Department of Anesthesiology and Critical Care

COVID-19: Physiology and Critical Care Management

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3.31.2020
Learning Objectives

- Describe the clinical epidemiology of COVID-19
- Understand the physiologic effects of COVID-19
- Explain the steps for providing critical care to a COVID-19 patient
What is COVID-19?

- Coronavirus Disease (COVID-19) is a respiratory tract infection
- It is caused by the virus: SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2
- Binds via the angiotensin-converting enzyme 2 (ACE2) receptor located on type II alveolar cells and intestinal epithelia

How is COVID-19 Defined?

- **Suspect case:**
  - A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease (e.g., cough, shortness of breath), AND with no other etiology that fully explains the clinical presentation AND a history of travel to or residence in a country/area or territory reporting local transmission of COVID-19 disease during the 14 days prior to symptom onset.
  - A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID19 case (see definition of contact) in the last 14 days prior to onset of symptoms;
  - A patient with severe acute respiratory infection (fever and at least one sign/symptom of respiratory disease (e.g., cough, shortness breath) AND requiring hospitalization AND with no other etiology that fully explains the clinical presentation

Source: World Health Organization
How is COVID-19 Defined?

- **Probable case**
  - A suspect case for whom testing for COVID-19 is inconclusive.
  - Inconclusive being the result of the test reported by the laboratory

- **Confirmed case**
  - A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.

Source: World Health Organization
What are the initial symptoms of COVID-19?
When would COVID-19 symptoms manifest after exposure?

When would COVID-19 symptoms manifest after exposure?

When would COVID-19 symptoms manifest after exposure?

What are the clinical syndromes associated with COVID-19?

- Uncomplicated upper respiratory tract viral infection or pneumonia
- Severe Pneumonia
- Acute Respiratory Distress Syndrome (ARDS)
- Sepsis and Septic Shock

### Timing

Within 1 week of a known clinical insult or new or worsening respiratory symptoms

### Chest imaging

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

### Oxygenation Impairment

<table>
<thead>
<tr>
<th>Level</th>
<th>PaO2/FIO2 Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>200 mmHg &lt; PaO2/FIO2 ≤300 mmHg</td>
</tr>
<tr>
<td>Moderate</td>
<td>100 mmHg &lt; PaO2/FIO2 ≤200 mmHg</td>
</tr>
<tr>
<td>Severe</td>
<td>PaO2/FIO2 ≤100 mmHg With PEEP or CPAP ≥5 cmH2O</td>
</tr>
</tbody>
</table>

Source: The ARDS Definition Task Force JAMA. 2012;307(23):2526-2533
What is the severity spectrum of COVID-19?

Mortality
- Overall - 2-3%
- Non-severe - 0.1%
- Severe, non-critical - 8%
- Critical – 40-60%

Who is at risk of severe COVID-19 illness?

- Older Age
- Chronic Lung Disease
- Heart Disease, Hypertension, Diabetes
- Immunosuppressed

Source: Center for Disease Control and Prevention
### What are the lab abnormalities associated with COVID-19?

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (N = 1099)</th>
<th>Disease Severity</th>
<th>Presence of Composite Primary End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nonsevere (N = 926)</td>
<td>Severe (N = 173)</td>
<td>Yes (N = 67)</td>
</tr>
<tr>
<td><strong>White-cell count</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR) — per mm³</td>
<td>4700 (3500–6000)</td>
<td>4900 (3800–6000)</td>
<td>3700 (3000–6200)</td>
</tr>
<tr>
<td>Distribution — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;10,000 per mm³</td>
<td>58/978 (5.9)</td>
<td>39/811 (4.8)</td>
<td>19/167 (11.4)</td>
</tr>
<tr>
<td>≤4000 per mm³</td>
<td>310/978 (33.7)</td>
<td>228/811 (28.1)</td>
<td>102/167 (61.1)</td>
</tr>
<tr>
<td><strong>Lymphocyte count</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR) — per mm³</td>
<td>1000 (700–1300)</td>
<td>1000 (800–1400)</td>
<td>800 (600–1000)</td>
</tr>
<tr>
<td>Distribution — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1500 per mm³</td>
<td>731/879 (83.2)</td>
<td>584/726 (80.4)</td>
<td>147/153 (96.1)</td>
</tr>
<tr>
<td><strong>Platelet count</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR) — per mm³</td>
<td>168,000 (132,000–207,000)</td>
<td>172,000 (139,000–212,000)</td>
<td>137,500 (99,000–179,500)</td>
</tr>
<tr>
<td>Distribution — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;150,000 per mm³</td>
<td>315/869 (36.2)</td>
<td>225/133 (31.6)</td>
<td>90/156 (57.7)</td>
</tr>
<tr>
<td>Median hemoglobin (IQR) — g/dL</td>
<td>13.4 (11.9–14.8)</td>
<td>13.5 (12.0–14.8)</td>
<td>12.8 (11.2–14.1)</td>
</tr>
</tbody>
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<tr>
<td></td>
<td></td>
<td>Nonsevere (N=926)</td>
<td>Severe (N=173)</td>
</tr>
<tr>
<td>Distribution of other findings — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-reactive protein ≥10 mg/liter</td>
<td>481/793 (60.7)</td>
<td>371/658 (56.4)</td>
<td>110/135 (81.5)</td>
</tr>
<tr>
<td>Procalcitonin ≥0.5 ng/ml</td>
<td>35/633 (5.5)</td>
<td>19/516 (3.7)</td>
<td>16/117 (13.7)</td>
</tr>
<tr>
<td>Lactate dehydrogenase ≥250 U/liter</td>
<td>277/675 (41.0)</td>
<td>205/551 (37.2)</td>
<td>72/124 (58.1)</td>
</tr>
<tr>
<td>Aspartate aminotransferase ≥40 U/liter</td>
<td>168/757 (22.2)</td>
<td>112/615 (18.2)</td>
<td>56/142 (39.4)</td>
</tr>
<tr>
<td>Alanine aminotransferase ≥40 U/liter</td>
<td>158/741 (21.3)</td>
<td>120/606 (19.8)</td>
<td>38/135 (28.1)</td>
</tr>
<tr>
<td>Total bilirubin ≥17.1 µmol/liter</td>
<td>76/722 (10.5)</td>
<td>59/594 (9.9)</td>
<td>17/128 (13.3)</td>
</tr>
<tr>
<td>Creatine kinase ≥200 U/liter</td>
<td>90/657 (13.7)</td>
<td>67/536 (12.5)</td>
<td>23/121 (19.0)</td>
</tr>
<tr>
<td>Creatinine ≥133 µmol/liter</td>
<td>12/752 (1.6)</td>
<td>6/614 (1.0)</td>
<td>6/138 (4.3)</td>
</tr>
<tr>
<td>D-dimer ≥0.5 mg/liter</td>
<td>260/560 (46.4)</td>
<td>195/451 (43.2)</td>
<td>65/109 (59.6)</td>
</tr>
</tbody>
</table>

What are the lab abnormalities associated with COVID-19?

Source:  
What are the imaging abnormalities associated with COVID-19?

What does lung ultrasound look like in COVID-19?

**Lung ultrasound**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickened pleural line</td>
<td><img src="image" alt="B lines" /></td>
</tr>
<tr>
<td>B lines (multifocal, discrete, or confluent)</td>
<td><img src="image" alt="Confluent B-lines" /></td>
</tr>
<tr>
<td>Confluent B lines</td>
<td></td>
</tr>
<tr>
<td>Small (centomeric) consolidations</td>
<td><img src="image" alt="Small consolidation" /></td>
</tr>
<tr>
<td>Both non-translobar and translobar consolidation</td>
<td></td>
</tr>
<tr>
<td>Pleural effusion is rare</td>
<td></td>
</tr>
<tr>
<td>Multilobar distribution of abnormalities</td>
<td></td>
</tr>
<tr>
<td>Focal B lines is the main feature in the early stage and in mild infection; alveolar interstitial syndrome is the main feature in the progressive stage and in critically ill patients; A lines can be found in the convalescence; pleural line thickening with uneven B lines can be seen in patients with pulmonary fibrosis</td>
<td><img src="image" alt="Larger consolidation" /></td>
</tr>
</tbody>
</table>

What are the imaging abnormalities associated with COVID-19?

What are the imaging abnormalities associated with COVID-19?

What happens to the lung in COVID-19?

What happens to the lungs in COVID-19?

Why does COVID-19 cause respiratory distress?

\[ P_{ALV} \]

- Resistance
- Lung compliance
- Chest wall compliance

Source: Nunn’s Respiratory Physiology
Why does COVID-19 cause respiratory distress?

- Work of Breathing: $P \times V$

- Work of Breathing can also be increased in CNS impairment, diaphragm weakness, and increased alveolar dead space

$P: 1/C_{RS} \times V + R_{AW} \times V'$
Why does COVID-19 cause respiratory distress?

Anatomic $V_D$ + Alveolar $V_D$

Why does COVID-19 cause respiratory distress?

- Alveolar flooding/consolidation
- Atelectasis
- Baby Lung

Source: Nunn’s Respiratory Physiology
What does COVID-19 cause hypoxemia?

What does COVID-19 cause hypoxemia?

- Mean Airway Pressure $\propto$ Oxygenation
  - Can increase inspiratory time, inspiratory pressure, and PEEP on the ventilator

- Don't Forget About Perfusion
  - Be Mindful of Alveolar Overdistention
  - Consider Microthrombi and Embolization
Evaluation and Diagnosis of COVID-19
How is COVID-19 Diagnosed?

- **Clinical suspicion is paramount**
  - Obtain contact and travel history

- **PCR assay**
  - Upper respiratory sample (e.g. nasopharyngeal swab) is recommended
  - In patients who are intubated, lower respiratory samples can be sample through endotracheal aspirate; bronchoscopy should be avoided due to risk of aerosolization
  - Consider resampling if assay is negative but clinical suspicion remains high

- Refer to UPHS guidelines: [http://accesspoint.uphs.upenn.edu/sites/preparedness/coronavirus](http://accesspoint.uphs.upenn.edu/sites/preparedness/coronavirus)

How is COVID-19 Diagnosed?

- Do not forget about other causes of respiratory disease
  - There are a number of circulating respiratory viruses, particularly influenza
  - Evaluate for bacterial infections
  - Consider non-respiratory causes (e.g. cardiac disease)
Critical Care Management of COVID-19
What are the guidelines for COVID-19 management?

Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected.

Interim guidance
13 March 2020

Coronavirus Disease 2019 (COVID-19)

Interim Clinical Guidance for Management of Patients withConfirmed Coronavirus Disease (COVID-19)

Summary of Recent Changes

Revisions were made on March 7, 2020, to reflect the following:

- Characteristics of patients with confirmed COVID-19 based on recent epidemiologic data from China, including characteristics of patients with COVID-19 admitted to the intensive care unit and data on pediatric cases
- Data regarding SARS-CoV-2 viral shedding among asymptomatic persons, and data from a recent report of viable SARS-CoV-2 isolation from stool
- Accessibility of investigational drug therapies for COVID-19 treatment through clinical trial enrollment in the United States
- Recently published pediatric surviving sepsis guidance
What is the most important part of COVID-19 treatment?

- All confirmed or suspected cases require isolation and airborne and contact precautions
- Providers need to use personal protective equipment, particularly with aerosolizing procedures (e.g. intubation, bronchoscopy, non-invasive ventilation)

Intubation Guidelines for Patients with known or suspected COVID-19 disease

1. Prior to intubation: Review and practice donning and doffing the appropriate respiratory protection, gloves, face shield, and clothing. Pay close attention to avoid self-contamination.
2. Before and after all procedures: Practice appropriate hand hygiene.

Clothing:
- Wear gowns, gloves, and a N95 or N95 fit-tested N95 respirator + face protector such as a shield.
- Use powered air-purifying respirators (PAPR) if tolerated.

Staffing:
- Limit the number of healthcare providers in the room where the patient is to be intubated.

Monitoring:
- Check standards, i.e., access, instruments, drugs, ventilator and suction.

Considerations:
- Avoid awake fiberoptic intubation unless specifically indicated.
- Atropine local anesthetic might aerosolize the virus. Consider using a video laryngoscope.

Plan for rapid sequence induction (RSI): RSI may need to be modified.
- If patient has very high alveolar arterial gradient and is unable to tolerate 30’s of apnea, or has a contraindication to succinylcholine. If manual ventilation is anticipated, small tidal volumes should be applied.

Oxygenation: 5 minutes of preoxygenation with oxygen 100% and RSI to avoid manual ventilation of patient’s lungs and potential aerosolization of virus from airways.

Check filters: Ensure bacterial viral high efficiency hydrophobic filter placed between facemask and breathing circuit or between facemask and resuscitation bag.

Intubate: Intubate and confirm correct position of tracheal tube.

Ventilate: Initiate mechanical ventilation and stabilize patient.

Clean equipment: All airway equipment must be decontaminated and disinfected according to appropriate hospital policies.
Remove protective equipment: Avoid touching hair or face before washing hands.
Before and after all procedures: Practice appropriate hand hygiene.
What is the next most important part of COVID-19 treatment?

- **Respiratory Support**
- **Hemodynamic Support**

Until immune response to the virus and recovery. May take 10-14 days.
How do we manage COVID-19 related respiratory failure?

- Management of severe COVID-19 is not different from management of most viral pneumonia causing respiratory failure
- The principal feature of patients with severe disease is ARDS
- Follow evidence-based treatment guidelines for ARDS

**Modifications to usual critical care**

- Admission of patients with suspected disease to private rooms when possible
- Use of medical face masks for symptomatic patients during assessment and transfer
- Maintain distancing of at least 2 m between patients
- Caution when using high-flow nasal oxygen or noninvasive ventilation due to risk of dispersion of aerosolized virus in the health care environment with poorly fitting masks
- Clinicians involved with aerosol-generating procedures should use additional airborne precautions including N95 respirators and eye protection

How do we manage COVID-19 related respiratory failure?

**Penn Medicine**

**COVID-19 (SARS-CoV-2):**

**EARLY CRITICAL CARE MANAGEMENT**

Last updated: 3/18/2020

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**EARLY INTUBATION**

- Early intubation if SpO₂ < 92% on 6L O₂
- NIV or high-flow nasal cannula **only in negative pressure rooms**. Time-limited trials (1-2 hrs) reasonable, but may not avoid ultimate intubation
- Call anesthesia as soon as possible
- Controlled intubation with appropriate PPE **in negative pressure room** (if patient can tolerate being moved)
- Use colorimetric CO₂ detector
- Anesthesia team should place orogastric tube
What are the evidence-based treatment for ARDS?

<table>
<thead>
<tr>
<th>Usual critical care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many patients with severe COVID-19 develop acute respiratory distress syndrome (ARDS). Evidence-based guidelines for ARDS in the context of COVID-19 include treatments such as</td>
</tr>
<tr>
<td>- Conservative intravenous fluid strategies</td>
</tr>
<tr>
<td>- Empirical early antibiotics for possible bacterial pneumonia</td>
</tr>
<tr>
<td>- Consideration for early invasive ventilation</td>
</tr>
<tr>
<td>- Lung-protective ventilation strategies</td>
</tr>
<tr>
<td>- Periodic prone positioning during mechanical ventilation</td>
</tr>
<tr>
<td>- Consideration of extracorporeal membrane oxygenation</td>
</tr>
</tbody>
</table>

What are lung-protective ventilation strategies?

PART I: 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 $V_T = 8 \text{ ml/kg PBW}$
4. Reduce $V_T$ by 1 ml/kg at intervals ≤ 2 hours until $V_T = 6\text{ml/kg PBW}$.
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 below.

General targets: $\text{Spo2 } 90-95\%$, $\text{paO}_2 60-80 \text{ mmHg}$, $P_{\text{plat}} \leq 30 \text{ cmH}_2\text{O}$, $\text{pH} > 7.25$

Source: ARDS Net:
Why is lung-protective ventilation important?

Mortality (Percent)

- 6 ml/kg IBW
- 12 ml/kg IBW

Reduces STRAIN: *tidal volume in relation to the functional residual capacity*

Reduces STRESS: *airway pressure in relation to pleural pressure*

Source: ARDS Net. NEJM 2000
What are the consequences of lung-protective ventilation?

▶ Hypercarbia
  - Lower Minute Ventilation
  - Ineffective ventilation – increased alveolar dead space
  - Ineffective ventilation – AutoPEEP from high RR

▶ Ventilator dyssynchrony
  - Potential need for increased sedation

▶ Potential for atelectasis

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**pH GOAL: 7.30-7.45**

**Acidosis Management: (pH < 7.30)**

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_I may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).

May give NaHCO₃

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Source: ARDS Net:
What if the plateau pressures are too high?

**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 $P_{plat} > 30 \text{ cm H}_2\text{O}$:** decrease $V_T$ by 1 ml/kg steps (minimum = 4 ml/kg).
- **If $P_{plat} < 25 \text{ cm H}_2\text{O}$ and $V_T < 6 \text{ ml/kg}$,** increase $V_T$ by 1 ml/kg until $P_{plat} > 25 \text{ cm H}_2\text{O}$ or $V_T = 6 \text{ ml/kg}$.
- **If $P_{plat} < 30$ and breath stacking or dys-synchrony occurs:** may increase $V_T$ in 1 ml/kg increments to 7 or 8 ml/kg if $P_{plat}$ remains $\leq 30 \text{ cm H}_2\text{O}$.

Source: ARDS Net:
How we can treat alveolar collapse and shunt?

Pre-recruitment

PEEP = 0 cmH20

Recruitment Maneuver

Post-recruitment

PEEP = 12 cmH20
Where should we set PEEP?

Be mindful of the potential adverse effects of PEEP: hypotension, hypoxemia, dead space
What other maneuvers are helpful to improve outcomes?

Start with lung-protective ventilation

If oxygenation remains low, consider with consultation →

Titrate PEEP/RM to optimize oxygenation + compliance

Neuromuscular Blockade

Prone Position

Inhaled Vasodilators

ECMO
Why would prone position be beneficial?

Source: (1) Guérin C et al. N Engl J Med 2013;368:2159-2168; (2) UpToDate
Prone ventilation for adult patients with acute respiratory distress syndrome
What are other management decisions for COVID-19?

**PART II: WEANING**

A. **Conduct a SPONTANEOUS BREATHING TRIAL daily when:**
   1. $\text{FiO}_2 \leq 0.40$ and $\text{PEEP} \leq 8$ OR $\text{FiO}_2 \leq 0.50$ and $\text{PEEP} \leq 5$.
   2. PEEP and $\text{FiO}_2$ ≤ values of previous day.
   3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
   4. Systolic BP ≥ 90 mmHg without vasopressor support.
   5. No neuromuscular blocking agents or blockade.

**ASSESS:** tolerance of SBT based on hemodynamics and respiratory mechanics

**CAUTION:** Improvements in oxygenation may not correlate with stabilization of inflammation

**CONSIDER:** extubation to helmet CPAP to limit aerosolization and maintain recruitment if available
What are other management decisions for COVID-19?

- Deeper sedation may be required during initiation resuscitation to facilitate ventilator tolerance
- Use of sedation protocols allows quicker liberation from the ventilator

Source: DJonghe et al Crit Care 2005; 33: 120-127
What are other management decisions for COVID-19?

- If persistent hypotension, be mindful that COVID-19 may cause cytokine storm syndrome and subsequent cardiogenic shock.
- Maintain high suspicion and use echocardiography along with EKG, lactate, capillary refill time and central venous oxygenation saturation.

**STABILIZATION**

- Insert arterial line and central line for vasopressors and blood draws as soon as possible (keep lines on one side to facilitate proning)
- Obtain norepinephrine so it can be readily started & escalated
- Assess intravascular volume to guide fluid management
- Early enteral nutrition is important

Ultrasound for IVC measurement
Central Venous Pressure
Dynamic Parameters (e.g. PPV) if appropriate

General targets: MAP 60-65 mmHg, Lactate < 2mmol/L, CRT < 3 secs
What are other management decisions for COVID-19?

- Consultation with Infectious Disease
- Low threshold for initiation of empiric antibiotics in severe disease
- Anti-viral therapy as dictated by ID protocols
- Follow microbiology studies

MEDICATION ORDERS

- Antiviral medications incompatible with Dobhoff tube; orogastric Salem sump tubes preferred
- When ordering, decrease frequency where possible to decrease contacts:
  - Daily enoxaparin preferred for DVT prophylaxis; SQ heparin at Q12 hours instead of Q8 hours
  - Daily stress ulcer prophylaxis, not Q12 hours
  - Limit insulin infusions (use Q6 hour SSI)
- Order MDIs instead of nebs