- Normalised target tidal volumes to predicted body weight (PBW), as per the ARDSNet ventilation strategy, does not take into account the varying proportion of lung that is not available for ventilation in ARDS (‘baby lung’ concept)

- The decrease in available lung for ventilation manifests as a decrease in respiratory system compliance (CRS)

- If two lungs are the same size, but the first lung has lower CRS, a delivered tidal volume calculated according to PBW will cause more mechanical stress in the first lung than the more compliant second lung

- Thus normalizing VT to CRS and using the ratio as an index to indicate the “functional” size of the lung may provide a better predictor of outcomes in patients with ARDS than VT alone

- This ratio is termed the driving pressure (ΔP = VT/CRS) and can be routinely calculated for patients who are not making inspiratory efforts as the plateau pressure minus positive end-expiratory pressure (ΔP = Pplat – PEEP)

The NEW ENGLAND JOURNAL of MEDICINE

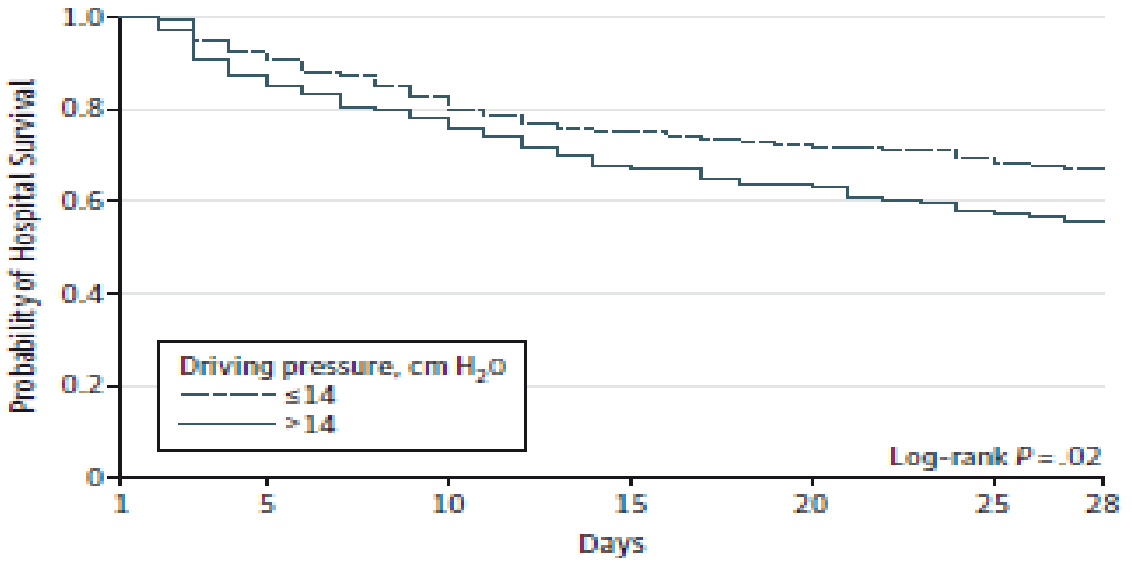
SPECIAL ARTICLE

Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slutsky, M.D.,

JAMA 2016, 315 : 788-800

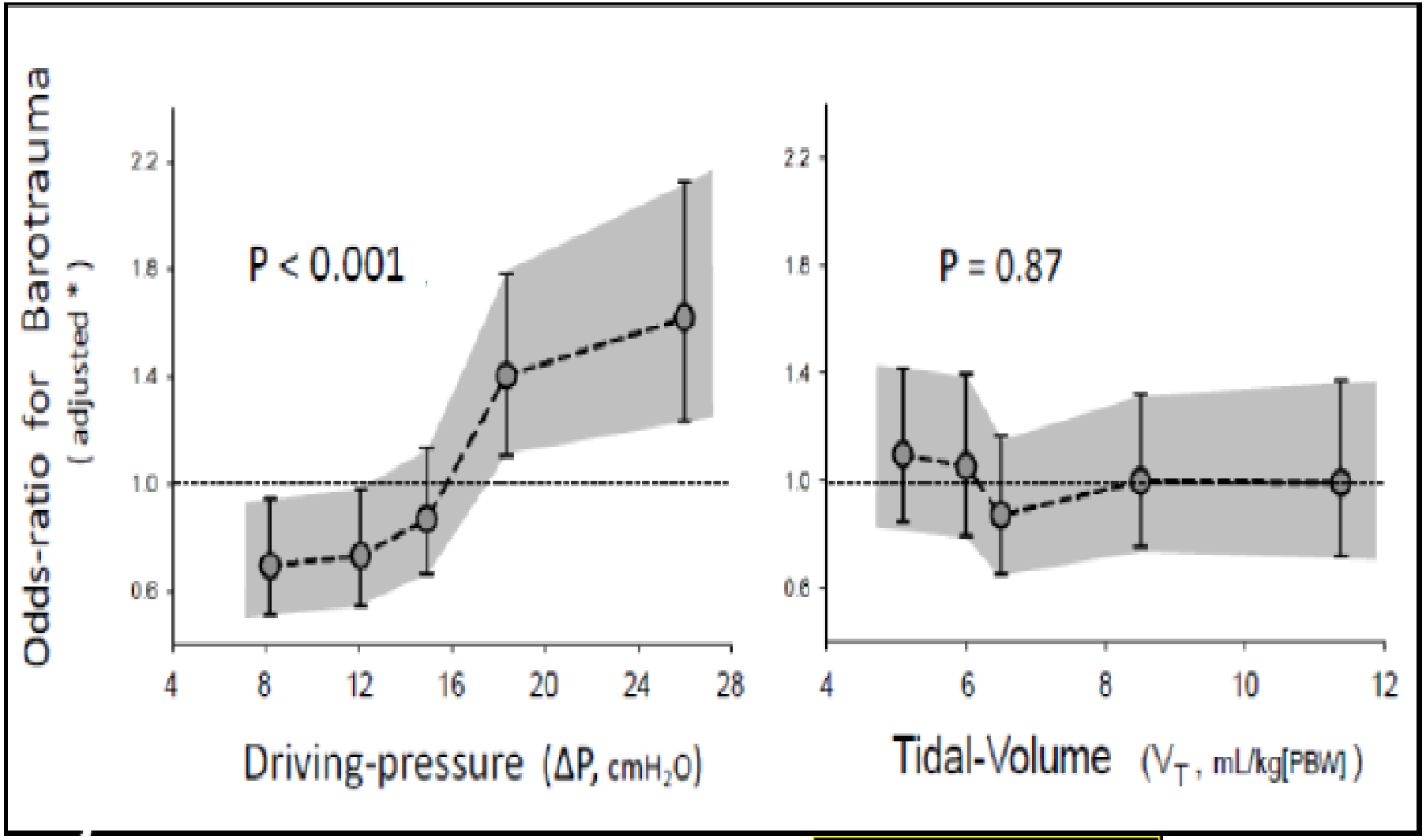
C Probability of hospital survival by driving pressure



No. at risk

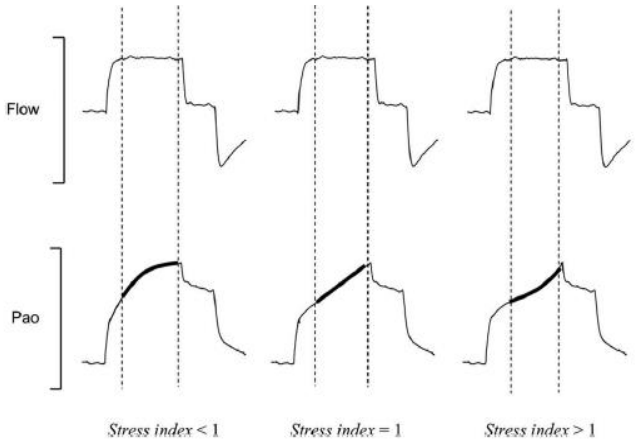
Driving pressure, cm H_2O							
≤14	370	342	306	277	266	254	245
>14	342	298	262	225	211	192	185

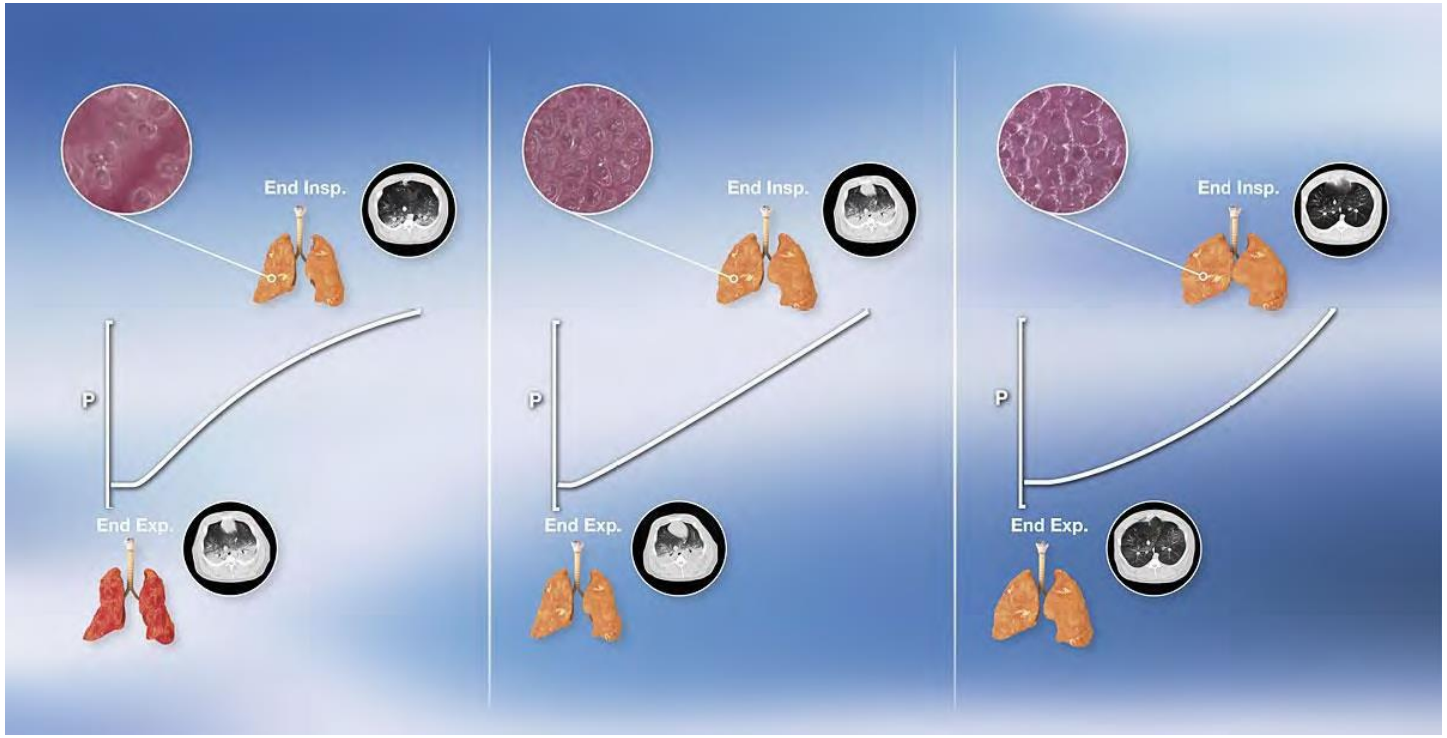
Driving Pressure, Not Tidal Volume Determines Barotrauma



Amato *et al* NEJM 2015

Stress index: one more





STRESS INDEX – WHAT'S THE EVIDENCE?

- Stress Index (SI) corresponds to CT evidence, SI=1 indicates tidal inflation only for normally aerated alveoli. Grasso S, CCM 2004

- ARDS patients normally show a small aerated region, which receives most of the tidal volume and is exposed to overdistension and stress due to alveolar wall tension Viera SR, AJRCCM 1999, Gattenoni L AJRCCM 1999

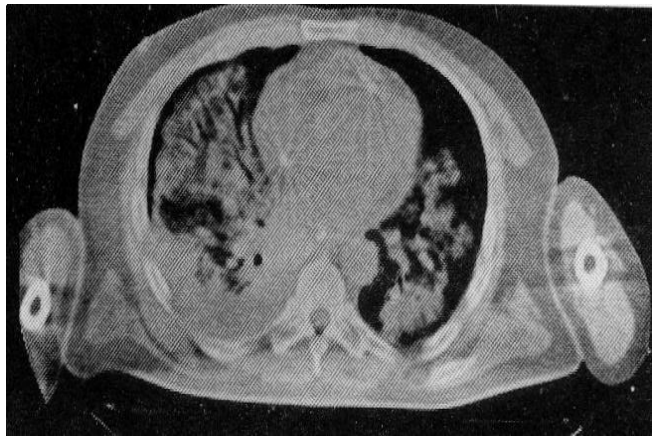
- Using the ARDSnet low tidal volume strategy in ARDS patients, 2/3 show no signs of hyperinflation while 1/3 show signs of hyperinflation. The latter group had higher pulmonary concentrations of inflammatory cytokines Terrangi PP, AJRCCM 2007

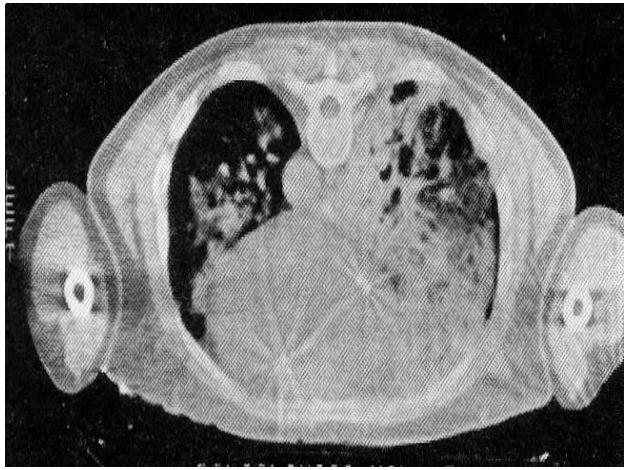
- By using ARDSnet for setting VT and titrating PEEP to a Stress Index level of 0.9-1.1, hyperinflation, dead space ventilation and inflammatory cytokines were reduced while improving hemodynamics Grasso S, AJRCCM 2005

Associated strategies : Position, NMBA

Prone position: Theoretical benefits

- Relieves the cardiac and abdominal compression
- Makes regional V/Q ratios and chest elastance more uniform
- Facilitates drainage of secretions
- Potentiates the beneficial effect of recruitment maneuvers





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prone Positioning in Severe Acute Respiratory Distress Syndrome

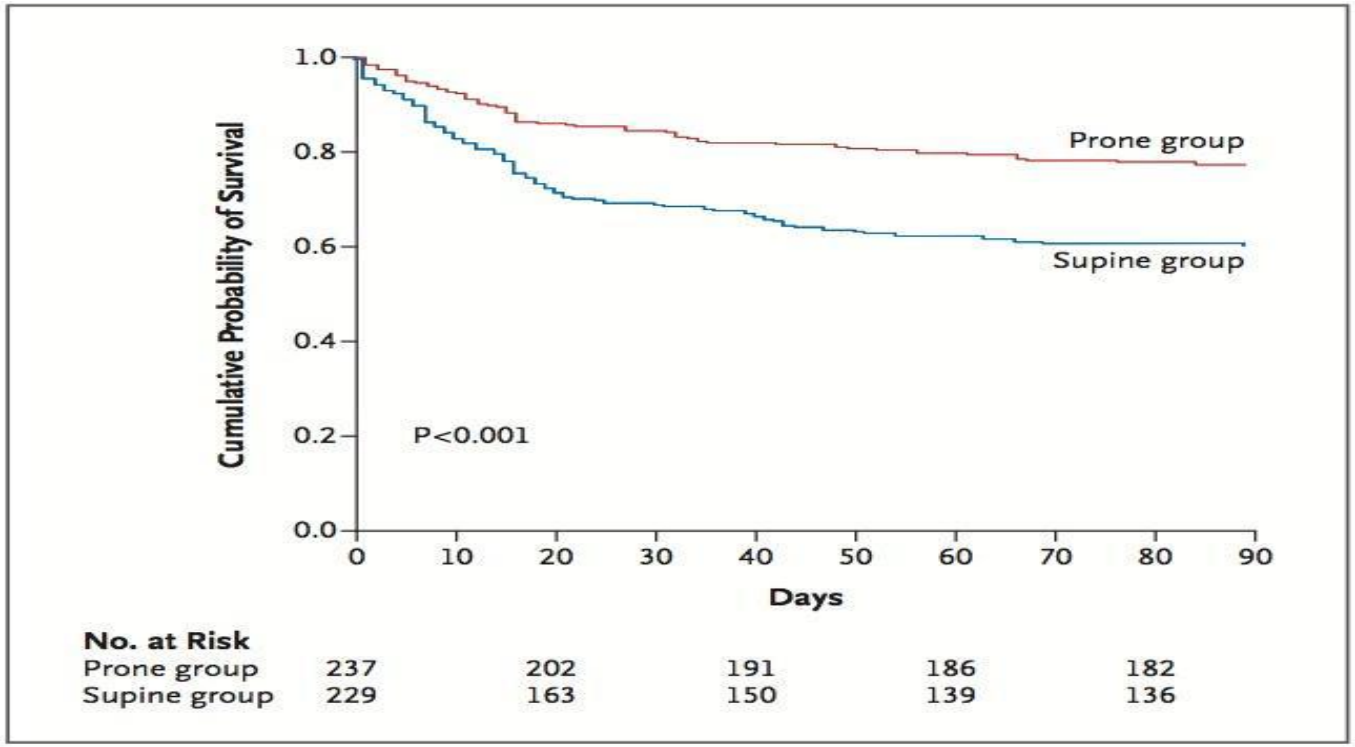
Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D.,

- Multicenter, prospective RCT
- 466 patients with severe ARDS
- Time from randomization to first PP session = 55 +/- 55 minutes
- Number of PP sessions per patient = 4 +/- 2
- PP session duration = 17 +/-3 hours

PROSEVA ClinicalTrials

N Engl J Med 2013.

	SP group (n=229)	PP group (n=237)	P value
No. deaths	75	38	
% death [95% CI]	32.8 [26.4-38.6]	16.0 [11.3-20.7]	0.0000256

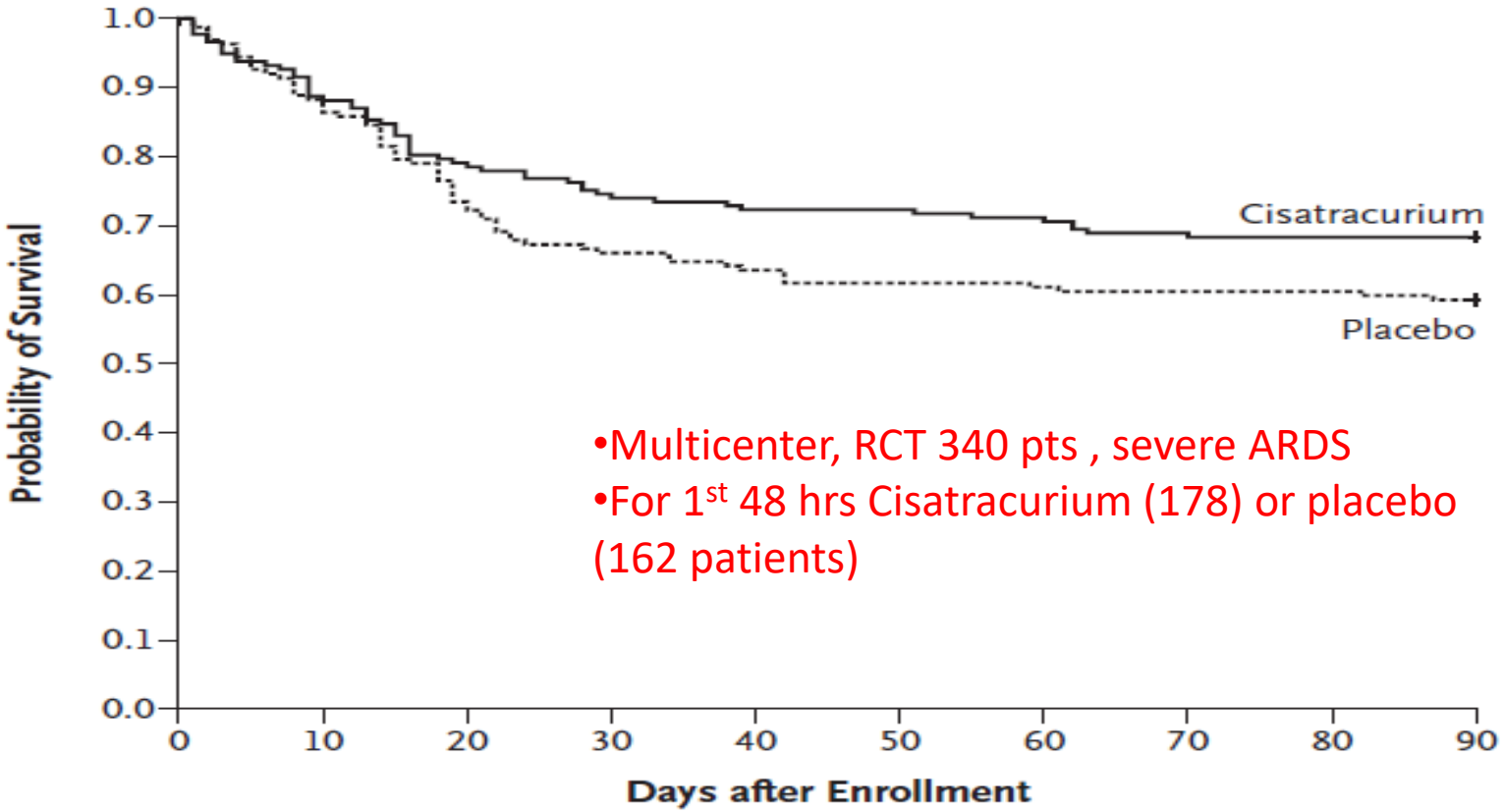


Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D.

N Engl J Med 2010;363:1107-16.

ACURASYS Study



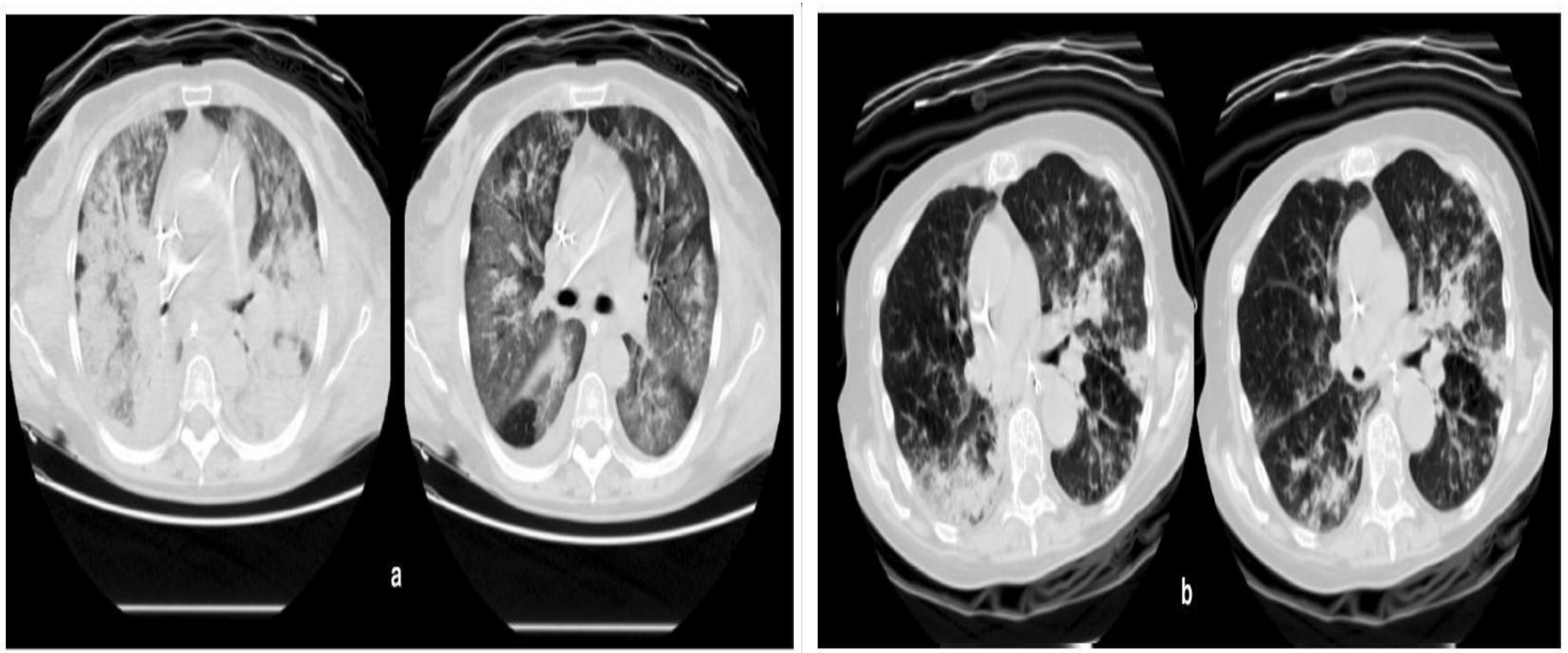
- Multicenter, RCT 340 pts , severe ARDS
- For 1st 48 hrs Cisatracurium (178) or placebo (162 patients)

Recruitment Maneuvers (RMs)

- Improving arterial oxygenation with short-lasting increases in intrathoracic pressures

  - CPAP up to 40 cm H_2O, maintained for 15 - 26 seconds
  - Intermittent sighs
  - Intermittent increase of PEEP
  - Increasing the ventilatory pressures to a plateau pressure of 50 cm H_2O for 1-2 minutes

Recruitment maneuvers to open the lungs and keep them open



Homogenous opacities with high potential for recruitment

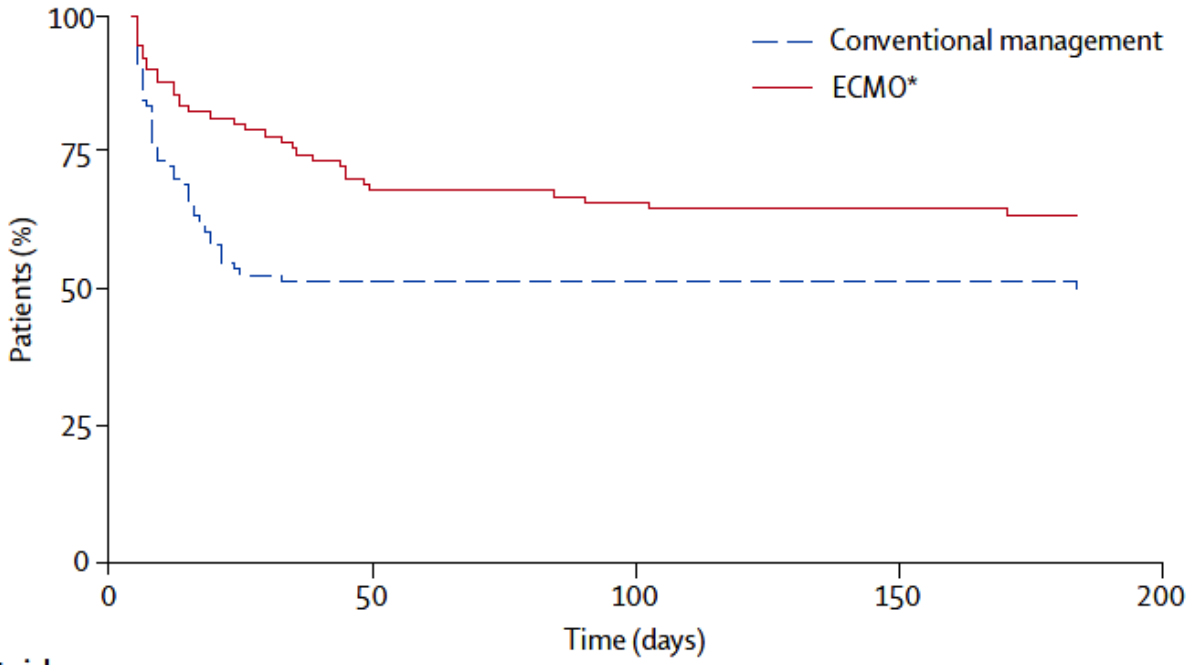
Heterogenous opacities with low potential for recruitment

Inverse ratio ventilation (IRV)

- Oxygenation can also be improved by increasing mean airway pressure with "inverse ratio ventilation."
- The inspiratory (*I*) time is lengthened so that it is longer than the expiratory (*E*) time (*I*:*E* > 1:1).
- With diminished time to exhale, dynamic hyperinflation leads to ↑ end-expiratory pressure, *similar to PEEP given by ventilator.*
- ↓ FI_{O2} to 0.60 to avoid possible oxygen toxicity,
- But no mortality benefit in ARDS has been demonstrated.

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Lancet 2009; 374: 1351–63



Patients at risk					
Conventional management	90	45	44	44	0
ECMO*	90	61	59	58	0

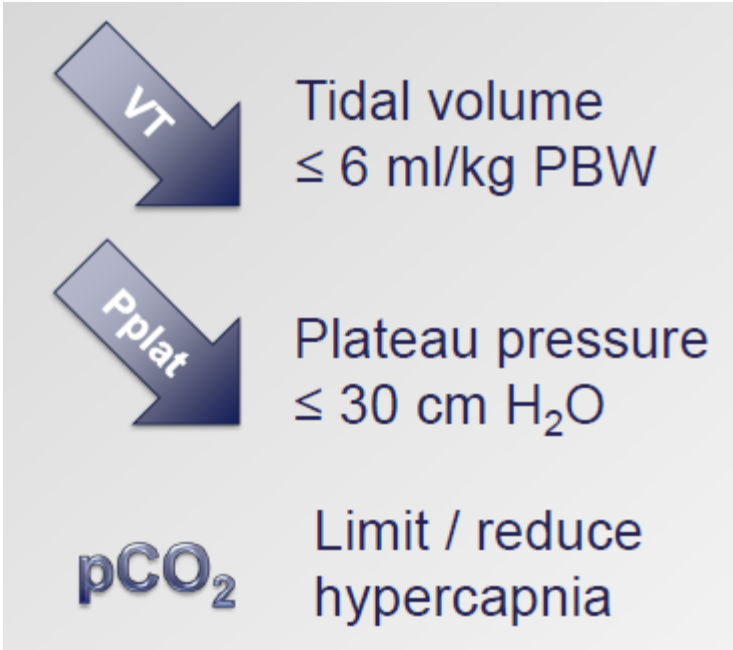
Transferring pts to ECMO centre significantly improve survival

Unwanted consequence: Permissive Hypercapnia

- Data show that PaCO2 levels of 60 to 70 mm Hg and arterial pH levels of 7.2 to 7.25 are safe for most patients
- Troublesome side effect brainstem hyper stimulation, which often requires neuromuscular blockade to asynchrony
- The risk of hypercapnic acidosis is determined by the benefit of maintaining low-volume ventilation to protect the lungs from volutrauma
- Contraindicated in pregnancy, ACS and raised ICP

ECCO2R in ARDS

ECMO	$ECCO_2R$
Indicated for treating refractory hypoxemia in the most severe cases of ARDS.	Indicated for facilitating lung protective ventilation in ALL stages of ARDS.



Evidence for $ECCO_2R$ in ARDS

Anesthesiology 2009; 111:826–35

Tidal Volume Lower than 6 ml/kg Enhances Lung Protection

Role of Extracorporeal Carbon Dioxide Removal

Pier Paolo Terragni, M.D., Lorenzo Del Sorbo, M.D.,* Luciana Mascia, M.D., Ph.D.,* Rosario Urbino, M.D.,* Erica L. Martin, Ph.D.,* Alberto Birocco, M.D.,† Chiara Faggiano, M.D.,† Michael Quintel, M.D.,‡ Luciano Gattinoni, M.D.,§ V. Marco Ranieri, M.D.‖*

Critical Care Vol 13 No 1 Zimmermann et al. 2009

Research

Pumpless extracorporeal interventional lung assist in patients with acute respiratory distress syndrome: a prospective pilot study

Open Access

Markus Zimmermann[1], Thomas Bein[1], Matthias Arlt[1], Alois Philipp[2], Leopold Rupprecht[2], Thomas Mueller[3], Matthias Lubnow[3], Bernhard M Graf[1] and Hans J Schlitt[4]

Intensive Care Med (2013) 39:847–856
DOI 10.1007/s00134-012-2797-6

ORIGINAL

Thomas Bein
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Matthias Lubnow
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Lower tidal volume strategy (≈ 3 ml/kg) combined with extracorporeal CO_2 removal versus 'conventional' protective ventilation (6 ml/kg) in severe ARDS

The prospective randomized Xtravent-study

SUPERNOVA: A Strategy of UltraProtective lung ventilation With Extracorporeal CO2 Removal for New-Onset moderate to seVere ARDS

ROLE OF NIV ?

- Delay in intubation-False hope
- No control over tidal volume
- High respiratory drive can generate high TV
- Pressure support may augment TV over 8-10ml/kg
    - Reducing PS to decrease TV will increase WOB
- Collapse of alveoli during expiration
- High PEEP may make patient prone to aspiration
- Negative pressure swings plus positive pressure support may allow transmural pressure to exceed 30 cmH2O

Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

JAMA. 2016 June 14; 315(22): 2435–2441.

NIV IN ARDS:REVISITED

- Total 83 patients involved
- Patients receiving helmet NIV had significantly lower rates of endotracheal intubation, more ventilator-free
- days, and a remarkably better mortality than patients with face mask ventilation
- face mask arm had a mortality of 56% at 90 days as compared to 35% in the helmet arm

Adaptive support ventilation for complete ventilatory support in acute respiratory distress syndrome: A pilot, randomized controlled trial

- Background:- A closed-loop mode, can minimize the work of breathing, and thus potentially improve the outcomes in ARDS.
- Forty-eight patients:- either ASV ($n = 23$) or VCV ($n = 25$) during the study period
- The mortality (VCV-36% vs ASV-34.7%), ease of use of mechanical ventilation, daily midazolam and vecuronium doses, and the number of ABGs performed were similar
- The duration ventilation, delta SOFA, ICU and hospital stay were comparable in the two groups.

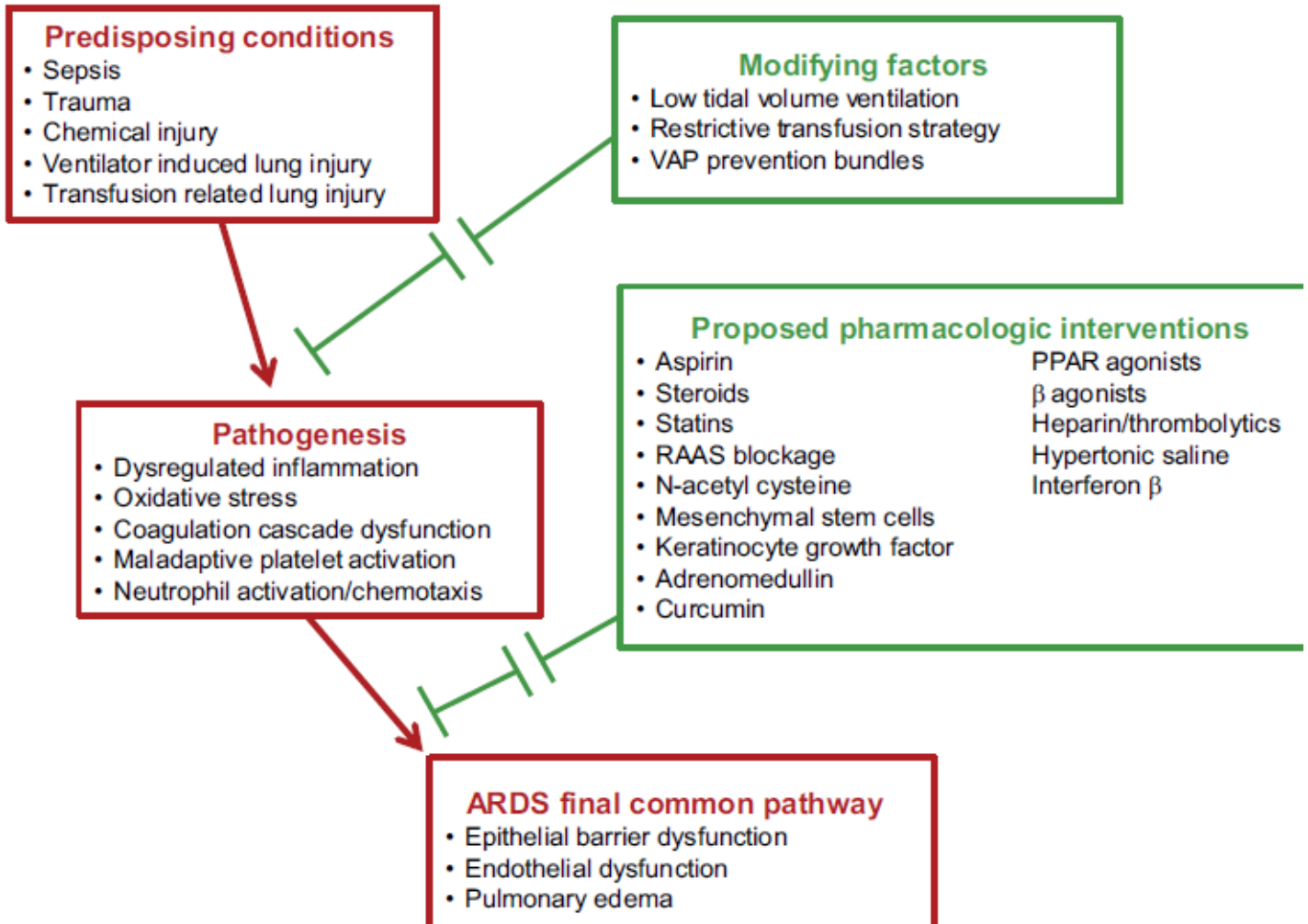
Respirology. 2013 Oct;18(7):1108-15

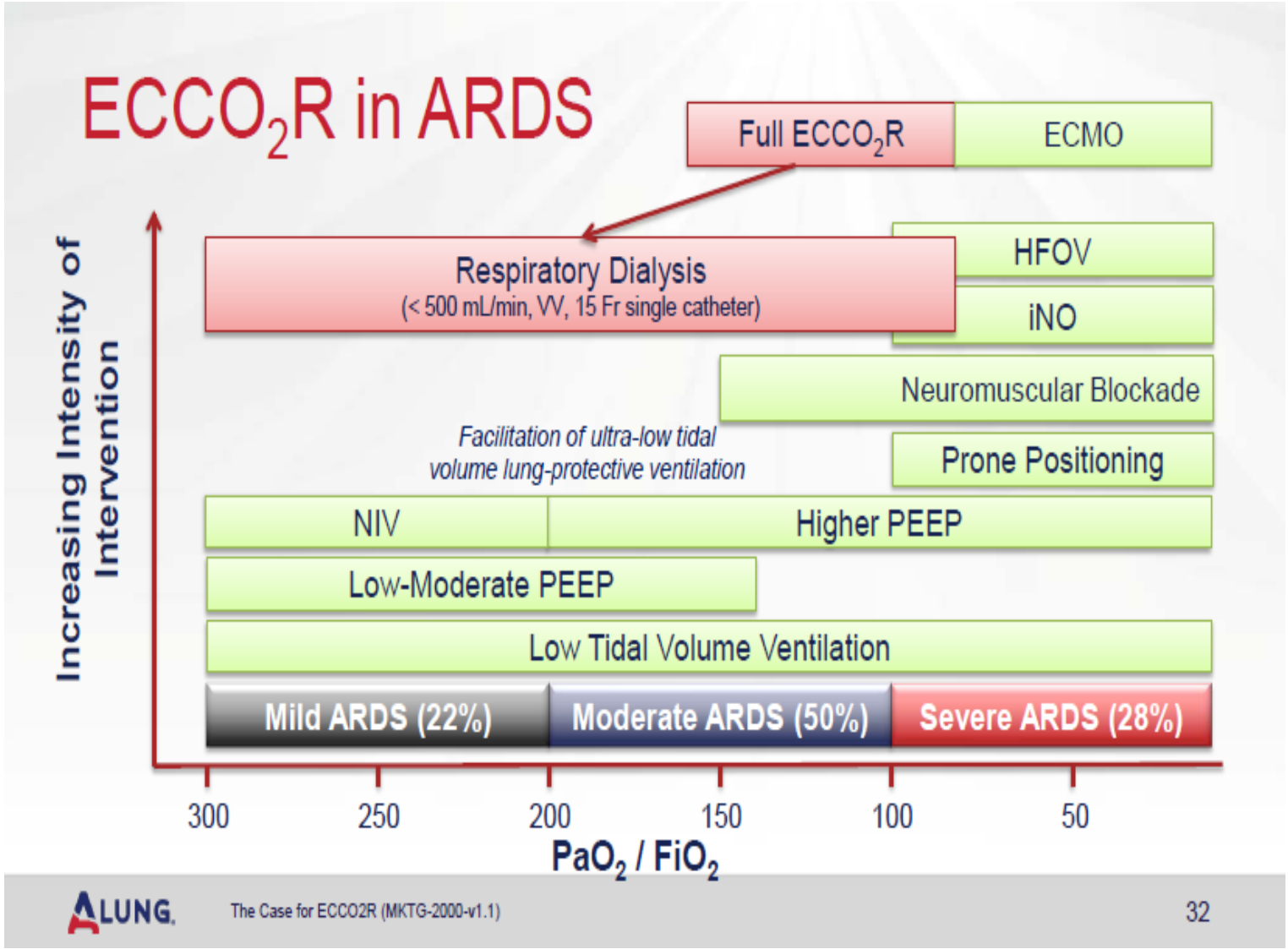
Emerging therapies for the prevention of acute respiratory distress syndrome

Ther Adv Respir Dis 2015, Vol. 9(4) 173–187

Carl A. Ruthman and Emir Festic

Interrupting the Progression to ARDS.




ECCO2R in ARDS
Full ECCO2R
ECMO
Respiratory Dialysis
(< 500 mL/min, VV, 15 Fr single catheter)
HFOV
iNO
Neuromuscular Blockade
Facilitation of ultra-low tidal volume lung-protective ventilation
Prone Positioning
NIV
Higher PEEP
Low-Moderate PEEP
Low Tidal Volume Ventilation
Mild ARDS (22%)
Moderate ARDS (50%)
Severe ARDS (28%)
Increasing Intensity of Intervention
300
250
200
150
100
50
PaO2 / FiO2
ALUNG.
The Case for ECCO2R (MKTG-2000-v1.1)
32

MV: A necessary evil in ARDS

"If correctly performed, mechanical ventilation "buys time" to allow other therapies to take effect; if performed incorrectly, it may kill the patient."

Dr. Luciano Gattinoni
CMAJ 2008;178:1174-1176

THANK YOU