Covid-ARDS Physiology

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COVID-19
Clinical presentation

Two clinical scenarios:

Based on Chinese Centers for Disease Control report on 72,314 patients

Mild disease (81%): non-pneumonia and mild pneumonia

Severe disease (14%): dyspnea, respiratory frequency ≥ 30/min, blood oxygen saturation (SpO2) ≤ 93%, PaO2/FiO2 ratio* < 300 and/or lung infiltrates > 50% within 24 to 48 hours

Critical disease (5%): respiratory failure, septic shock and/or multiple organ dysfunction (MOD) or failure (MOF)

* the ratio between the blood pressure of the oxygen (PaO2) and the percentage of oxygen supplied (FiO2)

“This Is Not ARDS”

People are saying this without appreciating Berlin definition

NYC hospitals presented different phenotypes locally

a) Vascular clot (giving heparin and lytics)

b) Mucus hypersecretion – bronching

c) Capillary leak – unclear

d) Alveolar flooding with high surface tension - recruitment

e) CHF from myocarditis

Research Question: perhaps Covid is affecting different cells in different patients e.g. non ACE2 mechanisms
Effect of Positive Pressure Ventilation on Surface Tension Properties of Lung Extracts

Lazar J. Greenfield, M.D., Paul A. Ebert, M.D., Donald W. Benson, M.D., Ph.D.

Activity. Overinflation of the lung results in depletion or alteration in surfactant which is essential to the maintenance of expanded alveoli at end-expiratory pressures. Prolonged positive pressure ventilation at normal pressure and volume does not alter surfactant and did not result in atelectasis in this study.
Experimental Pulmonary Edema due to Intermittent Positive Pressure Ventilation with High Inflation Pressures. Protection by Positive End-Expiratory Pressure$^1$-

HERBERT H. WEBB and DONALD F. TIERNEY

ARRD 1974

Fig. 3. Comparison of left lungs from rats ventilated with IPPB 14/0, PEEP 45/10, and HIPPB 45/0 (left to right). The perivascular groove is distended with edema in the lungs from rats ventilated with inspiratory pressure of 45 cm H$_2$O. The dark congested appearance of the lung ventilated with 45/0 is apparent.
ARDSNET

6 cc/kg ideal body weight

40% vs. 30% mortality comparing 12 cc/kg vs. 6 cc/kg

Lower is better

Goal is to do no mechanical harm with ventilator

NEJM 9/07
Fig. 1. A schematic diagram of an inspiratory waveform delivered during typical volume cycled ventilation. Pplat is based on an end-inspiratory hold. The driving pressure can be seen as the difference between the Pplat and the PEEP, but can also be calculated as the ratio of:

- Tidal volume = $V_t$
- Resistance = $(P_{IP} - P_{plat})/flow$
- Compliance = $V_t/(P_{plat} - PEEP)$
- Driving Pressure = $V_t/compliance$

Driving pressure = $P_{plat} - PEEP$
Covids are ‘recruitable’ by some reports

Recruitment is a vertical line on the PV Curve; overdistension is horizontal

Concomitant COPD increases compliance

Spontaneous breathing complicates matters
Esophageal and transpulmonary pressures in acute respiratory failure

Daniel Talmor, MD, MPH; Todd Sarge, MD; Carl R. O'Donnell, ScD; Ray Ritz, RRT; Atul Malhotra, MD; Alan Lisbon, MD; Stephen H. Loring, MD

Take Home: 6 cc/kg gives highly variable stretch on the lung

CCM 2006
Mechanical Ventilation Guided by Esophageal Pressure in Acute Lung Injury


Table 4. Clinical Outcomes.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Esophageal-Pressure–Guided (N = 30)</th>
<th>Conventional Treatment (N = 31)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-Day mortality — no. (%)</td>
<td>5 (17)</td>
<td>12 (39)</td>
<td>0.055</td>
</tr>
<tr>
<td>180-Day mortality — no. (%)</td>
<td>8 (27)</td>
<td>14 (45)</td>
<td>0.13</td>
</tr>
<tr>
<td>Length of ICU stay — days</td>
<td>Median: 15.5</td>
<td>13.0</td>
<td>0.16</td>
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<tr>
<td></td>
<td>Interquartile range: 10.8–28.5</td>
<td>7.0–22.0</td>
<td></td>
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</table>
Self Inflicted Lung Injury

• Traditional teaching is that you can’t pop your own lung
• High shear forces can occur at junctions of normal and abnormal lung – so called stress amplification
• Spontaneous breathing can generate lung stress even with atmospheric pressure at mouth ($P_L = P_{ao} - P_{pl}$)
• Kolobow ICM 1988 Induced lung injury by injecting salicylate into cisterna magna to stimulate ventilation but no lung injury when sheep were sedated and paralyzed.
Stress Concentration

- Estimated concentration of stress could be > 4 times that applied to the airway
- Airway pressure of 30 cmH$_2$O $\approx$ 140 cm H$_2$O in some regions

Mead, *JAP* 1970, 28(5):596
- Some of this is interesting but wild speculation:

- Initial lesion is vasoplegia i.e. loss of hypoxic vasoconstriction (HPV)
- Robust ventilatory response to hypoxia drives big tidal volumes
  With very compliant lungs (relief of dyspnea, corollary discharge)
- Lung injury is ‘self-infected’ based on stress (transpulmonary pressure) and strain (overcoming TLC locally)
- Starts to look like typical ARDS

His solution: ICU in Switzerland intubated and paralyzed very early and had 0/40 deaths compared to neighbors with >50% dead
We are given insufficient information about how/when these measurements were made to draw real conclusions.
Summary: Clinical Observations So Far for Covid and possible research ideas

- Hypoxemia out of proportion to lung infiltrates (? HPV problem)
- Compliance of lungs higher than expected (occasionally measured during spontaneous breathing giving spurious values)
- Cardiac function has been fairly normal by echo, central venous oxygen saturations and pressor requirements are ok
- Some patients abruptly deteriorate
- We have seen 3 ventilator induced pneumothorax which is typically rare in usual ARDS
- Response to inhaled pulmonary vasodilators has been generally poor
- Perhaps different cells are being affected in different patients (endothelial vs. vascular smooth muscle vs. T2 pneumocyte, goblet)
- Abnormalities in gas exchange, mechanics and control all seen

- Speculation among friends:
  - I wonder if proteases which are released in Covid pneumonia are degrading parenchyma leading to high compliance and pneumothorax
  - I have a theory about extremes of HPV (gas exchange vs. infection control)
  - I have a theory about extremes of chemosensitivity (severe asthma vs. ARDS)
Post-ICU Syndrome: Implications in the COVID-19 era

Amy Bellinghausen, MD, PGY6, PCCM fellow, UCSD

I have no conflicts of interest to disclose
PICS

• 42 previously healthy male
• Influenza pneumonia
• ~65 days in intensive care
  • Extracorporeal Membrane Oxygenation (ECMO) x17 days
• Multiple procedures
  • Tracheostomy, gastrostomy, central & arterial lines, percutaneous cholecystostomy and chest tube
• Discharged to nursing home
• Unable to walk
ICU Acquired Weakness

Common
  • 38-51% of ARDS patients
  • Multifactorial
    • Myopathy and/or Polyneuropathy

[Graph showing proportion of patients alive over time from discharge]

[Bar chart showing change in weight (%)]
ICU Recovery Clinic: Mr. G

- 45M with very severe ARDS
  - Paralyzed & proned, sent to UCSD for ECMO
  - Ambulated on ventilator, awake & communicative
  - Extubated after 5 days at UCSD, +delirium

- ICU Recovery Clinic - 20 days post discharge
  - Minimal complaints
  - Wife reported “He’s a little more forgetful”
  - Previously worked as aerospace machinist

- Cognitive testing – MoCA 11/30 (nl ≥ 26)
  - Sent for neuropsych testing
  - Cognitive rehab referral
ICU Recovery Clinic Visit = Hub and Spoke

• **Check in**
  • Screen for anxiety, depression, PTSD, insomnia

• **Critical Care MD**
  • Hear the ICU story
  • Cognitive testing
  • Identify functional deficits

• **Critical Care Pharmacist**
  • Reconcile medications
  • Review vaccines

• Referrals as needed
• Letter sent to primary MD