DR .HUSSAM BACHIR AL BARDAN

MD, MSC, PHD

PULMONARY AND CRITICAL CARE MEDICINE

16-10-2024

Hypoxemic respiratory failure

Respiratory system

- The respiratory system consists of two parts:

1-The lung performs gas exchange

2- pump ventilates the lung.

The pump

consists of:

- the chest wall, including the respiratory muscles
- the respiratory controllers in the central nervous system (CNS)
- linked to respiratory muscles through spinal and peripheral nerves.

- The diagnosis of respiratory failure is not clinical but based on arterial gas assessment
- it is defined by a

PaO_2 less than 60mmHg and/or $PaCO_2$ more than 45 mmHg.

- These values are not rigid; they must serve as a general guide in combination with the patient's history and clinical evaluation.
- Respiratory failure may be acute, chronic or acute on chronic, with clinical presentation being quite different between these types.

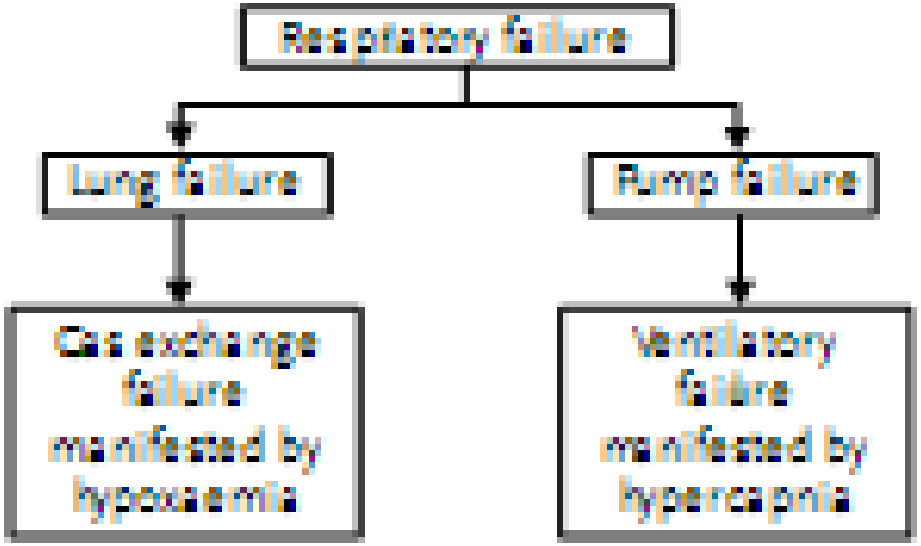

Respiratory failure
Lung failure
Pump failure
Gas exchange failure manifested by hypoxaemia
Ventilatory failure manifested by hypercapnia

Table 1. The most common causes of hypoxaemic ARF

Cardiogenic pulmonary oedema
ARDS and ALI
Alveolar haemorrhage
Lobar pneumonia
Atelectasis

ALI: acute lung injury.

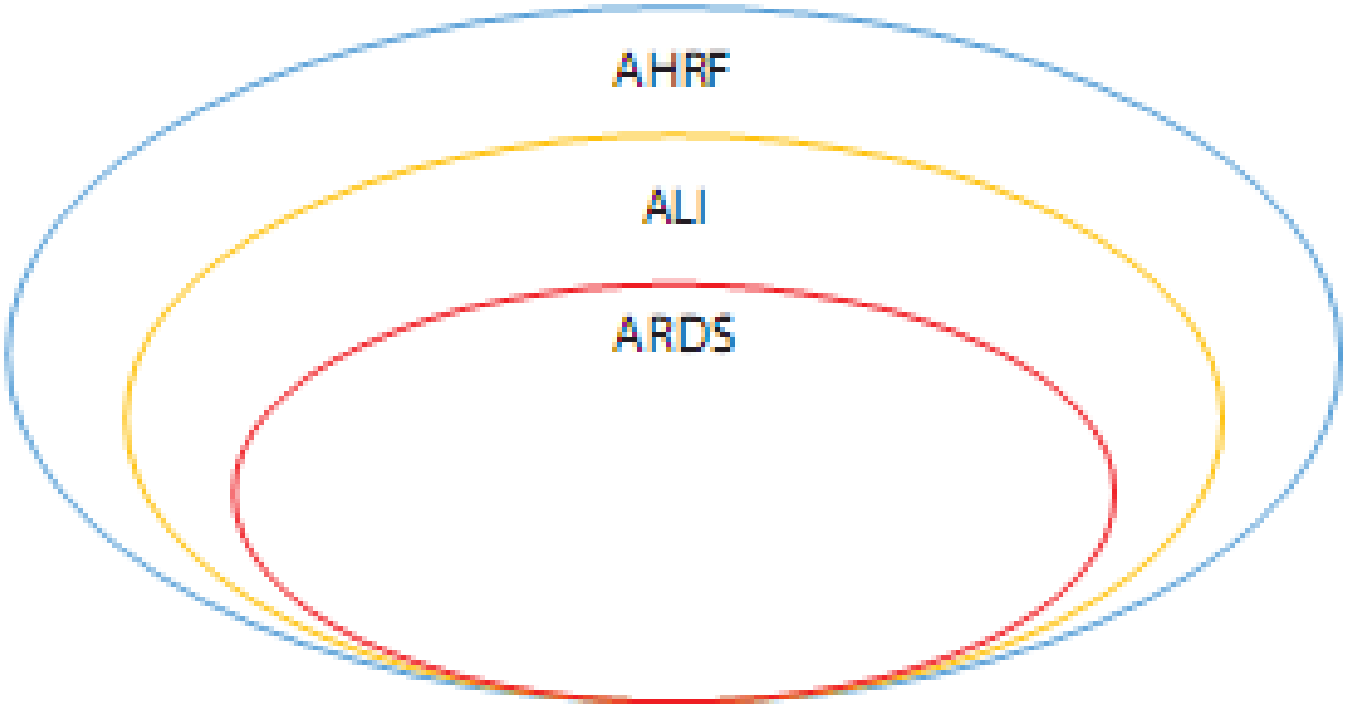

AHRF
ALI
ARDS

Table 2. Causes of acute hypercapnia

Decreased central drive
Drugs
CNS diseases
Altered neural and neuromuscular transmission
Spinal cord trauma
Myelitis
Tetanus
ALS
Poliomyelitis
Guillain–Barré syndrome
Myasthenia gravis
Organophosphate poisoning
Botulism
Muscle abnormalities
Muscular dystrophies
Disuse atrophy
Prematurity
Chest wall and pleural abnormalities
Acute hyperinflation
Chest wall trauma
Lung and airway diseases
Acute asthma
AECOPD
Cardiogenic and noncardiogenic oedema
Pneumonia
Upper airway obstruction
Bronchiectasis
Other causes
Sepsis
Circulatory shock

type I respiratory failure

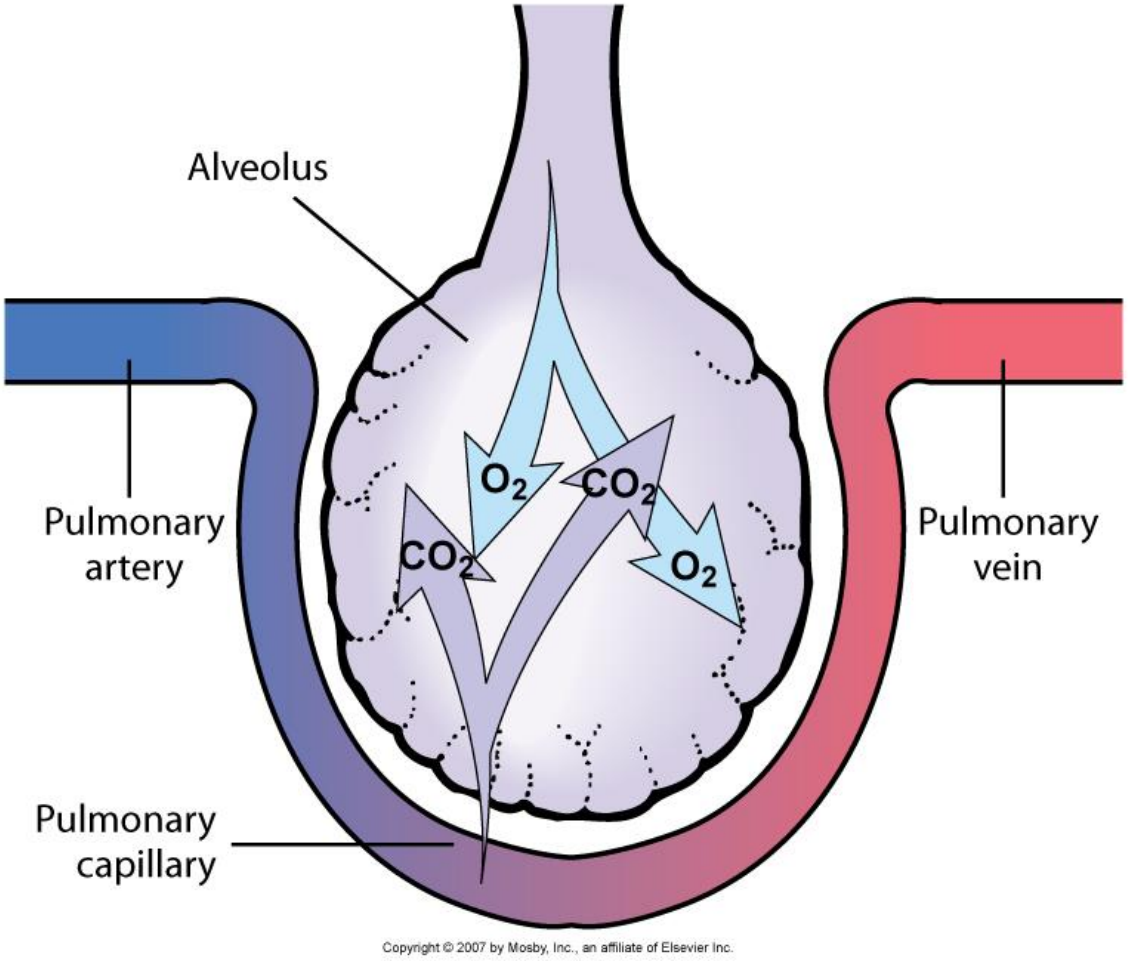
- Respiratory failure due to lung diseases (e.g. pneumonia, acute lung injury, acute respiratory distress syndrome (ARDS),emphysema or interstitial lung disease) leads to hypoxaemia with normocapnia or even hypocapnia (type I respiratory failure).

type I respiratory failure

Four pathophysiological mechanisms are responsible for hypoxaemic respiratory failure:

- ventilation/perfusion (V/Q) ratio inequalities
- shunt
- diffusion impairment
- hypoventilation.

Gas Exchange Unit



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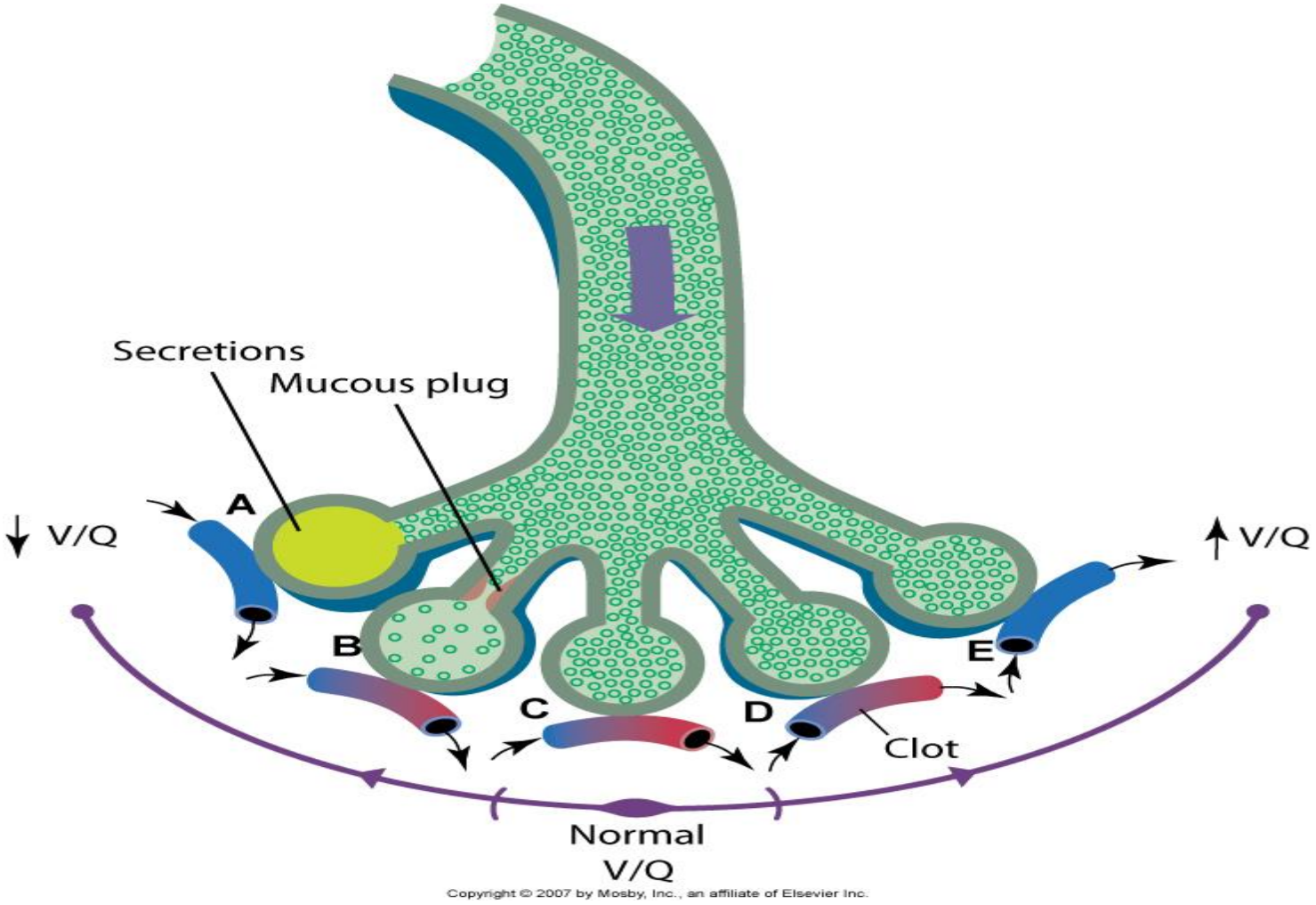
Range of V/Q Relationships



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- The range of $\dot{V}/\dot{Q}$ mismatching of the 300 million or so alveoli runs the spectrum from absence of ventilation **(shuntlike)** to absence of perfusion **(dead space).**

- These conditions cause an increased gradient (PAO2) and measured PaO2, as calculated in the equation

PAO2 - PaO2= (b p- 47 mm Hg) * 0.21 – (PaCO2/RQ) - PaO2

where 47 mm Hg represents the partial pressure of water vapor

RQ is respiratory quotient (regarded to be 0.8).

While breathing ambient air at sea level,

- PAO2=150-(PaCO2/0.8), and PAO2-PaO2 should be **10 to 15 mm Hg**.

- In contrast, generalized alveolar hypoventilation without $\dot{V}/\dot{Q}$ mismatch can result in hypercapnia plus hypoxemia with a normal $P_{A}O_2$ -$P_{a}O_2$.

type II respiratory failure).

- Failure of the pump (e.g. neuromuscular diseases or opiate overdose) results in alveolar hypoventilation and hypercapnia with parallel hypoxaemia (type II respiratory failure).

- The normal range of PaO2 varies with age as a result of the loss of effective alveoli during advancing age and can be approximated

from the following equation:

PaO2=100.1-0.32*(age in years).

Clinical Manifestations and Causative Conditions ofHypoxemia

- dyspnea, tachypnea, tachycardia, hypertension, cardiac arrhythmias (including bradycardia progressive to asystole in extreme cases)
- tremor, anxiety, delirium,and agitation.
- Often additional clinical manifestations are present that reflect the underlying causative condition(s).

Common Clinical Conditions Associated With Hypoxemic Respiratory Failure

- ALI/ARDS
- Pulmonary edema
- Diffuse alveolar hemorrhage
- Pulmonary embolism
- Interstitial lung disease
- Infectious pneumonia
- Pneumonitis
- Neoplasm
- Pulmonary contusion
- Atelectasis
- Emphysema
- Asthma
- Chronic bronchitis
- Bronchiolitis

Management Principles for Hypoxemic Respiratory Failure

Initial Evaluation and Stabilization

- BLS measures management of the airway ,breathing .
- Life-threatening respiratory distress will often require urgent endotracheal intubation and MV.
- Assessment of oxygenation and ventilation by arterial blood gas analysis is useful and pulse oximetry may provide continuous display of oxygenation including response to therapy.
- Initial evaluation should also include timely detection and management of urgent conditions such as airway obstruction or tension pneumothorax.

Supplemental Oxygen and Artificial Ventilation:

- Supplemental oxygen can be administered by a variety of interfaces including face mask, and nasal cannula with higher effective FIO2 being delivered with a tight-fitting nonrebreather mask.
- Mechanical ventilation, with delivery of positive-pressure breaths for alveolar ventilation as well as (PEEP) for alveolar recruitment and distention can be provided using a ventilator and delivered via an endotracheal or tracheostomy tube or with a tightly fitting mask applied to the face or nose.

- The addition of PEEP is particularly effective for improving oxygenation in the setting of diffuse lung disease and poorly compliant lungs as seen in ALI/ARDS and similar conditions.

ALI and Acute Respiratory Distress Syndrome

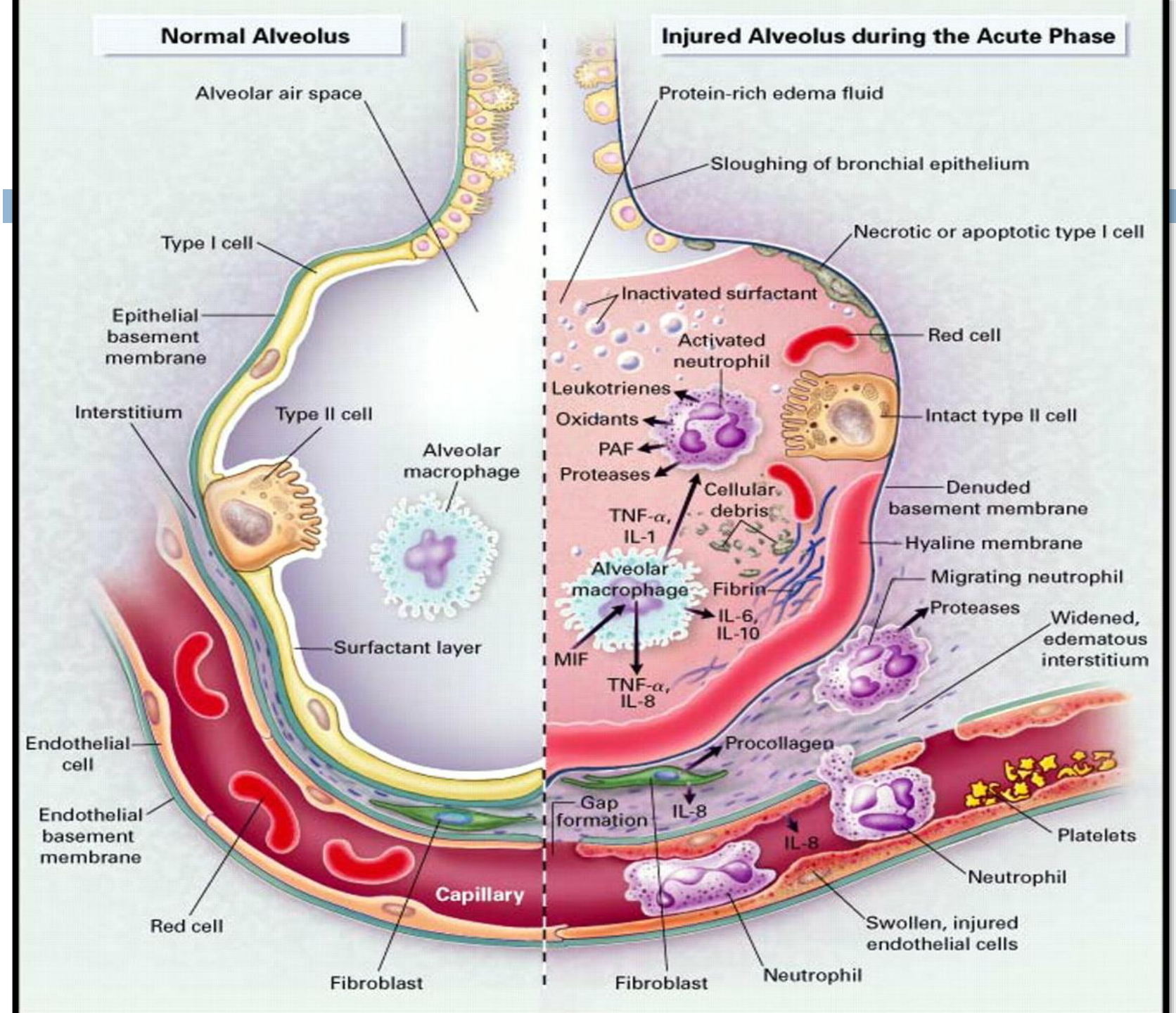
- ARDS was first described in 1967 as the acute onset of **hypoxemic respiratory failure** accompanied by **diffuse pulmonary infiltrates** in the absence of a cardiac failure and following an inciting event.

The acute respiratory distress syndrome (ARDS)

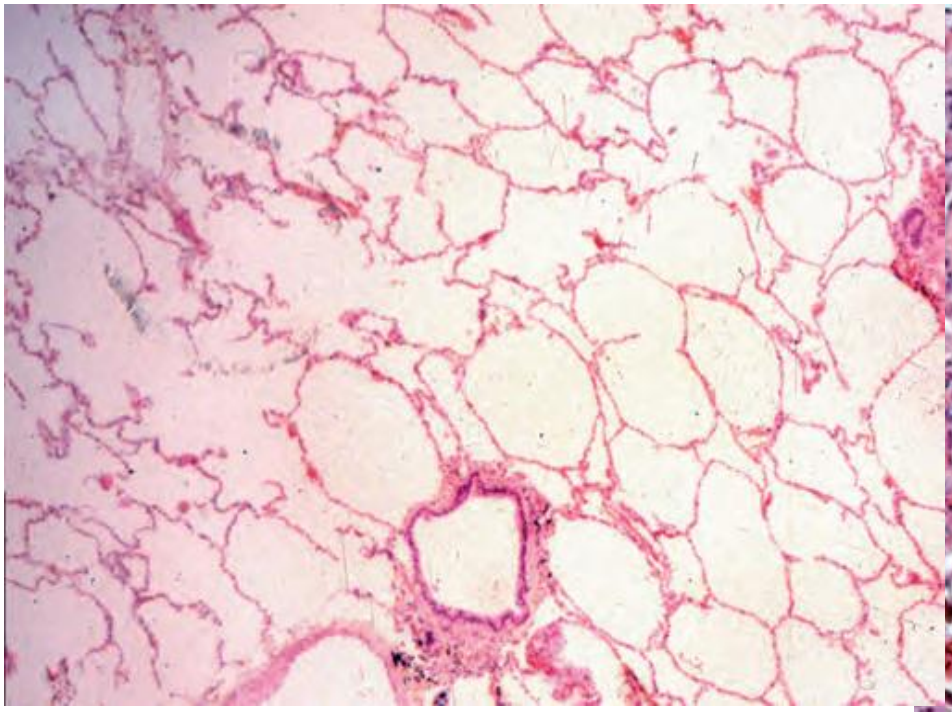
- is a form of **acute respiratory failure**
- **initiating injury or illness**
- **inflammatory events** developing in response

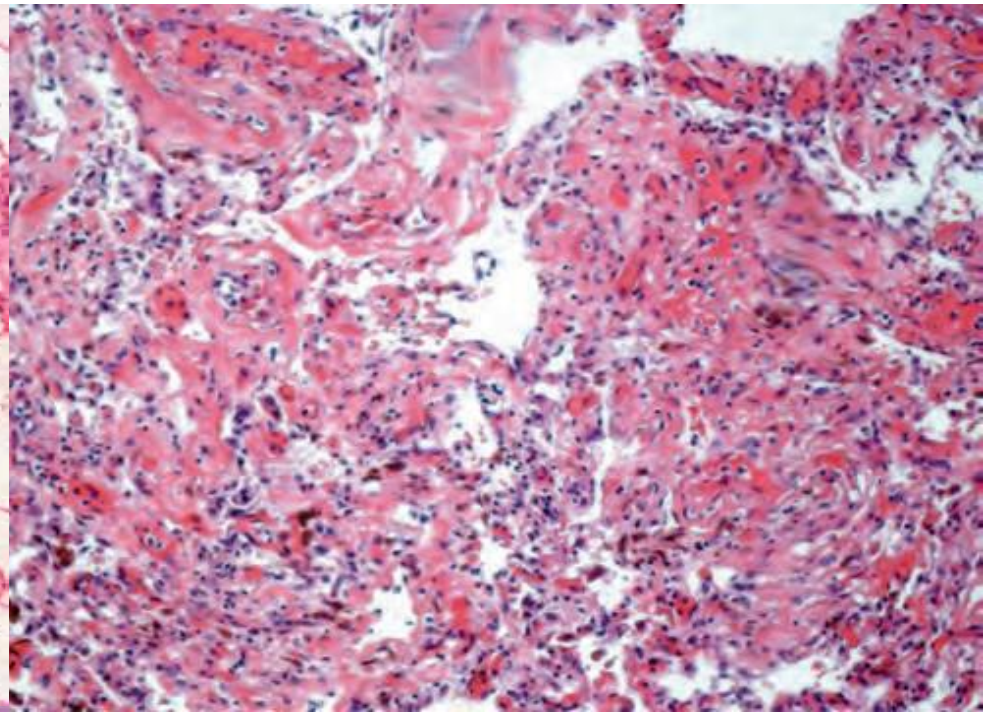
(In particular, activated neutrophils) aggregate and adhere to endothelial cells, releasing various toxins, oxygen radicals and mediators (e.g. arachidonic acid, histamine, kinins).

- **endothelial damage**
- **permeability pulmonary oedema**

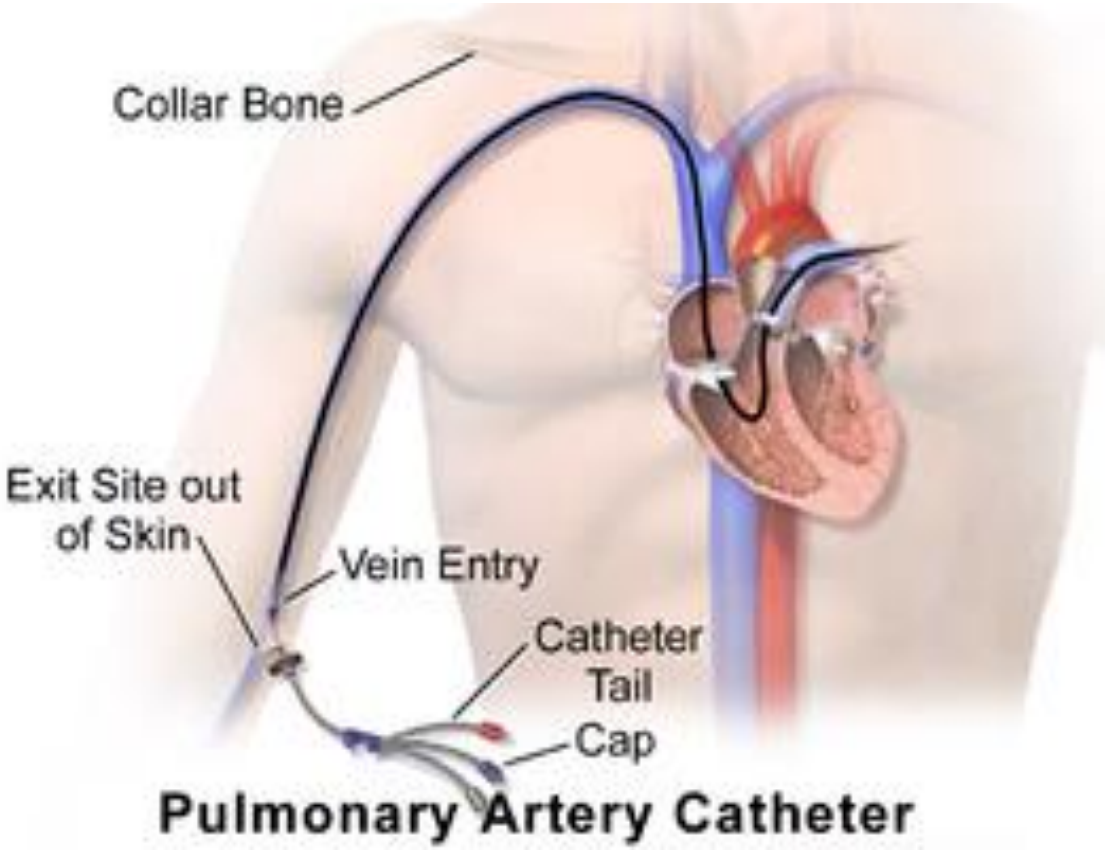

Normal Alveolus
Injured Alveolus during the Acute Phase
Alveolar air space
Type I cell
Epithelial basement membrane
Interstitium
Type II cell
Alveolar macrophage
Surfactant layer
Endothelial cell
Endothelial basement membrane
Capillary
Red cell
Fibroblast
Protein-rich edema fluid
Sloughing of bronchial epithelium
Necrotic or apoptotic type I cell
Inactivated surfactant
Activated neutrophil
Red cell
Leukotrienes
Oxidants
PAF
Proteases
Intact type II cell
Cellular debris
Denuded basement membrane
TNF-α, IL-1
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

- The alveoli become filled with a protein-rich exudate containing neutrophils and other inflammatory cells, and the airspaces show a rim of proteinaceous material: the hyaline membrane.





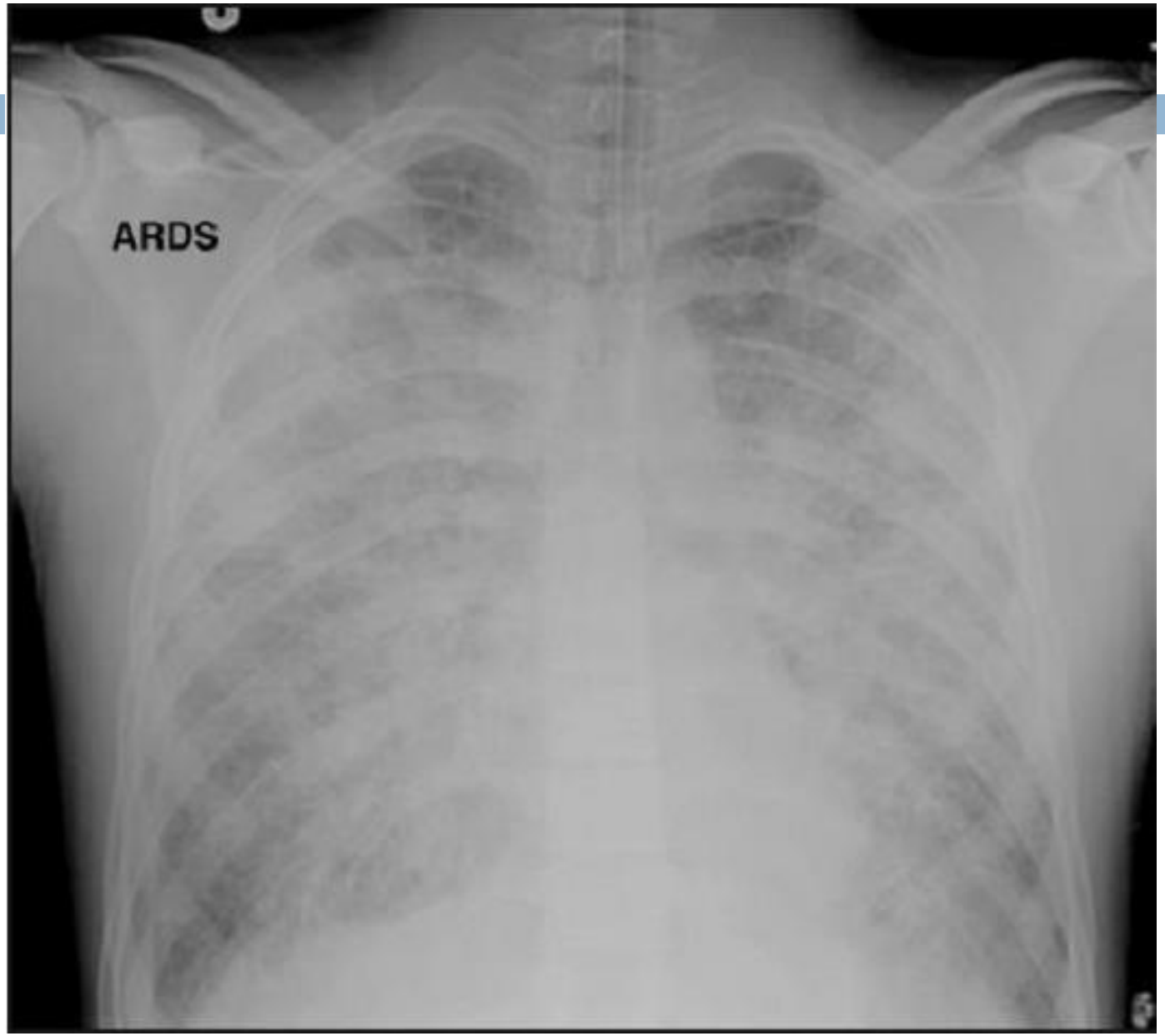
- The characteristic feature of pulmonary oedema in ARDS : **the PCWP is not elevated.**
- Measurement: passing a special balloon-tipped pulmonary artery catheter (e.g. **Swan–Ganz catheter)** via a central vein through the right side of the heart to the pulmonary artery.

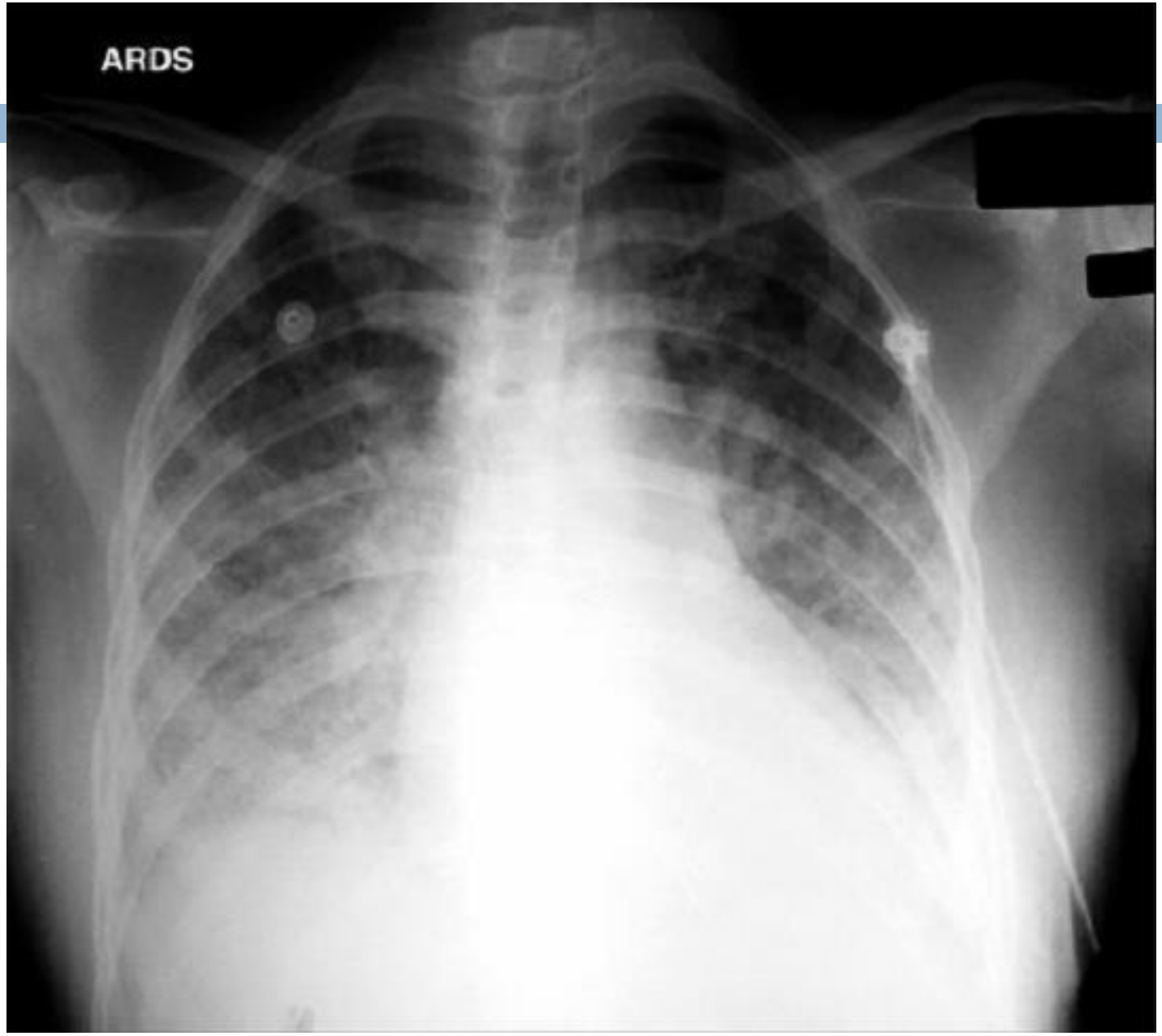

Collar Bone
Exit Site out of Skin
Vein Entry
Catheter Tail
Cap
Pulmonary Artery Catheter

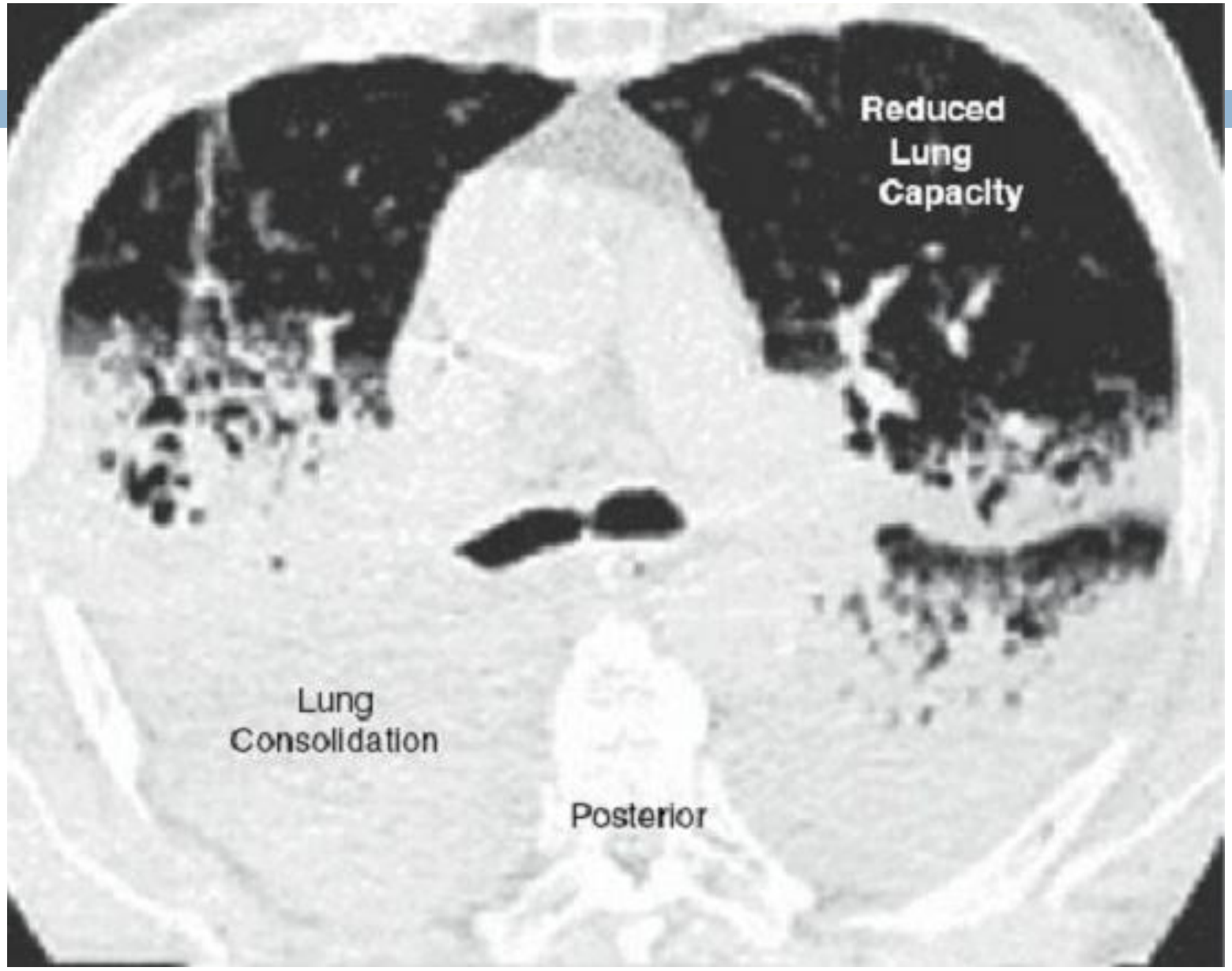
- pulmonary capillary wedge pressure reflects **left atrial pressure**.
- In ARDS, it is typically ≤18mmHg, whereas in cardiogenic pulmonary oedema, it is elevated.

American European Consensus Criteria for ALI and ARDS

- 1. Acute onset
- 2. Hypoxemia
    - a. ALI: PaO2\FIO2 <300 mm Hg
    - b. ARDS\ PaO2:FIO2 <200 mm Hg
- 3. Diffuse bilateral pulmonary infiltrates on frontal chest radiograph consistent with pulmonary edema; infiltrates can be patchy and/or asymmetric
- 4. Absence of left atrial hypertension based upon clinical assessment or PCWP ,18 mm Hg if measured


ARDS


ARDS


Reduced
Lung
Capacity
Lung
Consolidation
Posterior

Berlin Criteria

- (a) ALI was eliminated as a clinical entity, and the PaO2/FIO2 for ARDS was set at ″300 mm Hg
- (b) a requirement was added that the PaO2/FIO2 determination should be conducted at a positive end-expiratory pressure (PEEP) of 5 cm H2O
- (c) the wedge pressure measurement was eliminated (because of the diminished use of pulmonary artery catheters).

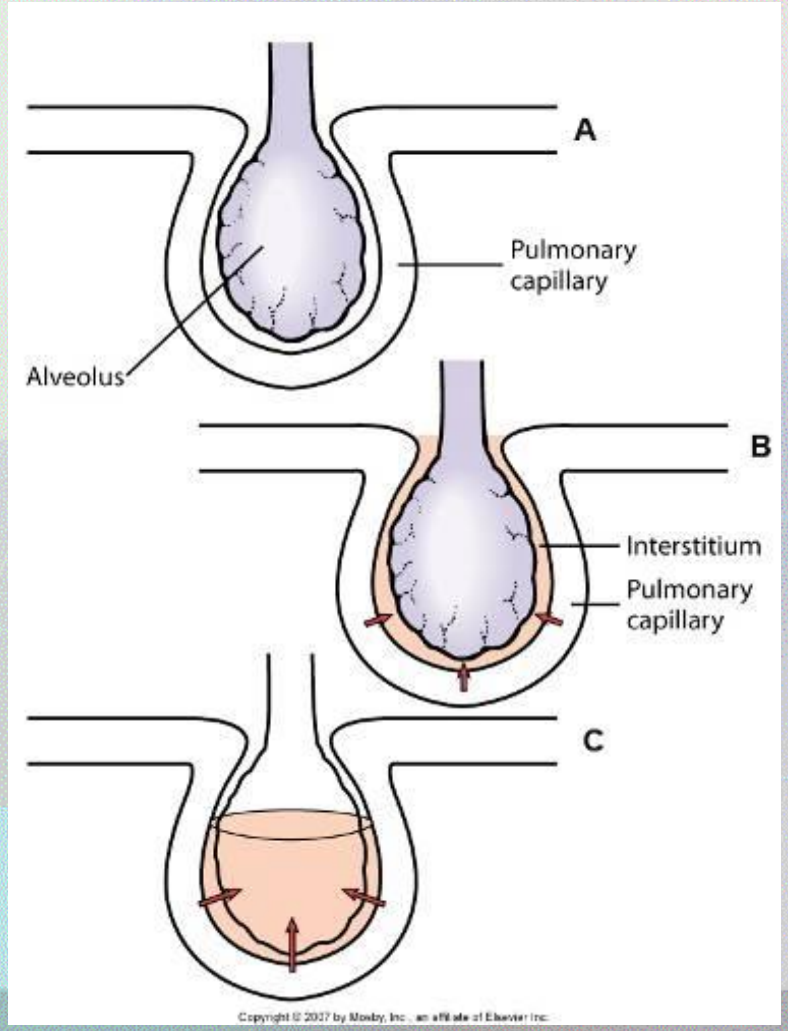
Common Causes of ALI/ARDS

- **Direct causes**
- **Pulmonary infection**
- **Aspiration injury (gastric contents, near drowning,blood, toxins)**
- **Inhalation injury (smoke, toxins)**
- **Trauma (contusion)Embolism (amniotic fluid, fat, air)**
- **Reexpansion injury,Reperfusion injury**
- **Indirect causes**
- **sepsis**
- **Shock**
- **Nonpulmonary trauma**
- **Transfusion-related lung injury**
- **Cardiopulmonary bypass**
- **Anaphylaxis**
- **Medications (opioids, salicylates, amiodarone, tocolytics,chemotherapy)**
- **Acute pancreatitis**

Clinical Features

- Clinical features of ALI/ARDS at the onset of illness include manifestations of hypoxemia as described above as well as signs and symptoms related to the underlying cause(s).
- It is noteworthy that the manifestations that are directly related to ALI/ARDS can **change over time.**

Stages of Edema Formation in ARDS



***A*, Normal alveolus and pulmonary capillary**

***B*, Interstitial edema occurs with increased flow of fluid into the interstitial space**

***C*, Alveolar edema occurs when the fluid crosses the blood-gas barrier**

Fig. 68-8

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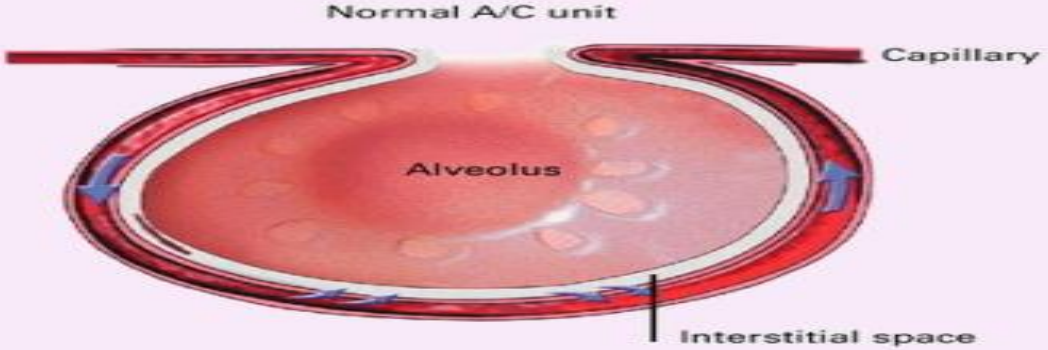
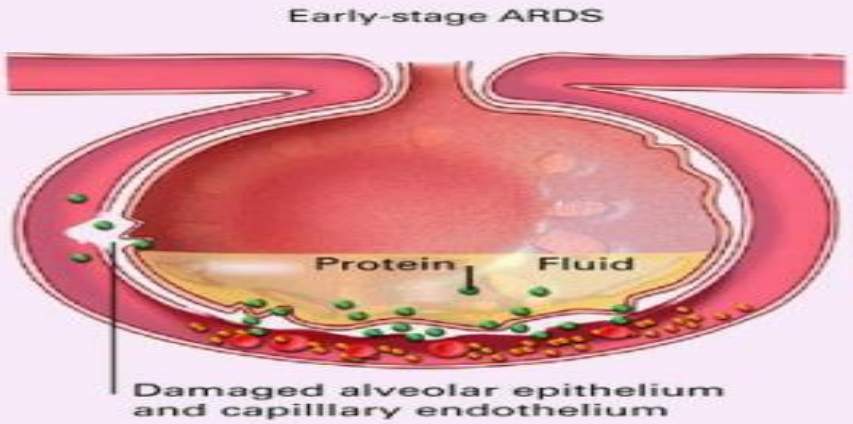
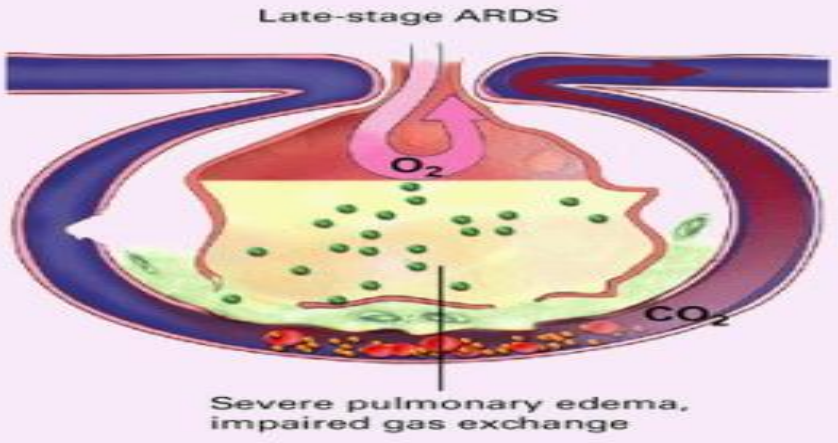

Normal A/C unit
Capillary
Alveolus
Interstitial space


Early-stage ARDS
Protein
Fluid
Damaged alveolar epithelium
and capilllary endothelium


Late-stage ARDS
O2
CO2
Severe pulmonary edema,
impaired gas exchange

An Overview of Management of ALI/ARDS

- treatment of the underlying cause
- support for gas exchange
- supportive and preventative measures such as adequate nutrition and prophylaxis against deep venous thrombosis, stress gastric ulceration, and ventilator-associated pneumonia
- application of evidence-based strategies for ventilation and medical care of ALI/ARDS
- rescue therapies for refractory hypoxemia in selected cases.

Lung protective ventilation

- limiting tidal volume (VT) to 6 mL/kg of predicted body weight (PBW), is a key component of contemporary management

- The largest trial of lung protective ventilation was conducted by the **ARDS Network** , and enrolled over 800 ventilator-dependent patients with ARDS who were randomly receive tidal volumes of 6 mL/kg or 12 mL/kg (using PBW).
- Ventilation with the lower tidal volume was associated with **a shorter duration of mechanical ventilation and a 9% absolute reduction in mortality rate** (40% to 31%, P= 0.007).

ARMA Trial

The New England
Journal of Medicine

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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

28 day mortality	
Intervention	Control
31%	40%
PEEP 8.9	PEEP 8.0

NIH ARDS Network trial
NEJM 2000;342:1301

	Low TV	High TV	P =
Mortality	31	40	0.007
Days of free MV	12	10	0.007
Days free of organ failure	15	12	0.006

Reducing from 12 to 6 ml/kg VT saved lives

ARDS

- effective alveolar volume is reduced substantially in ARDS—mimicking baby lungs in size—and that overdistention of functional alveoli impairs gas exchange and induces a state of inflammatory lung injury, called **ventilator-associated lung injury (VALI).**

- Second, many alveoli are prone to collapse either throughout the respiratory cycle or as lung volume and airway pressure decrease during exhalation—so-called **atelectrauma.**
- Recruiting these alveoli and maintaining them in an open state **improves gas exchange and reduces VALI** related to injury caused by repetitive alveolar collapse and recruitment.

- Third, high concentrations of oxygen are typically necessary to achieve sufficient cellular oxygenation but if administered for prolonged periods are associated with **pulmonary fibrosis** in animal models.

- Thus, current ventilatory strategies for ARDS focus on -using small VTs
  -sufficient PEEP to splint open alveoli
  - supplemental oxygen.

Permissive Hypercapnia

- A sequance of low TV ventilation is a **decrease in CO2 elimination** in the lungs, which can result in hypercapnia and respiratory acidosis.
- **Because of the benefits of low volume ventilation, hypercapnia is allowed to persist as long as there is no evidence of harm**
- The limits of tolerance to hypercapnia arterial PCO2 levels of 60 – 70 mm Hg and arterial pH levels of 7.2–7.25 are safe for most patients .

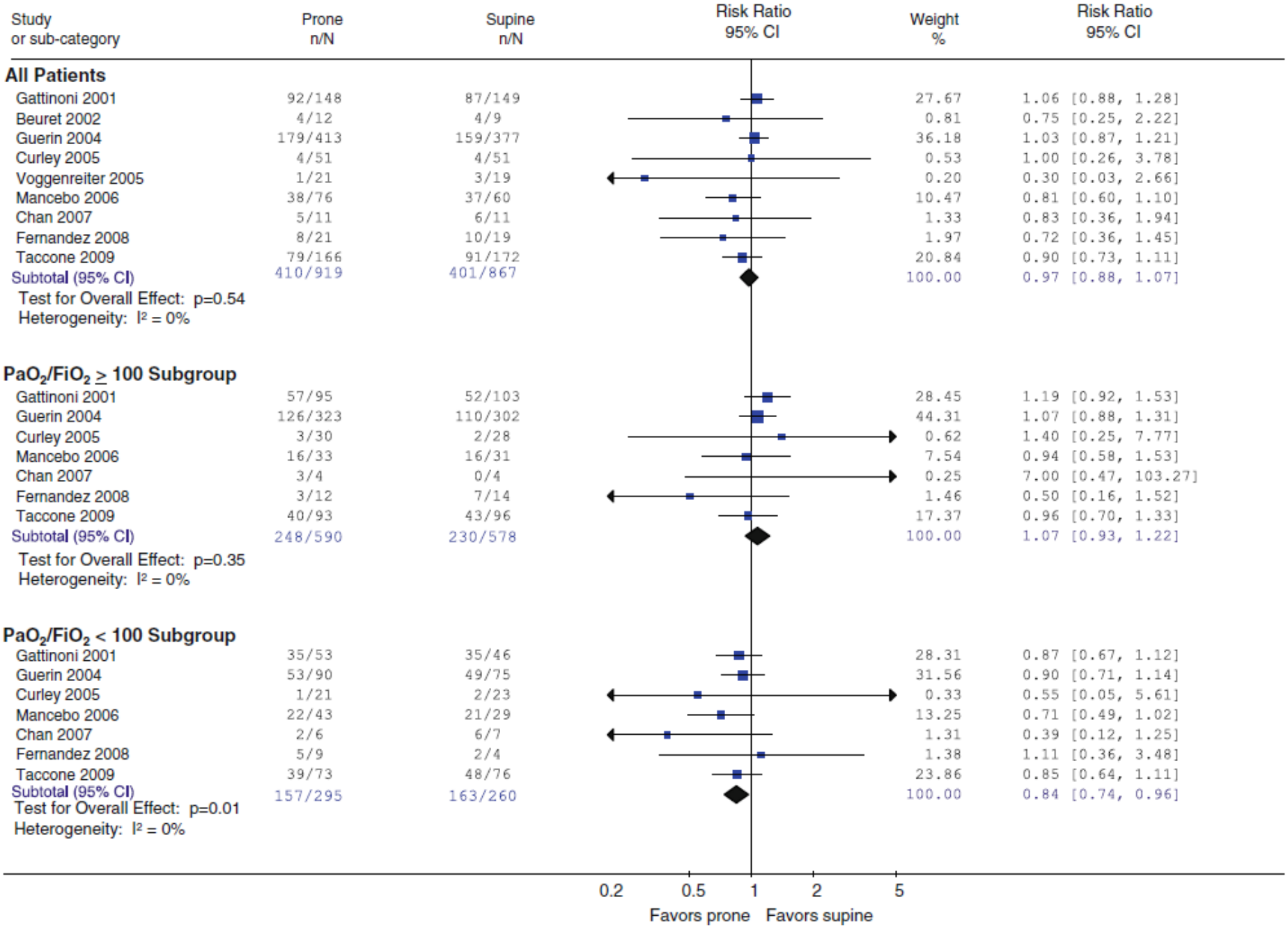
Prone Position in ARDS

Intensive Care Med
DOI 10.1007/s00134-009-1748-1

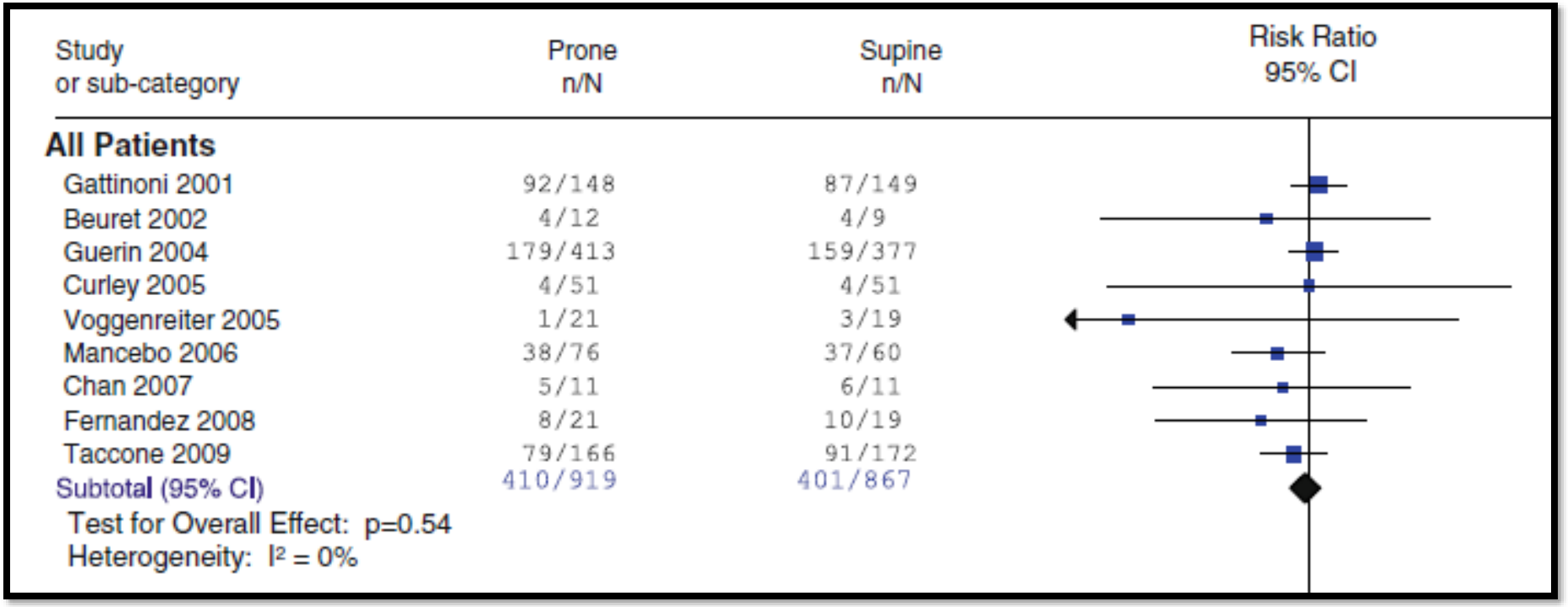
REVIEW

Sachin Sud
Jan O. Friedrich
Paolo Taccone
Federico Polli
Neill K. J. Adhikari
Roberto Latini
Antonio Pesenti
Claude Guérin
Jordi Mancebo
Martha A. Q. Curley
Rafael Fernandez
Ming-Cheng Chan
Pascal Beuret
Gregor Voggenreiter
Maneesh Sud
Gianni Tognoni
Luciano Gattinoni

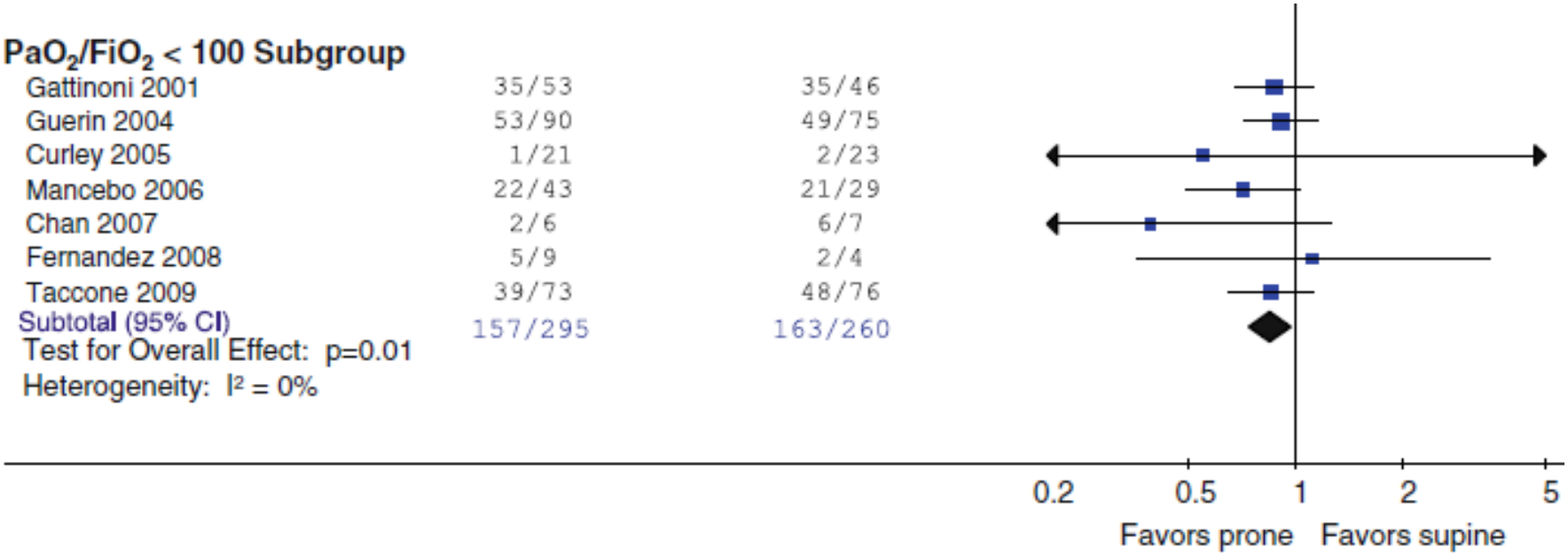
Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis


Study or sub-category
Prone n/N
Supine n/N
Risk Ratio 95% CI
Weight %
Risk Ratio 95% CI
All Patients
Gattinoni 2001 92/148 87/149 27.67 1.06 [0.88, 1.28]
Beuret 2002 4/12 4/9 0.81 0.75 [0.25, 2.22]
Guerin 2004 179/413 159/377 36.18 1.03 [0.87, 1.21]
Curley 2005 4/51 4/51 0.53 1.00 [0.26, 3.78]
Voggenreiter 2005 1/21 3/19 0.20 0.30 [0.03, 2.66]
Mancebo 2006 38/76 37/60 10.47 0.81 [0.60, 1.10]
Chan 2007 5/11 6/11 1.33 0.83 [0.36, 1.94]
Fernandez 2008 8/21 10/19 1.97 0.72 [0.36, 1.45]
Taccone 2009 79/166 91/172 20.84 0.90 [0.73, 1.11]
Subtotal (95% CI) 410/919 401/867 100.00 0.97 [0.88, 1.07]
Test for Overall Effect: p=0.54
Heterogeneity: I² = 0%
PaO2/FiO2 ≥ 100 Subgroup
Gattinoni 2001 57/95 52/103 28.45 1.19 [0.92, 1.53]
Guerin 2004 126/323 110/302 44.31 1.07 [0.88, 1.31]
Curley 2005 3/30 2/28 0.62 1.40 [0.25, 7.77]
Mancebo 2006 16/33 16/31 7.54 0.94 [0.58, 1.53]
Chan 2007 3/4 0/4 0.25 7.00 [0.47, 103.27]
Fernandez 2008 3/12 7/14 1.46 0.50 [0.16, 1.52]
Taccone 2009 40/93 43/96 17.37 0.96 [0.70, 1.33]
Subtotal (95% CI) 248/590 230/578 100.00 1.07 [0.93, 1.22]
Test for Overall Effect: p=0.35
Heterogeneity: I² = 0%
PaO2/FiO2 < 100 Subgroup
Gattinoni 2001 35/53 35/46 28.31 0.87 [0.67, 1.12]
Guerin 2004 53/90 49/75 31.56 0.90 [0.71, 1.14]
Curley 2005 1/21 2/23 0.33 0.55 [0.05, 5.61]
Mancebo 2006 22/43 21/29 13.25 0.71 [0.49, 1.02]
Chan 2007 2/6 6/7 1.31 0.39 [0.12, 1.25]
Fernandez 2008 5/9 2/4 1.38 1.11 [0.36, 3.48]
Taccone 2009 39/73 48/76 23.86 0.85 [0.64, 1.11]
Subtotal (95% CI) 157/295 163/260 100.00 0.84 [0.74, 0.96]
Test for Overall Effect: p=0.01
Heterogeneity: I² = 0%
0.2
0.5
1
2
5
Favors prone
Favors supine

Prone Position in ARDS Metanalysis



Prone Position in ARDS Metanalysis



Prone Position

- Switching from the supine to prone position can improve pulmonary gas exchange
- combining lung protective ventilation with prone positioning showed a lower than expected mortality rate in patients with severe ARDS (PaO_2/FIO_2 <100 mm Hg).
- Prone positioning creates **problems with nursing care (**e.g., airway care and skin care), but it may be the only measure available for refractory hypoxemia in hospitals with limited resources.

Fluid Management

- The lung consolidation in ARDS is an inflammatory exudate, and should not be influenced by fluid balance (for the same reason that diuresis will not clear an infiltrate caused by pneumonia).
- However, **avoiding a positive fluid balance will prevent unwanted fluid accumulation in the lungs**, which could aggravate the respiratory insufficiency in ARDS.

Critical Care Medicine

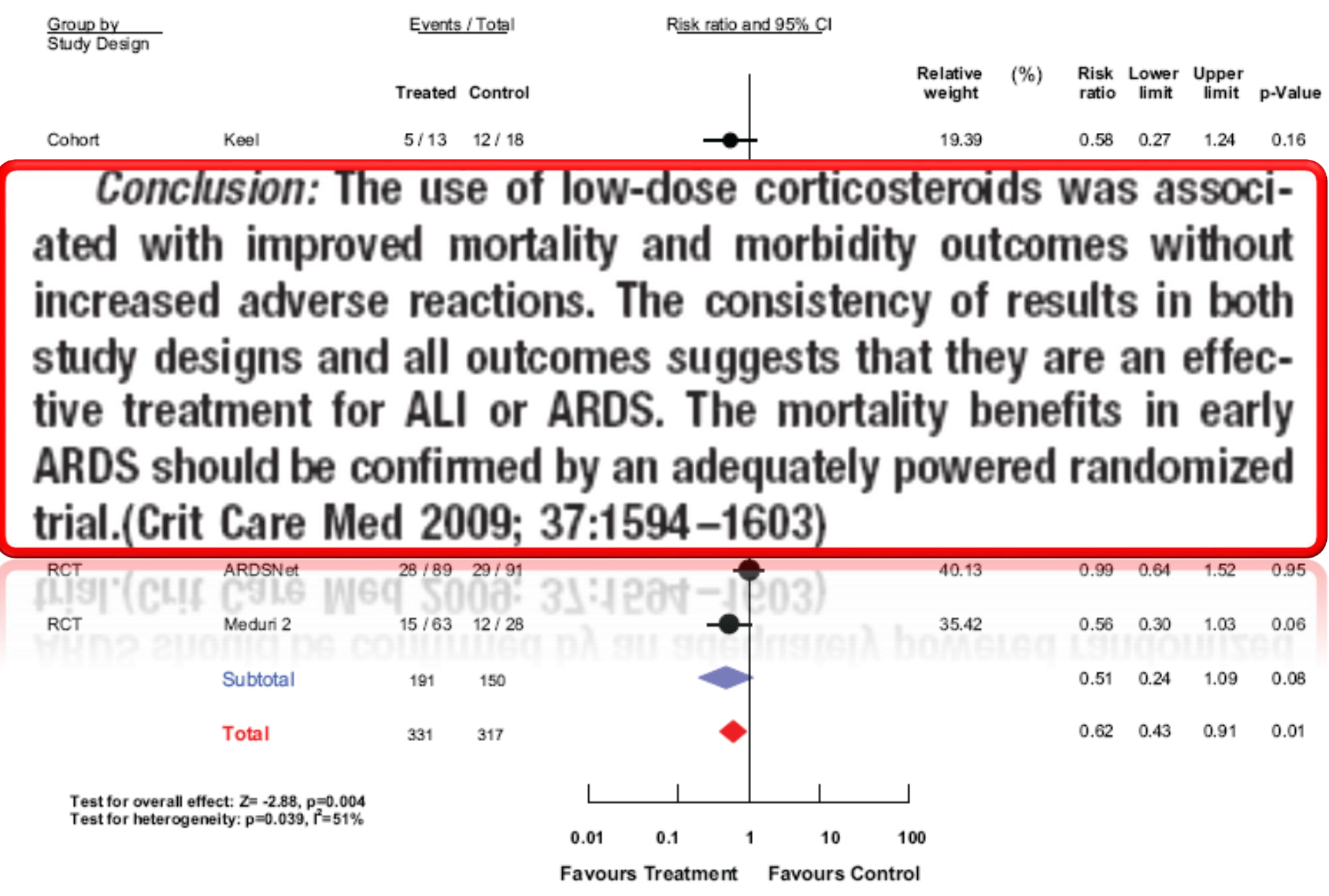
Society of Critical Care Medicine
The Intensive Care Professionals

Use of corticosteroids in acute lung injury and acute respiratory distress syndrome: A systematic review and meta-analysis*

Benjamin M. P. Tang, PhD; Jonathan C. Craig, PhD; Guy D. Eslick, PhD; Ian Seppelt, MBBS; Anthony S. McLean, MBBS

Crit Care Med 2009 Vol. 37, No. 5

Mortality

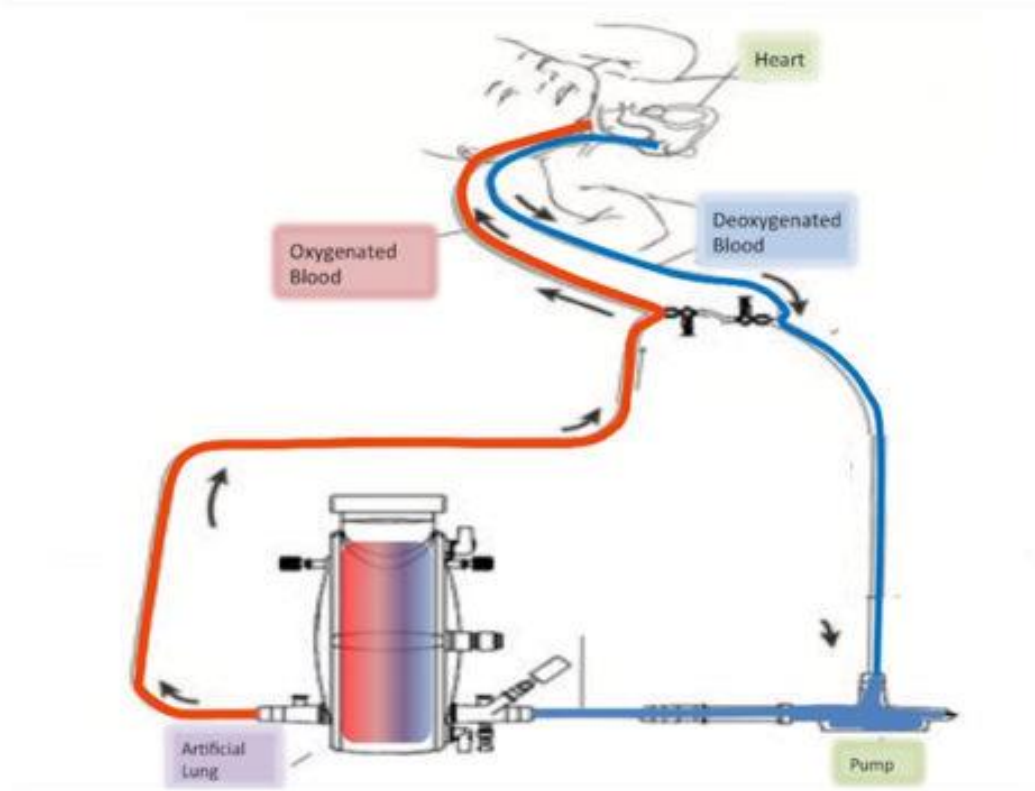


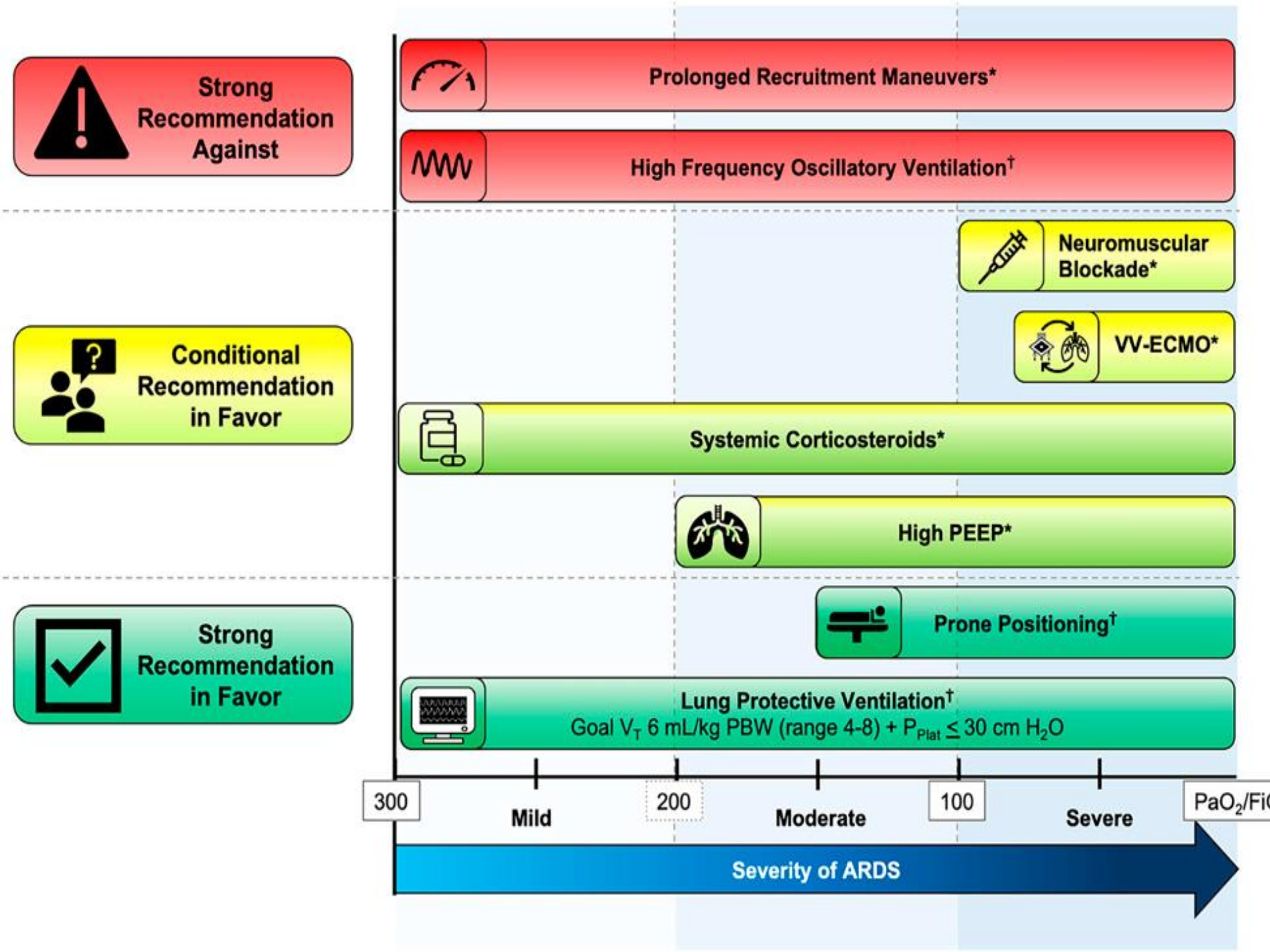
Conclusion: The use of low-dose corticosteroids was associated with improved mortality and morbidity outcomes without increased adverse reactions. The consistency of results in both study designs and all outcomes suggests that they are an effective treatment for ALI or ARDS. The mortality benefits in early ARDS should be confirmed by an adequately powered randomized trial.(Crit Care Med 2009; 37:1594–1603)

Corticosteroid Therapy

- there is evidence of other benefits provided by steroid therapy in ARDS, and these include a reduction in markers of inflammation (both pulmonary and systemic inflammation), improved gas exchange, shorter duration of mechanical ventilation, and shorter length of stay in the ICU .
- Steroid therapy is currently recommended only in cases of early severe ARDS and unresolving ARDS .

ecmo


Heart
Deoxygenated Blood
Oxygenated Blood
Artificial Lung
Pump


Strong Recommendation Against
Prolonged Recruitment Maneuvers*
High Frequency Oscillatory Ventilation†
Neuromuscular Blockade*
VV-ECMO*
Conditional Recommendation in Favor
Systemic Corticosteroids*
High PEEP*
Strong Recommendation in Favor
Prone Positioning†
Lung Protective Ventilation†
Goal V_T 6 mL/kg PBW (range 4-8) + $P_{Plat} \leq 30$ cm H_2O
300
200
100
PaO_2/Fi
Mild
Moderate
Severe
Severity of ARDS

Thank you