Acute Respiratory Distress Syndrome – with Special Reference to COVID-19

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When coronavirus kills, the lung condition ARDS can be the culprit. Here’s what you need to know.

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The Acute Respiratory Distress Syndrome (ARDS)

- ARDS is non-cardiogenic protein-rich pulmonary edema
- $\text{PaO}_2/\text{FiO}_2 < 300 \text{ mmHg}$ with bilateral infiltrates (Berlin)
- Approximately 200,000 cases per year in the US
- Mortality - 20-45%, depending on initial degree of hypoxemia
- Clinical disorders - pneumonia, sepsis, aspiration, & trauma
Pathogenesis of Acute Lung Injury – 2019
(Insights from Experimental & Clinical Studies)

- Alveolar endothelial & epithelial injury critical for severity of ARDS
- Role of neutrophils, platelets, & extracellular traps (NETs)
- Direct injury from pathogens and their products
- Non-pulmonary organ failure and co-morbidities contribute to higher mortality
ARDS in 2020: Better Understanding of Pathogenesis

Matthay M et al, Nature Rev, 2019
Clinical Features of ARDS in COVID-19

- Some patients present with pneumonia that does not require ICU care but may worsen in the second week of hospital care
- ICU care in 20-30% of hospitalized patients
- ARDS in 17-29% of hospitalized patients
- Mortality maybe 4-15% in ARDS patients
- Higher mortality with age > 70 years
Chest Radiographic and CT Findings of Unilateral Pneumonia in COVID-19

Kor Radiol Jnl Feb 2020
Chest Radiographic and CT Scans in COVID-19 With Bilateral Pneumonia

Kor Radiol Jnl Feb 2020
Bilateral Ground Glass Opacifications in COVID-19 leading to ARDS

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Lung Pathology in COVID-19 ARDS

A. Alveolar Edema       B. Protein exudates
C. Fibrin debris plus mononuclear cells
D. Hyperplastic type 2 alveolar cells + possible viral inclusions (arrow)
High Flow for Early Hypoxic Respiratory Failure for COVID-19 Patients with Worsening Respiratory Failure

Proportion Surviving vs Days since enrollment

- High Flow O$_2$
- Standard O$_2$
- NIPPV

P=0.02 by log-rank test

NEJM. 2015, 372, 2185-2196
Respiratory Treatment of COVID-19 ARDS

- Low tidal volume (4-6 ml/kg/IBW) with a plateau airway pressure < 30 cmH20 (NEJM, 2000)

- Positive end-expiratory airway pressure - moderate levels, maintain plateau airway pressure < 30 cmH20

- Neuromuscular blockade in significant ventilator dyssynchrony, high airway pressures, hypoxemia

- Prone positioning if PaO2/FiO2 less than 100-150 mmHg, usually with neuromuscular blockade (NEJM, 2013)
Biologic studies in after randomization provided insights into the how low tidal volume reduced lung injury in ARDS

Reduced Plasma Levels in Lower Tidal Volume Group

- Lower levels of IL-6
- Lower levels of IL-8
- Lower levels of TNR1
- Lower levels of SP-D

ARDS Network, NEJM, 2000

Crit Care Med, 2005
AJP:Lung, 2005
Mechanisms of Benefit for Reducing Lung Injury with Lung Protective Ventilation

Matthay, Ware, & Zimmerman. *JCI*, 2012
Prone Positioning in Severe Acute Respiratory Distress Syndrome

Focused primarily on moderate to severe ARDS (P/F < 150 mmHg)

Guerin NEJM 2013
Adjunctive Treatments for COVID-19 ARDS

- Inhaled nitric oxide (5-20 ppm) for refractory hypoxemia

- Fluid balance – moderate fluid resuscitation for intravascular fluid repletion

- Conservative fluid strategy, target 0.5 to 1.0 liters negative fluid balance daily (NEJM 2006)

- Dialysis with continuous veno-venous filtration for oliguric renal failure, pH <7.2, negative fluid balance

- ECMO if all else fails and patient qualifies by EOLIA criteria – focus on primary respiratory failure, exclude multi-organ failure, advanced age (NEJM 2018)
Possible Other Treatments for COVID-19 ARDS

- Glucocorticoids not recommended

- Experimental therapies being considered include anti-IL-6 or IL-6 receptor blocker therapy, Interleukin-1ra, interferon B - all have concerns

- Allogeneic Mesenchymal Stromal Cells attractive because in phase 2b trial for ARDS with good pre-clinical evidence for multiple mechanism of benefit, and safety profile favorable. We have DoD & NIH funded support for this trial which is ongoing

- High dose Vitamin C – favorable phase 2 trial (JAMA 2019) and part of our new phase 2 trial to launch in April 2020