MANAGEMENT OF RESPIRATORY FAILURE IN COVID PATIENTS

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LEARNING OBJECTIVES

• Summarize the Etiology and Pathophysiology of Respiratory Failure in Covid Patients
• Review General Clinical Strategies in Treating Covid Patients
• Evaluate Non-invasive Methods for Treating Respiratory Failure in Covid Disease
• Explore Various Invasive Strategies for Oxygenating and Ventilating Covid Patients
• Describe Adjunctive Therapies
• Furnish Selected Related Resources
DISCLAIMER:

This Presentation Represents a Combination of the Research Evidence, Complemented by Anecdotal Observation and Direct Experience. Research is Still Underway and Some of the Practices in Treating Covid Patients and Contents of This Presentation May Change Over Time as a Result.
COVID 19 -- RISK FACTORS

Serious medical conditions that increase the risk of serious illness from COVID-19 include:

- Serious heart diseases, such as heart failure, coronary artery disease or cardiomyopathy
- Cancer
- Chronic obstructive pulmonary disease (COPD)
- Type 2 diabetes
- Severe obesity
- Chronic kidney disease
- Sickle cell disease
- Weakened immune system from solid organ transplants

Other conditions may increase the risk of serious illness, such as:

- Asthma
- Liver disease
- Chronic lung diseases such as cystic fibrosis
- Brain and nervous system conditions
- Weakened immune system from bone marrow transplant, HIV or some medications
- Type 1 diabetes
- High blood pressure
ETIOLOGY OF COVID

• Infection with the new coronavirus (severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2) causes coronavirus disease 2019 (COVID-19).
• The virus appears to spread easily among people, and more continues to be discovered over time about how it spreads.
• Data has shown that it spreads from person to person mainly via respiratory droplets among those in close contact (within about 6 feet, or 2 meters).
• The virus then replicates…
• It can also spread if a person touches a surface with the virus on it and then touches his or her mouth, nose or eyes, although this isn't considered to be a main way it spreads.
COVID-19
HOW DOES IT AFFECT YOU?

Coronavirus Disease 2019 (COVID-19) is a pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2, also called SARS-CoV-2. Despite the widespread awareness regarding COVID-19, many are still unsure about how it affects the human body.

Left Lung
Trachea
Bronchus
Alveoli (SQ alveoli)

SARS-CoV-2 enters the body through the mouth, nose, or eyes and travels down the airway in the lungs. Alveoli are tiny sacs of air where gas exchange occurs.

Healthy

Gas Exchange
Each cap of air or alveolus is lined with capillaries where red blood cells release oxygen into the alveolus (O2) and carbon dioxide diffuses from the alveolus into the capillaries (CO2). This process is called diffusion. Type I alveolar cells facilitate gas exchange. Type II cells are thin enough that the oxygen can pass right through, and Type II cells secrete surfactant—a substance that lines the alveolus and prevents it from collapsing.

Infected

Viral Infection
The spike proteins covering the coronavirus bind ACE2 receptors primarily on type II alveolar cells, allowing the virus to infect the cells. The RNA “jumps” the cell, telling it to assemble many more copies of the virus and release them into the alveolus. The host immune response can respond to the infected cells and the new contagiousness infect neighboring cells.

Moderate

Impaired Gas Exchange
When the immune system accumulates the area of infection, it also kills healthy alveolar cells. This results in three things that hinder gas exchange:

1. Alveolar collapse due to loss of surfactant from type II cells
2. Less oxygen enters the bloodstream due to lack of Type II cells
3. More fluid enters the alveoli

Severe

Impaired Gas Exchange
When the immune system accumulates the area of infection, it also kills healthy alveolar cells. This results in three things that hinder gas exchange:

1. Alveolar collapse due to loss of surfactant from type II cells
2. Less oxygen enters the bloodstream due to lack of Type II cells
3. More fluid enters the alveoli

Immune Response

Macrophages release cytokines that activate inflammatory cells, releasing inflammatory cytokines and increasing the production of chemokines.

Fluid accumulates inside the alveoli.

Type I and II cells are destroyed, leading to collapse of the alveolus and causing Acute Respiratory Distress Syndrome (ARDS).
VARIABLE SEVERITY OF COVID – STILL SOMEWHAT A MYSTERY

2.3% of all cases died
1,023 of the 44,415 infected people, for which the breakdown is shown on the right, died. The case fatality rate is therefore 2.3%.

5% Critical cases
Critical cases include patients who suffered respiratory failure, septic shock, and/or multiple organ dysfunction/failure.

14% Severe cases
Severe cases include patients suffer from shortness of breath, respiratory frequency ≥ 30/minute, blood oxygen saturation ≤ 93%, PaO2/FiO2 ratio < 300, and/or lung infiltrates > 50% within 24–48 hours.

81% Mild cases
Mild cases include all patients without pneumonia or cases of mild pneumonia.

Cases that were not identified and not diagnosed
COVID 19
LUNG --
POST-MORTEM
General Clinical Strategies in Treating Covid Patients

- **Prevention**: Social distancing, Isolation & Quarantine

- **Medications**:
  - *Remdesivir* may offer some clinical advantage in patients with moderate to mild disease, but less so in the especially sick Covid patients.
  - Properly timed *steroids* seem to help some patients with the inflammatory phase of the disease called the cytokine storm.
  - Convalescent plasma (*obtained from recovered Covid 19 patients*) demonstrates a potential survival benefit and low risk in small studies.
  - Monoclonal Antibody infusion -
    - Indications: treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.
    - Dosage—1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous infusion over at least 60 minutes.
  - *Anticoagulants* may aid the approximately 20-30% of those with severe Covid disease who develop concomitant coagulopathies.
  - Though there was early hope for *hydroxychloroquine*, much of the enthusiasm has faded due to insufficient scientific evidence.

- **Respiratory Care**:
  - Oxygen Therapy
    - Low-Flow
    - High Flow
  - Non-Invasive Positive Pressure Ventilation (NIPPV)
  - Intubation & Invasive Mechanical Ventilation
  - ECMO
  - Adjunctive Therapies
    - ARDs-NET
    - Prone Positioning
    - Inhaled Pulmonary Vasodilators
    - Other Inhaled Agents
      - Bronchodilators
      - Mucolytics
THE OXYGEN THERAPY ARSENAL – COVID 19

1. NC @ 6 LPM
2. Venturi mask up to 50%
3. NC + Non-rebreather
4. HFNC
5. NIPPV: CPAP
6. Intubation
Covid 19 — Respiratory Care Algorithm—Earlier Intubation
Non-invasive Methods for Treating Respiratory Failure in Covid Disease

- Low Flow Oxygen
- High Flow Oxygen
- Non-invasive Ventilation
- Adjunctive Respiratory Therapies
  - Inhaled Vasodilators
    - INO
    - Prostacyclin
  - Prone Positioning
- Combining Strategies
LOW-FLOW OXYGEN

• Device: Nasal cannula 1 – 7 LPM
• Population: Mild to moderate hypoxemia and respiratory distress with Covid 19.
• Advantages:
  – Comfort & Ease of Use
  – Accessibility
  – Can be done in alternate sites including home.
  – Can be combined with other O2 devices (e.g., NRM)
• Limitations: Only Effective in treating mild/moderate disease.
HIGH FLOW OXYGEN THERAPY

- Devices:
  - Non-rebreather
  - High-Flow Nasal Cannula
- Advantages:
  - May avert intubation and mechanical ventilation in patients with mild/moderate disease.
  - Easy and relatively simple to set up.
- Disadvantages:
  - May delay but not eliminate intubation and mechanical ventilation, especially in those with moderate to severe disease.
  - Period checks needed risking clinician exposure.
  - Flows should be kept to a maximum of 30-35 LPM to reduce clinician risk due to aerosol.
  - Findings/Conclusion: **HFNO may be effective for Covid-2019 patients with mild to moderate acute hypoxemic respiratory failure.**
    - However, high-flow nasal oxygen failure was associated with a poor prognosis.
    - Male and lower oxygenation at admission were the two strong predictors of high-flow nasal oxygen failure.
NON-INVASIVE VENTILATION

• Population: Covid 19 patients with moderate hypoxemic and hypercapneic respiratory failure, and prohibitive breathing pattern/rate.

• Advantages:
  • May avert intubation and mechanical ventilation in patients with mild/moderate disease.

• Disadvantages:
  • May delay but not eliminate intubation and mechanical ventilation, especially in those with moderate to severe disease.
  • Not well tolerated by some patients.
  • Interference with adjunctive therapy such as proning, oral medication admin, nutrition.
  • Period checks needed risking clinician exposure.
  • Clinician risk due to aerosol.

• Citation: Honore P, Gutierrez L, Kugener L, et al., Compared to NIPPV, HFNC is more dangerous regarding aerosol dispersion and contamination of healthcare personnel: we are not sure. Crit Care. 2020 Aug 4;24(1):482.
HELMET NIPPV/CPAP

- Not (yet) approved for use in the US. But widely used elsewhere!
- Design: Case Series in a Canadian Hospital
- Findings:
  - For patients unable to tolerate facemask, NIPPV helmet provides an alternate interface.
  - In COVID-19 patients, the helmet interface may reduce the risk of virus exposure to health care workers from aerosolization.
  - Based on this experience, we recommend that helmet NIPPV be considered for the management of patients with COVID-19, whether the goal is to prevent immediate intubation or avoid post-extubation respiratory failure.
  - Randomized studies are needed to definitively validate the use of helmet NIPPV in this population.
COVID 19 INTUBATION CHECKLIST

• Purpose: Creation of a checklist for use during high-risk intubations of COVID-19 patients, which serves as a pragmatic bedside tool for clinicians

• Personnel: An intubating physician, respiratory therapist, and 2 nurses (ie, a code nurse at bedside and a Virtual Critical Care nurse working remotely).

• Medications:
  – Availability of additional neuromuscular blocking agents were added to the RSI kit.
  – The correct doses of all medications in the RSI kit were not known to everyone involved. An ICU pharmacist created simple weight-based dosing charts for all RSI medications

• Equipment: ICU respiratory therapists were trained on:
  – Intubation assisting, including the avoidance of manual ventilation, especially without a filter in place.
  – Appropriate assembly of the ventilator circuit, using high-efficiency particulate air filters attached to the airway and the importance of having all necessary equipment in the patient’s room at the outset!

• After intubation was completed, an immediate debrief should be conducted where possible. Intermittent debriefing should be done as an alternative or adjunctive.

TIMING OF INTUBATION IN COVID PATIENTS

• Some Covid patients were remarkably tolerant of moderate hypoxemia.
• Some patients who were tolerant of hypoxemia quickly decompensated and required emergent intubation.
• This caused the timing of intubation for Covid patients to be questioned.

• Hernadnez-Romieu, et al, (2020)
  • Retrospective Cohort Study of 231 patients admitted to ICU with Covid-19
  • Mortality did not differ by time of intubation (< 8 hrs, 8-24 Hrs> 24 hrs)

  • Design: Retrospective, Multicenter trial of 39 Covid-19 Patients
    – Findings: Early intubation was not associated with improved survival. This result may help in the efficient allocation of limited medical resources, such as ventilators.
Mortality of invasively ventilated Covid-19 patients was high and it was not easy to extubate. This raised concerns that HFNC & NIV were underutilized. This article takes a practical approach in describing how to use these techniques.
INVASIVE VENTILATORY STRATEGIES

• Modes
• Ventilation
  – VT
  – RR
  – Permissive Hypercapnea
• Oxygenation
  – FIO2
  – PEEP
• Adjunctive Maneuvers
  – Recruitment Maneuvers
ARDSNET: TIDAL VOLUMES AND PLATEAU PRESSURES

- Previously supported for use of ARDs in non-Covid patients.
- Therefore, is/was commonly used in Covid-19 Patients with ARDs.
- Start with a VT of 6-8 mls / Kg, and titrate as low as 4 mls / Kg to keep Plateau's ≤ 30.

**PLATEAU PRESSURE GOAL: ≤ 30 cm H₂O**
Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or VT.
- If Pplat > 30 cm H₂O: decrease VT by 1ml/kg steps (minimum = 4 ml/kg).
- If Pplat < 25 cm H₂O and VT< 6 ml/kg, increase VT by 1 ml/kg until Pplat > 25 cm H₂O or VT = 6 ml/kg.
- If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase VT in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H₂O.
ARDSNET: FIO2 AND PEEP

- Again, previously supported for use of ARDs in non-Covid patients.
ADJUSTING PEEP LEVELS

Pressure
Volume
UDP
LIP
"Best" PEEP Level
VENTILATOR SHARING FOR COVID 19

- **Definition:** Using one mechanical ventilator to ventilate more than one patient at a time.
- Theoretically possible; but at a minimum, *impractical and possibly outright unsafe.*
- Inadequate ability to individualize volumes, pressures, ventilation and oxygenation.
  - **Design:** Laboratory “Bench” research using specialized valves and circuits.
  - **Finding:** Of the strategies considered, shared PCV, with the inclusion of in-line pressure-relief valves in the individual inspiratory and expiratory limbs, offers the greatest degree of safety and lowest risk of catastrophic mechanical interactions.
Adjunctive Respiratory Strategies –
**PRONE POSITIONING IN MECHANICAL VENTILATION**

- Much Recent Research in proning Covid patients!
  
  - **Findings:** *Prone positioning is likely to reduce mortality* among patients with **severe ARDS** when applied for at least 12 hours daily.
  - Qualifications:
    - Do it early: within 48 hours on ARDS onset
    - Devise a protocol in advance. ETT dislodgment is a risk!
PRONE POSITIONING – SPONTANEOUS BREATHING PATIENTS

  – Study Design: Case Series of 10 Covid-19 patients in respiratory failure
  – Outcomes:
    • *Oxygenation rapidly improved after prone positioning*, and at 1 hour after assuming a prone position, median oxygen saturations had increased from 94% (IQR, 91–95%) to 98% (IQR, 97–99%)
    • *Patients reported improved dyspnea* with prone positioning.
    • Seven of the 10 patients did not require escalation of respiratory care.
    • Eight of the 10 patients did not require intubation.
PRONE POSITIONING – MECHANICALLY VENTILATED PATIENTS

• Citation: Sherlhamer M, Wesson P, Solari I, et al, Prone Positioning in Moderate to Severe Acute Respiratory Distress Syndrome due to COVID-19: A Cohort Study and Analysis of Physiology, Res Sq. 2020 Aug 17;rs.3.rs-56281.

  – Study Design: A cohort study at a New York City hospital of 335 Covid 19 patients who were intubated and mechanically ventilated with moderate to severe ARDS due to COVID-19.

  – Findings:
    • Prone positioning in patients with moderate to severe ARDS due to COVID-19 is associated with reduced mortality and improved physiologic parameters.
    • One in-hospital death could be averted for every eight patients treated.
RECRUITMENT MANEUVERS

• No studies which specially examine Lung Recruitment Maneuvers (LRM) in mechanically ventilated Covid patients.
• However, there is some evidence on their effectives in ARDS.

• LRM:
  – 30/30 or 40/40 – 30 cm H2O of PEEP for 30 seconds
  – APRV: Alternate 7.5 seconds at 40 cms followed by 7.5 seconds at 30 cm H2O for up to five minutes.

  – Design: Meta analysis of ten trials including 3,025 patients were analyzed.
  – Results:
    • LRM do not produce significant reduction of mortality in patients with ARDS.
    • However, they may shorten the length of hospital stay and improve oxygenation on the third day.
ADJUNCTIVE THERAPY – INHALED VASODILATORS

• Inhaled Nitric Oxide (INO)
• Prostacyclin
INO AND COVID

• Spontaneous Breathing Patients:
  - **Design:** Case series of 39 spontaneously breathing patients with moderate hypoxemia and Covid 19.
  - **Findings:** A total of 21 patients (53.9%) did not require invasive mechanical ventilation after treatment with iNO. Of the 21 patients, 20 were successfully discharged and there was 1 death.
  - **Discussion:**
    - These findings suggest that iNO therapy may have a role in preventing progression of hypoxic respiratory failure in Covid-19 patients.
    - Some researchers hypothesized that iNO may not simply improve oxygenation, but also potentially have an antiviral mechanism of action.
  - **Citation:** Parikh R, Wilson, Weinberg J, et al., Inhaled nitric oxide treatment in spontaneously breathing COVID-19 patients, Ther Adv Respir Dis, Jan-Dec 2020;14:175346620933510.

• Mechanically Ventilated Patients:
  - **Design:** Case Series of 10 patients with severe hypoxemia due to Covid
  - **Background:**
    - International guidelines, and experts in the field, all suggest considering iNO even for refractory hypoxemia due to COVID-19.
    - However, there are no strong clinical data to support this indication.
  - **Findings/Conclusion:** In this small series of 10 patients with severe hypoxemia due to COVID-19, it did not significantly improve arterial oxygenation.
  - **Citation:** Ferrari M, Santini A, Protti A, J Crit Care: Inhaled nitric oxide in mechanically ventilated patients with COVID-19. 2020 Aug 11;60:159-160
INO IN PREGNANT COVID PATIENTS

- **Design:** Case Series of six pregnant women with Covid treated at Mass. General
- **Method:** To treat pregnant patients meeting criteria for severe or critical COVID-19 with high-dose (160–200 ppm) nitric oxide by mask twice daily and report on their clinical response.
- **Findings:**
  - An increase in systemic oxygenation in each administration session and reduction of tachypnea in all patients in each session.
  - Three patients delivered a total of four neonates during hospitalization. At 28-day follow-up, all three patients were home and their newborns were in good condition. Three of the six patients remain pregnant after hospital discharge.
- **Conclusion:** Nitric oxide at 160–200 ppm is easy to use, appears to be well tolerated, and might be of benefit in pregnant patients with COVID-19 with hypoxic respiratory failure.
- **Citation:** Safaee Fakhr B; Wiegand S; Pinciroli R. et al, High Concentrations of Nitric Oxide Inhalation Therapy in Pregnant Patients With Severe Coronavirus Disease 2019 (COVID-19), Obstetrics & Gynecology: August 26, 2020
COVID 19 & INHALED EPOPROSTENOL (FLOLAN)

- Review of pharmacological therapeutics in treating mechanically ventilated Covid 19 patients suggests that Flolan should be considered in cases with refractory oxygenation.
- Should be administered with a vibrating mesh system in the ventilator circuit to minimize contaminating particles.
- Caution: Replacing expiratory filters in the ventilator circuit (breaking the circuit) to protect the ventilator from sticky glycine buffer may cause risks which outweigh benefits.
EXTRA CORPOREAL MEMBRANE OXYGENATION (ECMO)

• **Definition/Description:** ECMO involves bypassing the heart and lungs and having Oxygen added and CO2 extracted by a perfusion machine.

• In many states, though not NJ, Respiratory Therapists can perform ECMO and operate associated equipment.

• Currently, there is **insufficient evidence to show that ECMO offers a clinical advantage** in treating respiratory failure in Covid patients.


• **Findings:** Many patients have already been supported with ECMO during the current COVID-19 pandemic, and it is likely that many more may receive ECMO support, although, at this point, the role of **ECMO in COVID-19-related cardiopulmonary failure is unclear.**
**OTHER MEDICATIONS**

- **Inhaled Medications:**
  - Bronchodilators
    - SABA’s such as Albuterol
    - Atrovent
  - Mucolytics
    - 10% or 20% Mucomyst
    - 3% or 7% Saline to liquify secretions

- **Sedation with Mechanical Ventilation:** Versed, Propofol, Precedex.
  - Target a RASS -3 to -4 initially.
  - When respiratory failure improves and weaning is possible, lighten sedation for a RASS of -1 to -2.

- **Paralytics**
  - To facilitate ventilator synchrony and reduce ventilator pressures.
COMBINING STRATEGIES:

• Systemic Medications:
  – Antivirals, convalescent plasma, steroids, vaccines
• Spontaneously Breathing Patients (in addition to systemic meds) :
  – Oxygen Therapy + Pulmonary Vasodilators
  – Oxygen Therapy + Prone Positioning
• Mechanically Ventilated Patients (in addition to systemic meds)
  – ARDs-Net + Prone positioning + LRM + Pulmonary Vasodilators + Paralysis + Mucolytics + Systemic treatments (e.g., Anti-virals)
More Work to Be Done

• Much Yet to Be Discovered About Covid
  – Etiology - How it is transmitted, especially non-aerosol transmission..
  – Pathophysiology – Why some are Asymptomatic, and Others are so Vulnerable
  – Treatment – Most Therapies are only Marginally Effective.
  – Prevention—Vaccines?

• Many Articles were Submitted and Published Prematurely and had to be Retracted.

• Many Articles are Smaller and Less Scientifically Rigorous than Large, Randomized Control Trials (RCTs).

• Can Clinical Strategies be Combined to Produce a synergistic effect?

• If there is Another Wave, are we Better Prepared?

• What are the Longer-Term Impacts on our Healthcare Workforce and Society?
SELECTED REFERENCES


Honore P, Gutierrez L, Kugener L, et al., Compared to NIPPV, HFNC is more dangerous regarding aerosol dispersion and contamination of healthcare personnel: we are not sure. Crit Care. 2020 Aug 4;24(1):482.

• Johns Hopkins University -- Coronavirus Information: https://covidinfo.jhu.edu/


