

Acute respiratory distress syndrome and acute lung injury

Acute respiratory distress syndrome

- In 1967, Ashbaugh et al coined the term adult respiratory distress syndrome.
- Other names—
 - Acute respiratory distress syndrome
 - Adult hyaline membrane disease
 - Shock lung
 - Stiff lung syndrome
 - Non-cardiogenic pulmonary edema
 - Ventilator-associated lung injury
 - Traumatic wet lung
 - Transfusion wet lung
 - Post perfusion lung (Transplant lung: reperfusion pulmonary edema)

Acute respiratory distress syndrome

- It is a state of acute, diffuse alveolar damage characterised by increased capillary permeability, pulmonary edema and refractory hypoxemia.
- It is characterized by
 - acute onset of severe hypoxemia
 - signs of respiratory distress (dyspnoea, tachypnoea)
 - diffuse bilateral infiltrates in the CXR
 - no evidence of left atrial hypertension (PAWP < 18 mm Hg).



Incidence

- ARDS accounts for 10-15% of all ICU admissions
- ARDS mortality in trauma patients is 10-15% and in medical ICU patients is 60%.

The 1994 North American-European Consensus Conference (NAECC) criteria:

- **Onset** - Acute and persistent.
- **Radiographic criteria** - Bilateral pulmonary infiltrates consistent with the presence of edema.
- **Oxygenation criteria** - Impaired oxygenation with
 $P_{aO_2}/F_{iO_2} \leq 300$ mmHg (40 kPa) for ALI
 $P_{aO_2}/F_{iO_2} \leq 200$ mmHg (27 kPa) for ARDS.
- **Exclusion criteria** - Clinical evidence of left atrial hypertension or a pulmonary-artery wedge pressure of ≥ 18 mm Hg.

NAECC Limitations

- Solely on clinical criteria
- **Descriptive definition** - Permits inclusion of a multiplicity of clinical entities ranging from autoimmune disorders to direct and indirect pulmonary injury
- Does not address the cause of lung injury
- Does not provide guidelines on how to define acute
- The radiological criteria are not sufficiently specific
- Does not account for the level of PEEP used, which affects the Pao₂/Fio₂ ratio
- Does not specify the presence of extrapulmonary organ system dysfunction at the time of diagnosis
- Does not include the different specific mechanistic pathways involved in producing lung injury.

The 1998 NAEECC: Updated Recommendations

- The severity of ALI/ARDS should be assessed by the Lung Injury Score (LIS) or by the APACHE III or SAPS II scoring systems.
- The factors that affect prognosis should be taken into account. The most important of these are incorporated into the GOCA (Gas exchange, Organ failure, Cause, Associated disease) stratification system.
- It will be also useful to record aetiology, mortality, cause of death and follow-up information on the recovery and quality of life.

Stratification System of Acute Lung Injury-GOCA(Gas exchange, Organ failure, Cause, Associated disease)

Letter	Meaning	Scale	Definition
G	Gas exchange	0	$P_{aO_2}/F_{iO_2} \geq 301$
		1	$P_{aO_2}/F_{iO_2} 200 -300$
		2	$P_{aO_2}/F_{iO_2} 101 - 200$
		3	$P_{aO_2}/F_{iO_2} \leq 100$
	Gas exchange (to be combined with the numeric descriptor)	A	Spontaneous breathing, no PEEP
		B	Assisted breathing, PEEP 0-5 cmH ₂ O
		C	Assisted breathing, PEEP 6-10 cmH ₂ O
		D	Assisted breathing, PEEP ≥ 10 cmH ₂ O
O	Organ failure	A	Lung only
		B	Lung + 1 organ
		C	Lung + 2 organs
		D	Lung + ≥ 3 organs
C	Cause	1	Unknown
		2	Direct lung injury
		3	Indirect lung injury
A	Associated diseases	0	No coexisting disease that will cause death within 5 yr
		1	Coexisting disease that will cause death within 5 yr but not within 6 mo
		2	Coexisting disease that will cause death within 6 mo



Lung injury score

Four components:

1. Chest radiograph
2. PEEP score
3. Hypoxemia score
4. Respiratory system compliance score

Lung injury score

Chest radiograph	
No alveolar consolidation	0
Alveolar consolidation confined to 1 quadrant	1
Alveolar consolidation confined to 2 quadrant	2
Alveolar consolidation confined to 3 quadrant	3
Alveolar consolidation confined to 4 quadrant	4

Hypoxemia score	
Pao ₂ /Fio ₂ > 300	0
Pao ₂ /Fio ₂ -225-299	1
Pao ₂ /Fio ₂ -175-224	2
Pao ₂ /Fio ₂ -100-174	3
Pao ₂ /Fio ₂ <100	4

PEEP score	
<5cm H ₂ O	0
6-8cm H ₂ O	1
9-11cm H ₂ O	2
12-14cmH ₂ O	3
>15cm H ₂ O	4

Respiratory system compliance score	
>80 ml/cmH ₂ O	0
60-79ml/cmH ₂ O	1
40-59ml/cmH ₂ O	2
20-39ml/cmH ₂ O	3
<19cm/mlH ₂ O	4

- The score is the sum calculated by adding the sum of each component and dividing by the number of components used.

	Score
No lung injury	0
Mild to moderate	0.1-2.5
Severe lung injury	>2.5

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The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material

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The Berlin definition of ARDS

- Three mutually exclusive categories of mild, moderate and severe ARDS were created for the better separation of prognosis and better treatment selection.

Acute respiratory distress syndrome			
Timing	Within 1 week of a known clinical insult or new/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 (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present		
	Mild	Moderate	Severe
Oxygenation ^b	200 < PaO ₂ /FiO ₂ ≤ 300 with PEEP or CPAP ≥5 cmH ₂ O ^c	100 < PaO ₂ /FiO ₂ ≤ 200 with PEEP ≥5 cmH ₂ O	PaO ₂ /FiO ₂ ≤100 with PEEP ≥5 cmH ₂ O

ARDS acute respiratory distress syndrome; PaO₂, partial pressure of oxygen; FiO₂, fraction of inspired oxygen; PEEP, positive end-expiratory pressure; CPAP, continuous positive airway pressure.

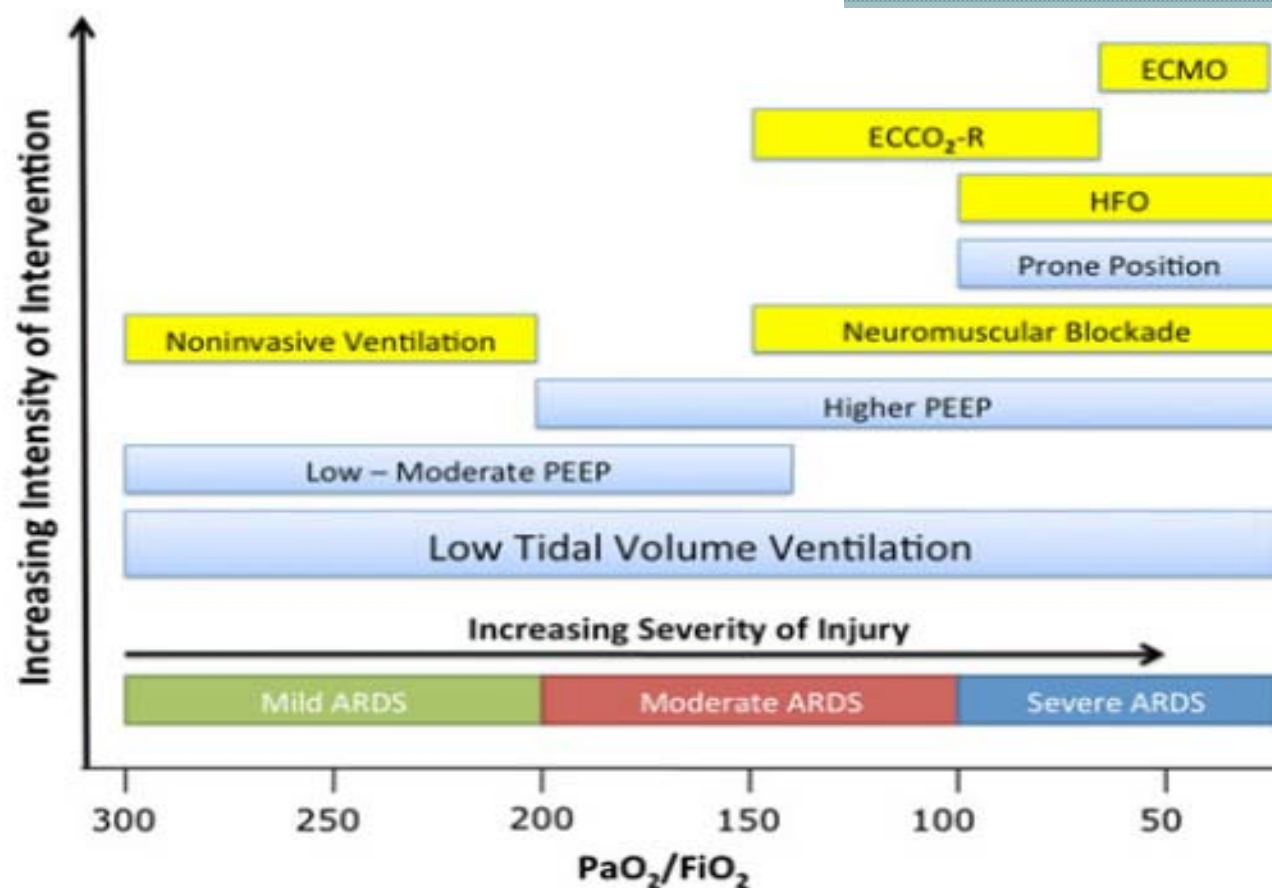


Fig. 1 Aligning Therapeutic Options with The Berlin Definition (adapted from [48] with permission). This figure depicts potential therapeutic options according to the severity of ARDS. Boxes in yellow represent therapies that in the opinion of the panel still require confirmation in prospective clinical trials. This figure is just a model based on currently available information. In the coming years, various aspects of the figure will likely change; proposed cut-offs may move, and some therapies may be found to not be useful, while others may be added



DIRECT LUNG INJURY

Common causes

- Pneumonia
- Aspiration of gastric contents

Less common causes

- Pulmonary contusion
- Fat emboli
- Near-drowning
- Inhalational injury
- Reperfusion pulmonary edema after lung transplantation or pulmonary embolectomy

INDIRECT LUNG INJURY

Common causes

- Sepsis
- Severe trauma with shock and multiple transfusions

Less common causes

- Cardiopulmonary bypass
 - Drug overdose
 - Acute pancreatitis
 - Transfusions of blood products
-



Risk factors predictive of increased mortality in ALI/ARDS

- Advanced age
- Comorbid diseases
- Sepsis
- Liver dysfunction/ cirrhosis
- Non-pulmonary organ dysfunction
- Organ transplantation
- HIV infection
- Active malignancy
- Chronic alcoholism
- Mechanism of lung injury



Pathophysiology

3 phases –

1. Exudative/ Inflammatory
2. Proliferative
3. Fibrotic

1. Exudative Phase

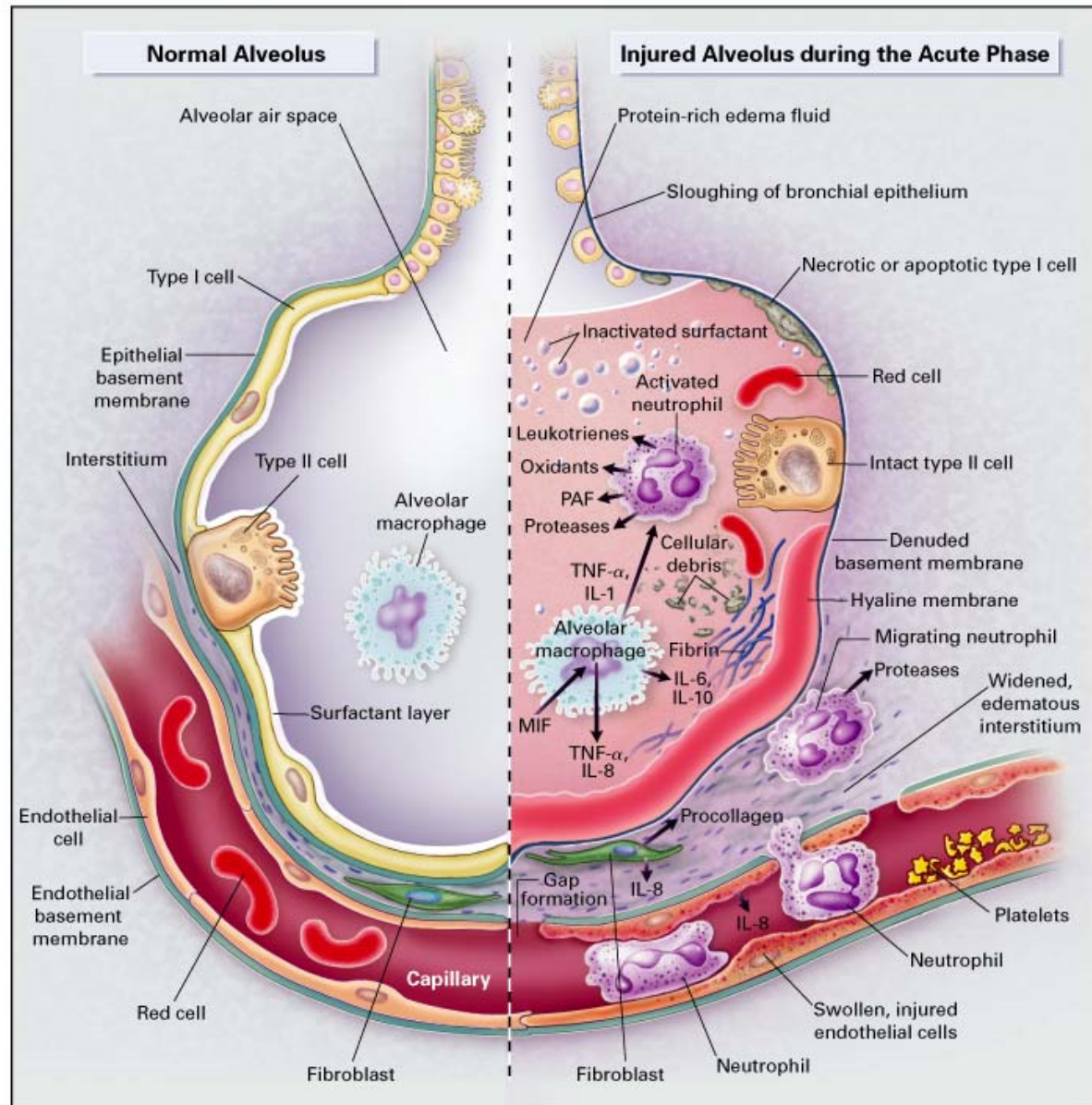
Alveolar macrophages release pro-inflammatory cytokines (TNF- α , IL-1, IL-6, IL-8)

Attract neutrophils to the lungs

Release reactive oxygen species and proteolytic enzymes (e.g., neutrophil elastase)

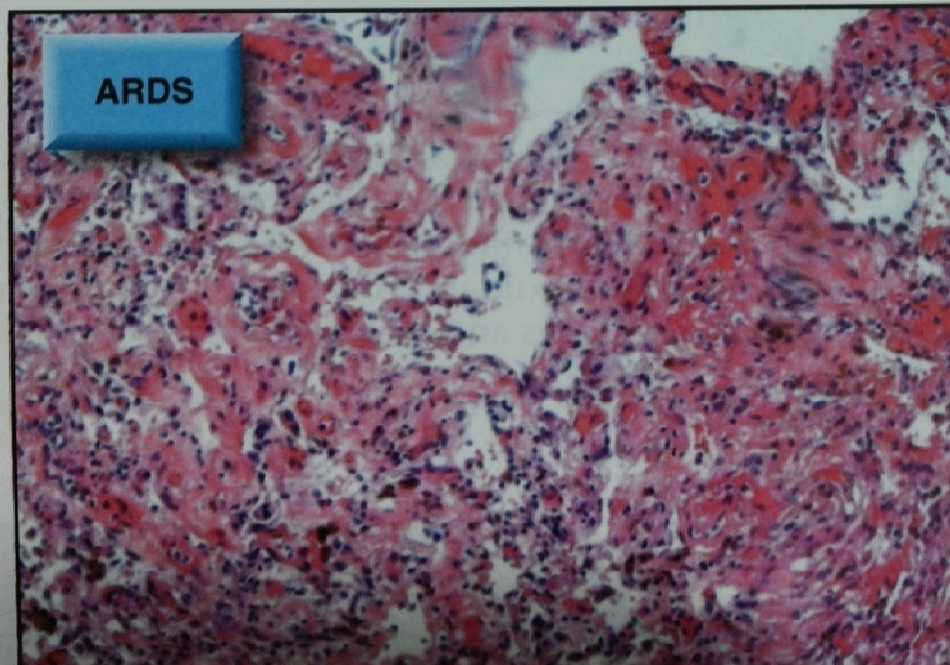
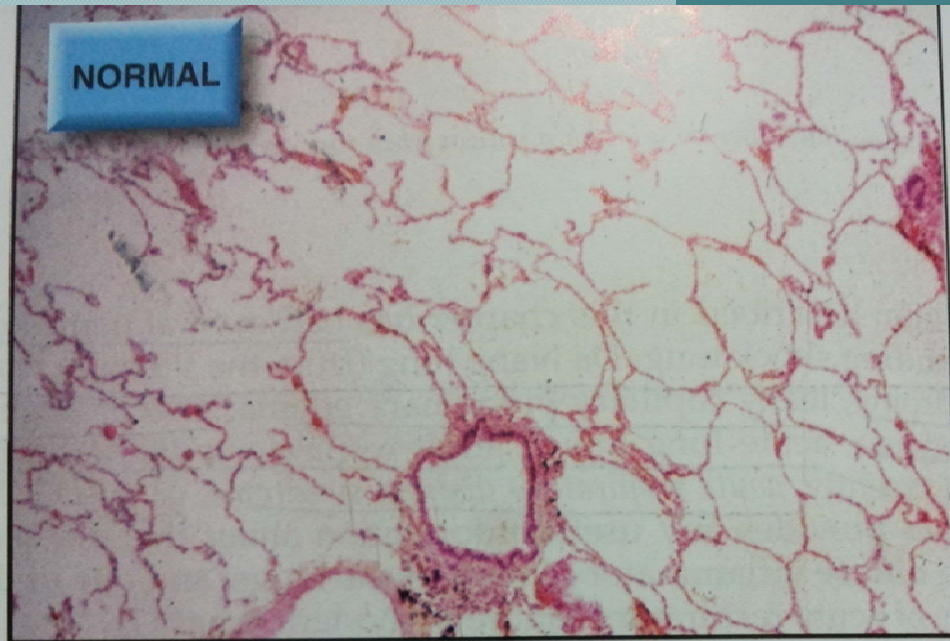
Damage of the alveolar epithelium and the endothelium

Proteinaceous edema fluid filling alveolar space



Exudative phase

- Commences within 24 hours of injury
- Lasts 1-7 days
- Diffuse alveolar damage and microvascular injury
- Hyaline membrane formation
- Decreased surfactant production
- Basement membrane disruption
 - Type I pneumocytes destroyed
 - Type II pneumocytes preserved
- Surfactant deficiency
 - inhibited by fibrin
 - decreased type II production
- Atelectasis/alveolar collapse



2. Proliferative phase

- 7-14 days
- Proliferation of inflammatory cells and fibroblasts → Obliteration of airspaces, atelectatic alveoli & poorly compliant lung leads to
 - persistent hypoxemia
 - development of hypercarbia
 - fibrosing alveolitis
 - pulmonary hypertension



3. Fibrotic phase

- >14 days
- Extensive fibroblast proliferation
- Deposition of collagen and proteoglycans
- Involvement of the pulmonary vasculature from edema - intractable pulmonary hypertension



Physiological changes in the lungs

- Ventilation-perfusion mismatch
- Intrapulmonary shunting
- Decreases lung compliance (stiff lung)
- Life threatening hypoxia
- Increased work of breathing
- Ventilatory failure with hypercapnia



Clinical features

- Dyspnoea/ laboured breathing- COMMONEST
- Tachypnoea/ hyperventilation
- Tachycardia
- Hypotension and peripheral vasoconstriction with cold extremities
- Cyanosis
- Scattered crackles
- Agitation
- Lethargy
- Obtundation

Management

3 cornerstones:

1. Recognizing patients with acute lung injury and ruling out other causes of acute hypoxemia
2. Identifying and treating the underlying disease
3. Mechanical ventilation to secure oxygenation and ventilation whilst protecting the lung from ventilation-induced lung injury

Approach to clinical diagnosis

1. Chest x ray

- **Early stages**- interstitial edema
- **Established cases**- full blown pulmonary edema
- Not reliable : “**normal**” for a period of time (hours - days) following the precipitating event [e.g. sepsis]
- Progression to diffuse, bilateral alveolar infiltrates within 4 - 24 hours after the first abnormal radiographic signs appear
- **Diagnostic confusion:** cardiac failure, pneumonia, pulmonary embolism

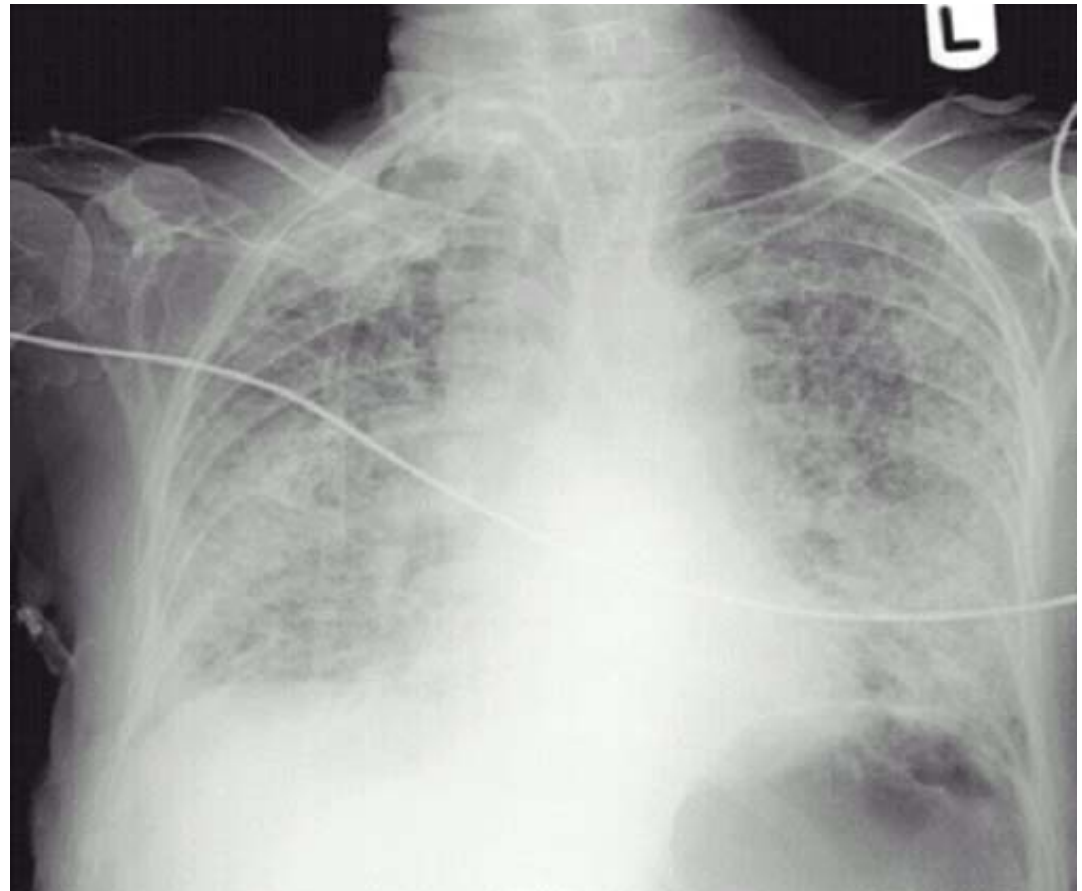
TABLE 3–2.—Radiographic Criteria Differentiating Acute Respiratory Distress Syndrome (Noncardiogenic Edema) From Cardiogenic Edema*

Criteria	ARDS	Cardiogenic Edema
Major		
Cardiomegaly	Unusual	Present
Kerley's lines	Unusual	Present
Large pleural effusions	Unusual	Present
Opacities	Patchy/peripheral*	Diffuse
Minor		
Air bronchograms	Often present	Rare
Hilar haze	Infrequent	Present
Peribronchial cuffing	Unusual	Present

*Adapted from Putman CE: Cardiac and noncardiac edema: Radiologic approach, in Goodman LR, Putman CE (eds): *Critical Care Imaging*. Philadelphia, WB Saunders, 1992, pp 107–136.

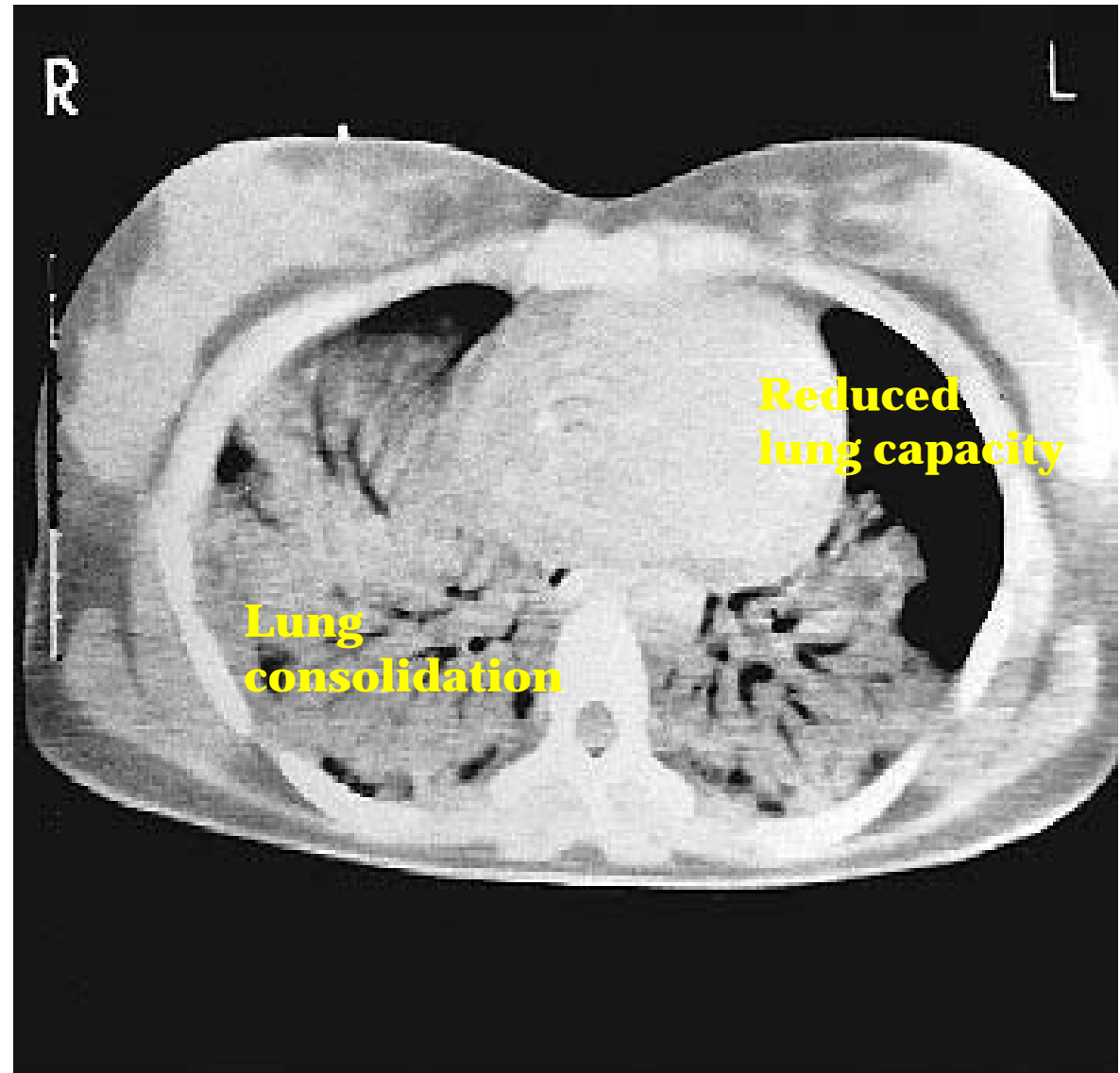
- ***Homogenous infiltrates & absence of pleural effusion – more characteristic of ARDS***

- As alveolar filling continues-**Ground glass appearance** or ***white-out*** of all lung fields
- CXR's are influenced by the effects of therapy-
 - *IV Fluids can increase alveolar content*
 - *Diuretic agents may decrease total content*
 - *PEEP increases lung inflation thereby reducing regional lung density*



2. CT Scan

- On CT imaging, the lung consolidation is confined to the posterior lung regions, which are dependent regions in supine position.
- The uninvolved lung in the anterior portion represents the functional portion of the lung.



3. **Laboratory studies** –

- ✓ ABG-
 - Initial stages- hypoxemia with hypocapnia, respiratory alkalosis
 - Later stages- hypoxia, hypercapnia, respiratory and metabolic acidosis
- ✓ Leukocytosis/Leucopenia/anemia are common
- ✓ Renal function / liver function abnormalities
- ✓ Von willebrand's factor or complement in serum may be high
- ✓ Acute phase reactants like ceruloplasmin or cytokine (TNF,IL-1,IL-6,IL-8) may be high.

4. **Echocardiography** – method to detect cardiac causes of respiratory failure

5. **Invasive hemodynamic monitoring** –

- Insertion of a Swan Ganz catheter- not essential
- Pulmonary edema with pulmonary wedge pressure <18 mm Hg in presence of normal colloid oncotic pressure

6. **Pulmonary compliance-**

- <30ml/ cm H₂O
- Easily measured in mechanically ventilated patients

7. **Full bacteriological screen** –

- Blood , urine and tracheal aspirate cultures
- Culture of other body secretions and discharges
- Culture of bronchoalveolar lavage fluid.

8. **Bronchoalveolar Lavage** –

- **Very reliable & underutilized**
- In normal subjects, less than 5% of cells are neutrophils. In patients with ARDS, upto 80% cells are neutrophils.
- Lavage fluid is rich in protein in patients of ARDS as the inflammatory exudates are rich in protein.
Hydrostatic edema: Lavage protein/ Plasma protein < 0.5
ARDS : Lavage protein/ Plasma protein > 0.7
- **Presence of a marker of pulmonary fibrosis called procollagen peptide III (PCPIII) correlates with mortality.**

Ventilatory management in ARDS

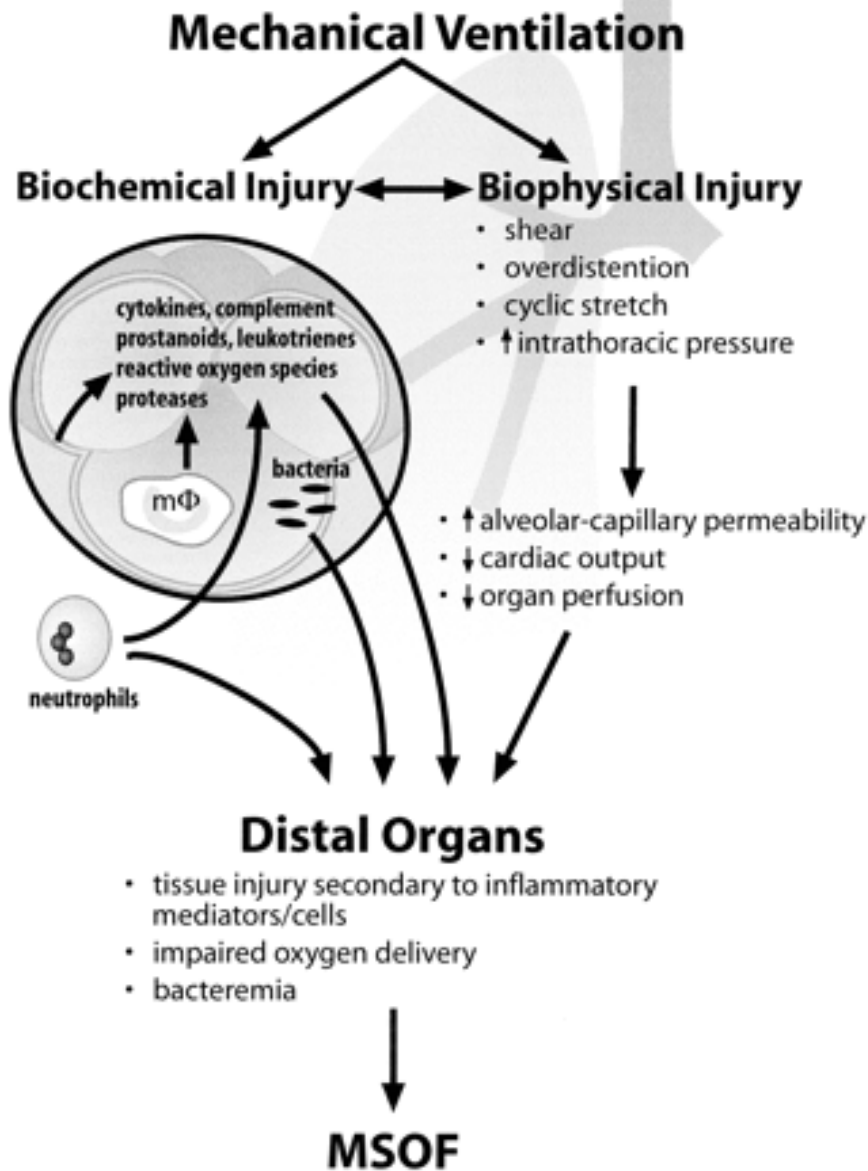
- In the early stages of ARDS, the hypoxia may be corrected by 40 to 60% inspired oxygen with CPAP.
- If the patient is well oxygenated on $\leq 60\%$ inspired oxygen and apparently stable, then close ward monitoring, continuous oximetry and regular blood gas estimation is required.

Indications of ventilatory support

- ✓ Inadequate Oxygenation($\text{PaO}_2 < 60\text{mm Hg}$ on $\text{FiO}_2 \geq 0.6$)
- ✓ Rising or elevated PaCO_2 ($\geq 45\text{ mmHg}$)
- ✓ Clinical signs of incipient respiratory failure

Conventional mechanical ventilation

- Tidal volumes are 12-15ml/kg
- In ARDS, the functional portion of the lungs is greatly reduced
- High inflation volumes results in overdistension and rupture of the distal airspaces.
- **Ventilator associated lung injury:**
 - High inflation pressure - Barotrauma
 - Over distension - Volutrauma
 - Repetitive opening & closing of alveoli - Atelectrauma
 - SIRS & cytokines release - Biotrauma.



• **Mechanical ventilation can be a source of multi-organ failure.**

• The lung with ALI or ARDS are particularly prone to ventilator associated lung injury:

- Collapsed, consolidated, less compliant areas (Dependant)
- Functional areas (non dependant) are reduced.

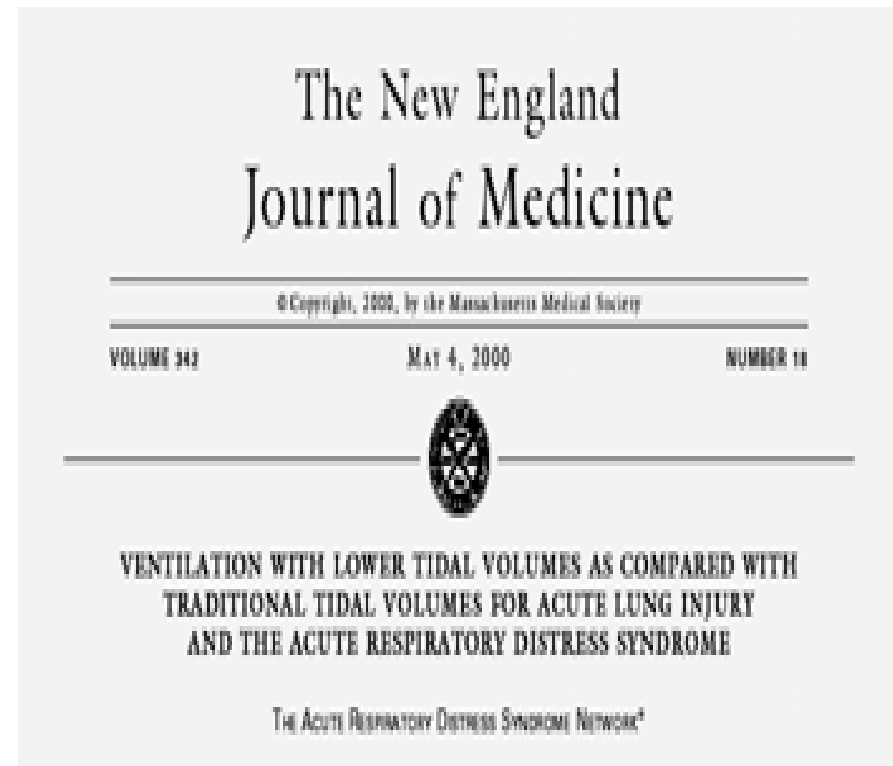
Lung protective ventilation

- Tidal volumes – 6ml/kg
- Limits risk of volutrauma and biotrauma
- Uses positive end expiratory pressure to limit the risk of atelectrauma.
- Currently, the only therapy that has been proven to be effective at reducing mortality in ALI/ARDS in a large, randomized, multi-center, controlled trial is a protective ventilatory strategy.

Tidal Volume Strategies in ARDS

ARDS conducted trials-

- Low tidal volume ventilation 6ml/kg predicted body wt., limited end inspiratory pressure (pplat) 30cm H₂O in one group and 12ml/kg tidal volume in the other group.
- Results suggested-decreased mortality from **40% to 31%**





NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

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 $V^T = 6$ ml/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

Oxygenation goal: (PaO₂ 55-80 mmHg or SpO₂ 88-95%)

- Use a minimum PEEP of 5 cm H₂O. Consider use of incremental FiO₂/PEEP combinations-

Lower PEEP/higher FiO₂

FiO₂	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

FiO₂	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO₂

FiO₂	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

FiO₂	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

Plateau pressure goal:

$\leq 30 \text{ cm H}_2\text{O}$

- Check P_{plat} (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V^T
- If **P_{plat} > 30 cm H₂O**: decrease V^T by 1ml/kg steps (minimum = 4 ml/kg)
- If **P_{plat} < 25 cm H₂O and V^T < 6 ml/kg**, increase V^T by 1 ml/kg until P_{plat} > 25 cm H₂O or V^T = 6 ml/kg
- If **P_{plat} < 30 and breath stacking or dys-synchrony occurs**: may increase V^T in 1ml/kg increments to 7 or 8 ml/kg if P_{plat} remains < 30 cm H₂O

pH Goal: 7.30-7.45

Acidosis Management:

- If **pH 7.15-7.30**: Increase RR until pH > 7.30 or paCO₂ < 25 (Maximum set RR = 35).
- If **pH < 7.15**: Increase RR to 35.
- If **pH remains < 7.15**, V^T may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).
- NAHCO₃ infusion

Alkalosis Management: Decrease ventilation rate if possible.

I: E RATIO GOAL: duration of inspiration must be less than the duration of expiration (1:1 to 1:3; no inverse ratio).

Weaning

A. Conduct a **spontaneous breathing trial** daily when:

1. $\text{FiO}_2 \leq 0.40$ and $\text{PEEP} \leq 8$
2. PEEP and $\text{FiO}_2 \leq$ values of previous day
3. Patient has acceptable spontaneous breathing efforts.
(May decrease ventilation rate by 50% for 5 minutes to detect effort.)
4. Systolic BP ≥ 90 mmHg without vasopressor support.
5. No neuromuscular blocking agents or blockade.

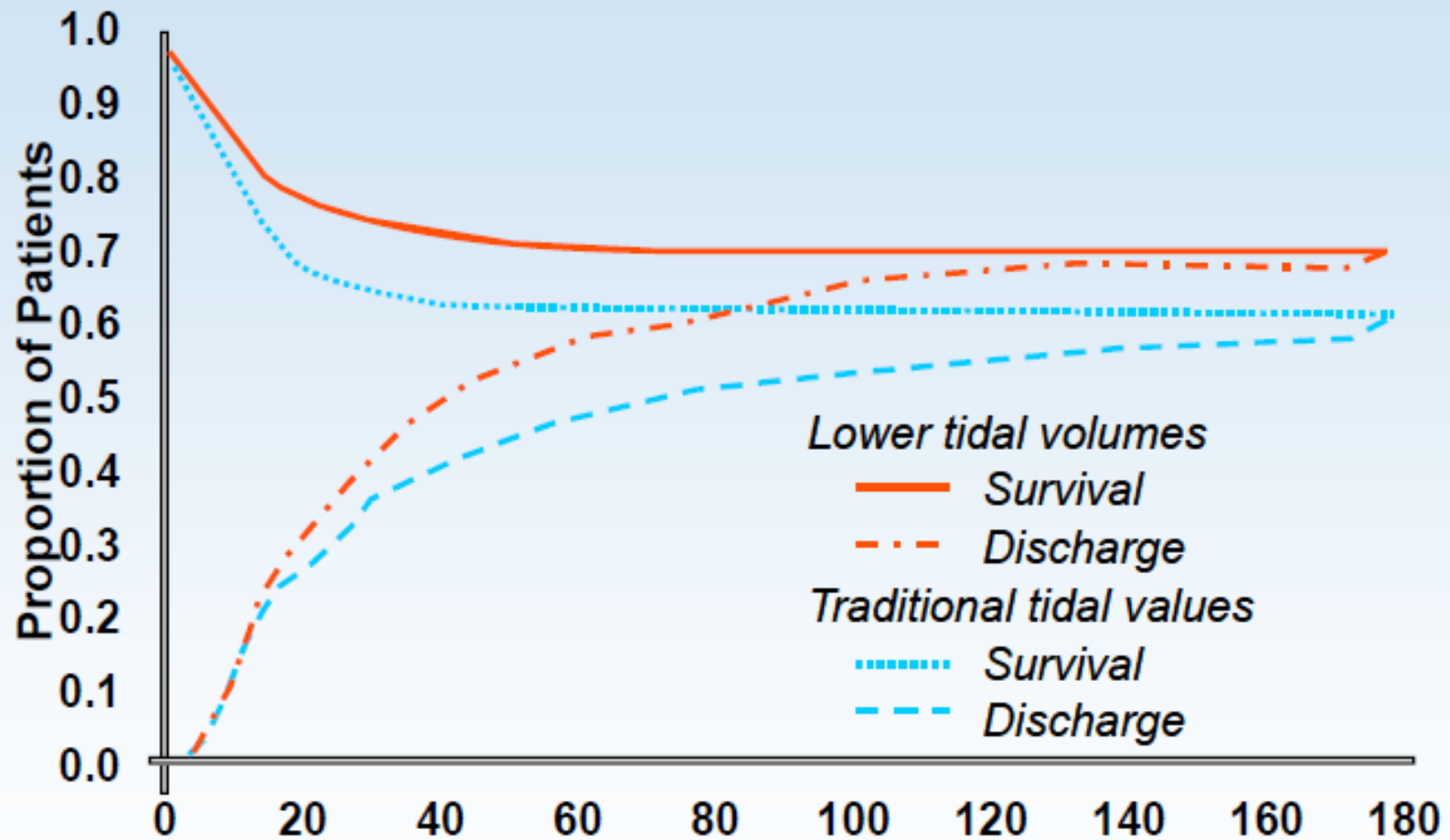
Weaning

B. Spontaneous breathing trial (SBT):

If all above criteria are met for at least 12 hours, initiate a trial of upto 120 minutes of spontaneous breathing with **FiO₂ < 0.5 and PEEP < 5:**

1. Place on T-piece, trach collar, or CPAP ≤ 5 cm H²O with PS ≤ 5
2. Assess for tolerance as below for up to two hours
 - a. SpO₂ ≥ 90 : and/or PaO₂ ≥ 60 mmHg
 - b. Spontaneous V^T ≥ 4 ml/kg PBW
 - c. RR ≤ 35 /min
 - d. pH ≥ 7.3
 - e. No respiratory distress (distress= 2 or more)
 1. HR $> 120\%$ of baseline
 2. Marked accessory muscle use
 3. Abdominal paradox
 4. Diaphoresis
 5. Marked dyspnoea
3. If tolerated for at least 30 minutes, consider extubation
4. If not tolerated resume pre-weaning settings.

ARDS Network: Improved Survival with Low V_T



ARDS Network: Main Outcome Variables

	Low Vt	Traditional Vt	p Value
Death before discharge home and breathing without assistance (%)	31.0	39.8	0.007
Breathing without assistance by day 28 (%)	65.7	55.0	< 0.001
No. of ventilator-free days, days 1 to 28	12 ± 11	10 ± 11	0.007
Barotrauma, days 1 to 28 (%)	10	11	0.43
No. of days without failure of nonpulmonary organs or systems, days 1 to 28	15 ± 11	12 ± 11	0.006

Consequences of low tidal volume ventilation :

- Reduction in CO₂ elimination via lungs – hypercapnia , respiratory acidosis , increased cardiac output.
- Increased cerebral blood flow, cerebral edema, intracranial hemorrhage
- Leads to brainstem stimulation-hyperventilation

Contraindications of low tidal volume ventilation:

- Increased intracranial pressure
- Stroke
- Acute or chronic myocardial ischemia
- Severe pulmonary hypertension
- Right ventricular failure
- Severe metabolic acidosis
- Sickle cell anemia
- TCA overdose
- Beta blockers
- Pregnancy

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

Systematic Review and Meta-analysis

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Context Trials comparing higher vs lower levels of positive end-expiratory pressure (PEEP) in adults with acute lung injury or acute respiratory distress syndrome (ARDS) have been underpowered to detect small but potentially important effects on mortality or to explore subgroup differences.

Objectives To evaluate the association of higher vs lower PEEP with patient-important outcomes in adults with acute lung injury or ARDS who are receiving ventilation with low tidal volumes and to investigate whether these associations differ across prespecified subgroups.

Data Sources Search of MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (1996-January 2010) plus a hand search of conference proceedings (2004-January 2010).

A strategy employing higher PEEP along with low tidal volume ventilation should be considered for patients receiving mechanical ventilation for ARDS. This suggestion is based on a [2010 meta-analysis](#) of 3 randomized trials (n=2,229) testing higher vs. lower PEEP in patients with acute lung injury or ARDS, in which ARDS patients receiving higher PEEP had a strong trend toward improved survival.

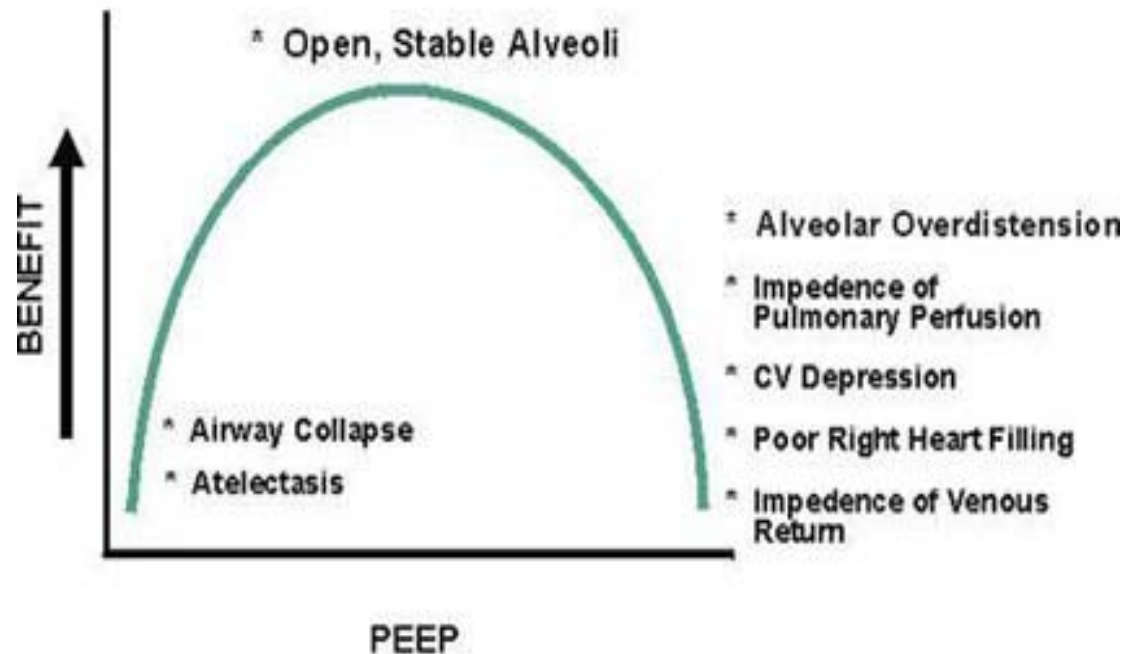
Role of PEEP in ARDS

- PEEP avoids repetitive opening and collapse of atelectatic lung units – could protect against VILI
- Improves arterial oxygenation
- Lung is kept open by using PEEP to avoid end expiratory collapse
 - Preserves inspiratory recruitment
 - Re-establish end expiratory lung volume
 - Prevent surfactant loss in airway
 - Decreases intrapulmonary shunt

- **Optimal /Best PEEP:**

It is the minimum PEEP necessary to maintain adequate PaO₂ at non toxic FIO₂ .

- It is required for optimization of arterial oxygenation without introducing risk for oxygen toxicity and VILI, with least effect on haemodynamics, oxygen delivery and airway pressures.



Adverse effects of PEEP

1. Decreased cardiac output
 2. Increased pulmonary edema formation
 3. Increased dead space & increased resistance of the bronchial circulation
 4. Increased lung volume and stretch during inspiration → lung injury or barotrauma.
- These adverse effects are more pronounced in patients with direct lung injury

Recruitment maneuvers

Application of continuous positive airway pressure aimed at recruiting or opening totally or partially collapsed alveoli.

- The most well known method of recruitment maneuver is sustained application of CPAP of 30- 50 cm H₂O for 30 seconds
- Periodic recruitment with a series of traditional sigh breaths
- Intermittently raising PEEP over several breaths
- Extended sigh maneuver with step wise increase in PEEP while V_t is decreased
- Intermittent application of pressure controlled ventilation with incremental high PEEP

Other approaches to ventilatory management

- 1. Pressure control mode** – PCV limits maximal peak airway pressure , end inspiratory pressure.
- 2. Inverse ratio ventilation with PCV** – inspiratory time > expiratory time , some case reports – patients with refractory hypoxemia responded to PCV IRV
 - Due to intrinsic PEEP , alveolar recruitment
 - Can compromise cardiac output – risk of non pulmonary organ dysfunction
 - Used as salvage mode



3. Modes that allow spontaneous breathing during positive pressure ventilation –

BiPAP, APRV- airway pressure cycles between higher and lower levels of PEEP

- Decreases- intrathoracic pressure
- Improved ventilation perfusion mismatch
- Improved cardiac output
- Decreases shunt fraction , dead space
- Less patient ventilator asynchrony

4. High frequency oscillatory ventilation (HFOV)

- Delivers small tidal volumes (1-2 ml/kg)
- Rapid oscillations (300 cycles/min)
- Ventilation is achieved by oscillation of air around set airway pressure
- Constant airway pressures maintain open lung, optimize lung recruitment
- Lower V_t – less alveolar distension
- High mean pressures- higher end expiratory lung volumes and recruitment- improvement in oxygenation
- Disadvantages:
 - A special ventilator is required
 - Aerosolized bronchodilators are ineffective
 - Cardiac output is decreased due to high mean airway pressures



Adjuncts to protective lung ventilation

- Permissive hypercapnia
- Fluid and hemodynamic management
- Inhaled nitric oxide
- Prone position ventilation
- Tracheal gas insufflation
- Steroids
- Nutritional support
- Other drug therapies



1. Permissive hypercapnia

- Low tidal volume ventilation results in hypercapnia.
- Clinicians have allowed hypercapnia to persist in patients of ARDS as long as there is no evidence of harm.
- Clinical trials have shown that arterial pCO₂ level of 60-70 mmHg and arterial pH of 7.2-7.25 are safe for most of the patients.

2. Fluid management

- **NIH/ARDS Network Fluid Management Trial (The FACTT Study) – FACTT (Fluid and Catheter Therapy Trial; 2005-6)** - fluid restriction results in improved outcome (may reduce pulmonary edema due to increased pulmonary vascular permeability).
- **FACTT – fluid management protocol based on –**
 1. Mean arterial pressure $>60\text{mmHg}$
 2. Urine output $>0.5\text{ml/kg}$
 3. Effectiveness of circulation $\text{CI} >2.5\text{l/min/m}^2$
 4. Intravascular pressure –CVP $<4\text{mmHg}$
- **Result** – improved lung function, improved central nervous system function, less sedation, mechanical ventilation , less complications
- Avoiding a positive fluid balance in ARDS patients reduces the time on mechanical ventilation and also mortality.

3. Haemodynamic management

- **ARDSNet FACTT** compared hemodynamic management guided - **CVP/PAC SUPPORT** – use of PAC increases mortality
 - PAC allows measurement of central venous and pulmonary arterial pressure, pulmonary artery occlusion pressure , mixed venous blood gases, cardiac output.
 - no added benefit, increasing complications
 - CVP better indicator of measurement than PAC

Inotropes

- **Dobutamine is preferred-** because vasodilators increase intrapulmonary shunt
- Dopamine – constricts pulmonary veins , rise in pulmonary capillary hydrostatic pressure

4. Prone ventilation

- Routine use of prone positioning in all patients with ALI / ARDS cannot be currently recommended due to a lack of clinical data support.
- **Indications:**
 - as an adjunctive therapy to improve oxygenation in established ALI and ARDS
 - considered in patients who require PEEP >12 cmH₂O and a FiO₂ >0.60
- should better be used early within 36 hours of the onset of ARDS
- optimum duration unknown

PATIENT LYING PRONE ON VOLLMAN PRONE POSITIONER



Prone position

- **A**telectasis and ventilation perfusion mismatch appear to be dependent on gravity - improves oxygenation
- **Mechanism –**
 - ✓ Increased FRC
 - ✓ Change in regional diaphragmatic motion
 - ✓ Perfusion redistribution – better oxygenation
 - ✓ Improved clearance of secretions
- **Limitations:**
 - ✓ Need extra care- prevent pressure necrosis
 - ✓ Secure ET
 - ✓ Dislodgement of line or chest tube
 - ✓ Hemodynamic instability

GATTINONI AND COLLEAGUES – multicentre prospective randomized trial (2001)-No survival advantage, salvage therapy

Prone position

Absolute contraindications

- Burns or open wounds on the face or ventral body surface
- Spinal instability
- Pelvic fractures
- Life-threatening circulatory shock
- Increased intracranial pressure

Complications

- Facial and periorbital edema
- Pressure sores
- Accidental displacement of the endotracheal tube, thoracic or abdominal drains, and central venous catheters
- Airway obstruction
- Hypotension
- Arrhythmias
- Vomiting



5. Inhaled nitric oxide

- Selectively dilates pulmonary capillaries
- Decreases pulmonary capillary pressure
- Selectively vasodilates ventilated areas of lung
- Inhibit neutrophils activation
- Used as a **salvage therapy** to improve oxygenation
- Adverse effects- methemoglobinemia, renal dysfunction.

6. Tracheal gas insufflation

- Delivering fresh gas through modified ET just above carina
 - Removes CO₂ rich gas- from trachea, small airways
 - Reduces anatomic dead space

Risks-

- Tracheal erosion
 - Oxygen toxicity due to increased Fio₂
 - Hemodynamic compromise
 - Barotraumas
-
- Salvage therapy

7. Steroids

- Steroid therapy is currently recommended only for early severe and unresolving ARDS:
- **Early severe ARDS** ($\text{PaO}_2/\text{FiO}_2 < 200$ mmHg, PEEP=10 cm H₂O):
 - Methylprednisolone IV loading dose of 1 mg/kg over 30 min, followed by 1 mg/kg/day for 14 days, then taper over next 14 days and then discontinue.

Steroids

Unresolving ARDS

- In cases where ARDS has not started to resolve after 7 days, high dose steroid therapy should be started (but it should not begin after 14 days of onset)
- Methylprednisolone IV loading dose of 2 mg/kg over 30 min, followed by 2 mg/kg/day for 14 days, then 1 mg/kg/day for next 7 days. Gradually taper the dose and discontinue therapy at 2 weeks after extubation.
- 5 days after the patient is able to ingest oral medications, oral prednisone or prednisolone can be started as a single daily dose.

8. Nutrition

- **Goals-**
 - Provision of adequate nutrition
 - Prevention and treatment of deficiencies

Enteral nutrition superior because

- Prevents bacterial translocation
 - Lowers levels of TNF, arterial glucagon & epinephrine
 - Lesser febrile responses
 - Lower incidence of infection
 - Less costly
- However parenteral maybe needed in some patients

Other drug therapies

- **Prostaglandin E 1**- pulmonary vasodilatation , anti inflammatory effects on neutrophils and macrophages
- **Aerosolized prostacyclin** – selective pulmonary vasodilatation of ventilated lung areas
- **Almitrine** – selective pulmonary vasoconstrictor of non ventilated areas of lung
- **Surfactant** – prevents collapse, protects against inflammation and infection
- **N-acetylcysteine, procysteine, lisofylline**
- **Anti oxidants** – protect against oxidant damage
- **Partial liquid ventilation**- PFC, liquid PEEP
- **Anti inflammatory drugs** – ibuprofen
- **Antifungal**- ketoconazole
- **Recombinant activated protein C**
- **ECMO/ ECCOR**
All used as salvage modalities , no benefit seen.

Clinical course outcome

- **Most ARDS related deaths occur within first 2 wks, one third occurring by day 7 and two third by 14 day.**
- **Most common cause of death--** sepsis, associated multiorgan failure
- **Long term sequelae-** impaired pulmonary, neurologic, musculoskeletal, cognitive, and psychosocial functions.
- **Pulmonary sequelae-** impaired diffusion capacity, restrictive or obstructive abnormalities. Restoration of normal lung function occurs in a substantial proportion.
- **Physical and neuromuscular sequelae-** low exercise capacity, weakness, decreased muscle mass.
- **Cognitive and psychological sequelae-** impaired memory, reduced attention, decreased concentration, depression and anxiety.

RVF in acute lung injury

- ARDS involves not only alveoli but also capillaries → constant pulmonary HTN → acute cor pulmonale in 20-25% of patients
- Diagnosis- Echocardiography
- Considering the poor prognosis of patients suffering from such acute right ventricular (RV) dysfunction, RV protection by appropriate ventilatory settings-
 - including strict limitation of Pplat,
 - diminution of positive end-expiratory pressure (PEEP),
 - control of hypercapnia,
 - prone positioning

Conclusion

- The management strategies for ARDS patients. should focus on-
 - Lung protective ventilation strategy
 - Low tidal volume (6 ml/kg)
 - Optimal peep and Pplat
 - Oxygenation goal- PaO₂ -55-80 mmHg /SpO₂ – 88-95%
 - Conservative fluid management
 - Treat the underlying cause.



Thank you