ARDS
The Good, the Bad and the Ugly
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Objectives

- Origins
  - Review ARDS definition
  - Original definition
  - Berlin definition

- The Syndrome

- Current State

- Treatment & Prognosis

- Synopsis + Practical Approach
• ARDS is a syndrome

• Imprecise classification

• Pathophysiology does not exist in all patients

• ARDS and ventilation strategies: most important for intermediate-severe and severe ARDS

• Mechanical concept: increase lung homogeneity with PEEP and Prone Positioning

• Driving pressure
Syndrome without a Gold Standard

• Heterogeneous
• Multiple mechanisms leading to same clinical presentation
• No gold standard
• Other fields without a gold standard
  ● Sepsis
  ● Frailty
  ● Shock
  ● Asthma
  ● COPD
  ● Depression
  ● Etc...
ARDS as a Syndrome

- Incidence ~10-15% of ICU patients
- ~20% of patients who are ventilated meet criteria of ARDS
- ~80% of ARDS patients (diagnosed with), require mechanical ventilation

- Increased fluid in the interstitium
- Decreased alveolar diffusion and alveolar collapse
- Inhomogeneity in the lung – V/Q mismatch
ARDS Risk Factors

- Pneumonia – most common, outside hospital cause (Strep pneumo, Legionella, PCP, Staph aureus, gram negatives); hospital: staph, pseudomonas
- Aspiration (up to 1/3 of patients can develop ARDS)
- Shock – particularly Septic Shock, worse with chronic EtOH
- Trauma
- Pancreatitis
- CABG
- Fat embolism
- Fluid resuscitation - transfusion
Physiology

- Normal lungs – small amount of interstitial fluid
  - Retained intravascular protein – maintenance of oncotic pressure
  - Normal interstitial lymphatics – facilitate drainage of tissue, fluid returns to circulation
  - Tight junctions – between alveolar epithelial cells

- ARDS – abnormal fluid, present both in the interstitium and also alveoli = Injured Lungs
  - Impaired gas exchange
  - Decreased compliance
  - Increase pulmonary arterial pressure
Phases of ARDS

Diffuse Alveolar Damage

Exudative stage

- Edema
- Hyaline membranes

Proliferative stage

- Interstitial inflammation
- Interstitial fibrosis

ARDS in 1967 – clinical phenotype

**AECC DEFINITION** (AMERICAN EUROPEAN CONSENSUS CONFERENCE)

**ARDS**
- **ACUTE ONSET**
- **SEVERE HYPOXEMIA** \( \text{PaO}_2 / \text{FiO}_2 < 200 \) (irrespective of PEEP)
- **B/L OPACITIES on chest X Rays.**
- **ABSENCE OF LVF** (clinical examination / Rt heart catheterise PCWP < 18 mm Hg)

New term – **ALI (acute lung injury)** – \( \text{PaO}_2 / \text{FiO}_2 < 300 \)
(same cause and pathophysiology)
AECC ARDS Definition

- CXR unreliable
- Poor inter-observer agreement on PAOP
- P/F Ratio – treatment dependent – Vt, PEEP, FiO2
- Left atrial hypertension – coexistent with ALI
- ALI vs. ARDS – not useful terminology – folks used ALI/ARDS
- ALI used for all P/F < 300
Problems?

- Reliability
- Validity
- Feasibility
- No Gold standard!
Modified Definition Attempt

- Rapid onset hypoxemia
- Acute radiographic abnormalities
- Non-cardiogenic origin
- Decreased lung compliance
- Predisposition
Direct vs. Indirect ARDS

• Examples:
  ● Trauma – crush then aspirates?
  ● Ortho injuries with marrow embolization? Vs. huge transfusion
  ● Patients have both!
  ● No difference in mortality (REVIEW WHICH PAPER)

• Berlin decided to not include it!
Berlin Definition (2012, replaced AECC 1994)

- Respiratory symptoms begun within 1 week of clinical insult – New or Worsening during past week

- Bilateral opacities – consistent with pulmonary edema (CXR OR CT)
  - Not fully explained by effusions, lobar collapse, lung collapse, or pulmonary nodules

- Symptoms Not fully explained by: 1) cardiac failure, or fluid overload

- Impairment of oxygenation – defined by PaO2/FiO2 (“P-F ratio”) on a PEEP of 5mmHg (minimum PEEP required)
  - Mild – P-F ratio 200-300, less than 300
  - Moderate – P-F ratio 100-200
  - Severe – P-F ratio less than 100
Berlin Definition

- An Evolution NOT a Revolution
- Focus on predictive validity

Main changes:
- Introduces a framework
- Eliminated ALI
- 3 simple categories – Mild, Moderate, Severe
- Minimal PEEP level for assessing gas exchange
- Allows diagnosis in non intubated patients
- Allows for CT diagnosis
- Empiric evaluation – do not need a complex definition
- Education provided to help enhance reliability
What does the Fox Say

- When Diffuse Alveolar Damage (DAD) is used as a reference standard, the Berlin Definition is 89% sensitive and 63% specific.
- Based on clinical criteria alone, used to diagnose ARDS, approximately 45% have DAD on biopsy.

- DAD on biopsy
  - Mild ARDS – 12%
  - Moderate ARDS – 40%
  - Severe ARDs – 58%

- Severe ARDS for >72 Hrs?
  - 69% of patients had DAD on pathology.
Corticosteroids for Blastomycosis-Induced ARDS*: A Report of Two Patients and Review of the Literature

Tim Lahm, MD; Sheila Neese, MD; Aaron T. Thornburg, DO; Michael D. Ober, MD; George A. Sarosi, MD, FCCP; Chadi A. Hage, MD, FCCP
Ventilation + PEEP

V/Q Mismatch

• FiO2
• Alveolar Ventilation
• Alveolar Recruitment

• Increased Shunting
• Increased Deadspace
• Minute Ventilation Requirements
Decreased Lung compliance

- Heterogeneous
- Stiff ?, poorly aerated lung
- Loss of compliance, results in small tidal volumes being too much for the lungs inspiratory capacity -> this increases airway pressures
Pulmonary Hypertension

- Occurs in 25% of patients
- Hypoxic vasoconstriction
- Vascular compression by positive airway pressure
- Parenchymal destruction
- *cor pulmonale is rare
Supportive Care

• Sedation
  - High PEEP
  - Low Tidal Volume
  - Balance of morbidity and mortality with prolonged sedation in ARDS vs benefits of Lung-Protective Ventilation
  - Case for Benzos? Sedation for several days, long-acting agents, hemodynamic consequences

• Paralysis
  - For Moderate to Severe (P-F Ratio 120 or less) there is a 90-day mortality benefit
  - Some notion of more ventilator-free days
  - In general, ICU-acquired neuromuscular weakness is the same (neuropathy vs myopathy)

• Swan-Ganz? Vs. CVC
  - No difference in: mortality, lung function, Vent-free days, ICU-free days at 28 days
  - Hypotension and Dialysis use is the same
  - More complications with Swan-Ganz (PAC)
Supportive Care

• Feeding
  ● Mixed results
  ● No role for routine Omega-3 FA and anti-oxidants
  ● Fewer side-effects with initial trophic feeds
  ● Avoid over-feeding (CO2 production)

• Fluid Balance
  ● Conservative fluid strategy – increases Vent. free days
  ● Concept of Lasix + Albumin
    ● Addition of albumin to furosemide significantly improved oxygenation, with greater net negative fluid balance and better maintenance of hemodynamic stability (Martin et al. 2005).
Prone Positioning

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**Supine position**
- Ventral lung (overdistended)
- Dorsal alveolus (collapsed)

**Prone position**
- Ventral lung (decreased overdistention)
- Dorsal alveolus (decreased collapse)

Physiology of prone positioning in acute respiratory distress syndrome, UpToDate
Pressure – time curve (volume – oriented mode)

Driving Pressure
Vt/C
Outcome

- Patient factors
  - Older age
    - 24% age 15-19
    - 60% age 85 years or older
  - Obesity?
  - Comorbidities
  - Overall ~040%
  - Infection and/or multiorgan dysfunction are better predictors of mortality than respiratory parameters (SOFA, APACHE III)
Outcome

- Disease-related factors
  - Hypoxemia
  - Pulmonary vascular dysfunction
    - No longer practical to measure transpulmonary gradient (mean PA – Wedge), or pulmonary vascular resistance
  - Extravascular/Lung Fluid (permeability)
  - High dead-space fraction early in ARDS course
- Underlying cause
  - Trauma less mortality than medical causes
  - Severe EtOH use + ARDS
  - DAD on biopsy is correlated with worse prognosis
Outcome

• Treatment factors
  • Fluid balance
  • Steroids – early is bad
  • Transfusion requirements
  • Late intubation
The Ugly

• No Direct/specific therapy
• Most clinical evidence based on old definition (AECC)
• Disconnect between pathology and diagnosis based on clinical criteria
• Global mortality for ARDS, for in-hospital mortality is still 40%
  ● Differential mortality – e.g. Trauma vs. Sepsis, Specialized Centre vs. Rural Centre
• Non-specific treatments have not shown benefit:
  ● Steroids
  ● Statins
  ● Anti-inflammatory mediators
The Bad

• Syndrome
• Difficult to Define
The Good

- Improved Definition
  - Better operator characteristics
  - Better Internal Validity

- Mortality is suspected to be decreasing with ARDS
  - 35%, 40%, 46% for mild, moderate, and severe ARDS

- We have a better understanding of strategies:
  - Volume Status/fluid balance
  - Lung protective strategy for all patients – ideally 6 cc/kg
    - Low Vt
    - High PEEP
    - Driving pressure
  - Prone positioning