COVID-19

Treatment of Severe Disease

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Topics for discussion

1. Recognition of severe disease and ICU triage
2. Modalities of respiratory support and respiratory monitoring
3. Intubation of patients with severe COVID-19
4. Ventilator management of severe COVID ARDS
5. Prone positioning, intubated and non-intubated
6. General critical care for severe COVID-19
7. Preparation for a COVID-19 surge
Case 1

- 59-year-old man with cough and fever for six days. Son and daughter-in-law were sick a week ago but recovered. No past medical history. Works as a cook, never smoker, no drugs or alcohol.
- T 38, HR 105/min SBP 130/80 SpO2 95% on 2L NC oxygen
- Looks well, able to walk, talk and eat.
- COVID screen positive
- Ferritin 2400, CRP 17, D-dimer 1.3
Triage

• Admitted to hospital because of hypoxia
• Triaged to general medical floor
• Treated with Tylenol, cough syrup and oxygen
• Enoxaparin 40 mg QD for DVT prophylaxis
• ID consultation for Remdesivir
Day 2

• Patient agrees for Remdesivir treatment
• Patient reports that he feels the same
• Oxygen requirement is now 3-4 L/min, O2 saturation 90-95%
• “does not appear to have increased work of breathing”
• Continues to have high temperatures
• Tachycardic 100-110/min
• Repeat CRP, ferritin and D-dimer are increase by almost 2X
Day 3

- MICU consulted for dyspnea and hypoxia requiring 5L/min oxygen with SpO2 88-90%
- MICU “RR 30/min, 15L/min NRM with SpO2 90%, unable to speak full sentences, transfer to MICU for high flow oxygen and respiratory monitoring. US DVT”
Hospital course

- Specific therapy
  - Remdesivir x 10 days, Tocilizumab x 1
  - Convalescent plasma x 1
  - Full dose anticoagulation for chronic DVT
  - Antibiotics for a secondary UTI
  - SC insulin for new diagnosis of diabetes

- Respiratory support
  - High flow oxygen 60L/min
  - Weaned down to nasal cannula
  - Awake prone position was used intermittently as tolerated by the patient
  - Talking and eating throughout his stay

- Discharged home on anticoagulation and oral anti-diabetics after two weeks in the hospital
Case 2

• HPI: 48-year-old female with history of obesity and diabetes mellitus. One week of fever, and myalgias, multiple sick family members.
• Exam: T 39, HR 90, RR 24/min, SPO2 88% RA, 95% on 2L/min, obese, no distress, talking full sentences
• Labs: COVID positive, high ferritin 1000, D-dimer of 1.94, CRP 19
• CXR: Bilateral infiltrates
• US DVT negative
Hospital course

• Treated with CPAP 10, FiO2 60%
• Intermittent prone positioning as tolerated during NIV breaks
• Tocilizumab and hydroxychloroquine
• Full recovery and discharged to home
Case 1&2 – Topics for discussion

1. Recognition of severe disease and ICU triage
2. Modalities of respiratory support and respiratory monitoring
3. Awake prone positioning
Recognition of severe disease

- Physiologic parameters
  - HR, RR, Pulse oximetry
  - “work of breathing”
- Chest X-findings
- Laboratory markers (ferritin, D-dimer, CRP)
- Age and co-morbidities
ICU triage for severe disease

- ICU triage is always context sensitive
- Strong considerations for ICU triage
  - 6L/min NC oxygen for SpO2 92%
  - RR > 30 /min (manually counted for 1 minute)
  - Excessive work of breathing
  - Rapidly increasing oxygen requirements
  - Clinician gestalt
- Formal policy regarding ICU triage is helpful
  - Removes decision fatigue
OXYGEN DELIVERY SYSTEMS

Device: Nasal Cannula
Flow: 1 - 6 L/min
FiO2: 25 - 40%
(~4%/L of flow)

Device: Face Mask
Flow: 5 - 10 L/min
FiO2: 40 - 60%

Device: Face Tent
Flow: 10 - 15 L/min
FiO2: ~40%

Device: Venturi Mask
Flow: 2 - 15 L/min
(based on valve)
FiO2: 24 - 60%
(precisely controlled)

Device: Non-Rebreather
Flow: 10 - 15 L/min
FiO2: 80 - 95%

Device: High Flow Nasal Cannula
Flow: up to 60 L/min
FiO2: 21 - 100%
A: FiO2 25%, SpO2 93-94% pO2 75 mm Hg
B: FiO2 25%, SpO2 90%, pO2 62
Pulse oximetry went down by 3 or 4%
But partial pressure of oxygen went down by 17%

Respiratory Monitoring by Pulse Oximetry
High flow oxygen

- High flow oxygen system
  - 40-60L/min with heated and humidified nasal prongs
  - FiO2 titrated independent of air flow.
- FLORALI trial – acute hypoxic respiratory failure
- Comfort, mild CPAP effect, easier to prone
Non-invasive ventilation

- CPAP or BiPAP
- Helps oxygenation, relieve work of breathing
- May help overcome upper airway obstruction in obese patients
- Concern for tolerability over the long term
- Aspiration risk
- Ventilator induced lung injury by excessively large tidal volumes under high pressure
- May "delay" intubation
Awake prone positioning

- PROSEVA 2013 for intubated patients
- Multiple case series described of awake proning in COVID-19
- Benefits oxygenation, redistributes inflammation
- Dependent on patient cooperation and tolerability
- Intensive Care Society – timed position changes for COVID-19
Awake prone positioning
Case 3

• HPI: 70-year-old man with history of poorly controlled diabetes and hypertension presented with two weeks of fever, sore throat and myalgias. Now with cough and dyspnea.

• Exam: T 37, HR 90, SpO2 82% (RA, 95% on 2L/min NC), BP 140/80. Looked “ill”, normal size and built, bilateral crackles on auscultation. Talking full sentences, not using accessory muscles

• Labs: COVID screen positive, TWC 15, lymphocyte count was low, Glucose 250, Lactate 3.5, Ferritin 16 mg/ml, CRP 5, D-dimer 0.8
Day 2-4

- Treated with hydroxychloroquine, remdesivir IV
- Oxygen support escalated to 6L/min nasal cannula
- Worsened dyspnea and tachypnea
- L sided pleuritic chest pain
- Moved to MICU, started on NRM oxygen at 10L/min
- Awake prone positioning – poorly tolerated
- CT Angiogram to rule out PE
Day 5

- Patient is intubated and placed on mechanical ventilation
- Low tidal volume ventilation with permissive hypercapnia
- Very severely hypoxic even on 100% FiO2
- Deep sedation, neuromuscular blockade
- PEEP titration is done by driving pressure
- Plateau pressures < 28, measured lung compliance is lower normal
- After an hour, patient starts to desaturate, worsened hemodynamics
- Peak pressure alarms sounding, lung US suggests PTX
Hospital Course

- Develops severe RV failure and refractory shock, multiorgan dysfunction, renal failure, possibly bacterial superinfection, stress ulcer bleeding
- Treated with ventilatory support, paralytics, INO2, chest tube drainage
- Vasopressors, CRRT, anticoagulation with low dose heparin
- Remdesivir, Tocilizumab and HCQ
- Broad spectrum antibiotics
- IV steroids
- Dies after one month of ICU stay
Case 4

- 63-year-old lady with past history of diabetes mellitus and obesity admitted with one week of cough and fevers. Multiple family members with COVID-19. Husband hospitalized with severe disease.
- T 39, HR 100/min, RR 30/min, SPO2 90% on 6L/min
- Admitted to ICU, subsequently intubated, started on MV
Case 3 & 4 - Topics of discussion

3. Intubation of patients with severe COVID-19
4. Ventilator management of severe COVID ARDS
5. Prone positioning, intubated and non-intubated
6. General critical care for severe COVID-19
The decision to intubate

- Composite assessment
  - Vital signs
  - Clinical assessment
  - Patient views and preferences
  - Resources available
- Never a consequence of pre-determined indices
- Failure of alternatives
- "If you are considering intubation, and the patient cannot talk you out of it, intubate them"
- Does intubation and mechanical ventilation change improve the trajectory of disease in the absence of a disease modifying treatment?
The assumptions behind the benefit of IMV

“Early” intubation
- Use traditional indices for and paradigms for institution of IMV, especially hypoxia
- Proponents argue lower mortality in ventilated patients
- Avoids P-SILI
- “do something now before it’s too late”

“Late” intubation
- Permissive hypoxia – “silent- happy hypoxic”
- Proponents argue lower overall ICU mortality
- Avoids antecedent risks of invasive life-support system
- “if it ain’t broke, don’t fix it”

## Rates of IMV

Comparison of the rates of IMV across a sample of epidemiological actions


<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Hospitalized (n)</th>
<th>ICU Admission (n)</th>
<th>Invasive Mechanical Ventilation</th>
<th>Percent of ICU Patients</th>
<th>Percent of Hospitalized Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Richardson 4</td>
<td>New York City</td>
<td>5,700</td>
<td>1,281</td>
<td>1,151</td>
<td>89.9</td>
<td>20.2</td>
</tr>
<tr>
<td>Petrilli 17</td>
<td>New York City</td>
<td>1,999</td>
<td>534*</td>
<td>445</td>
<td>83.3</td>
<td>22.3</td>
</tr>
<tr>
<td>Goyal 13</td>
<td>New York City</td>
<td>393</td>
<td>NA</td>
<td>130</td>
<td>NA</td>
<td>33.1</td>
</tr>
<tr>
<td>ICNARC 14</td>
<td>UK</td>
<td>NA</td>
<td>3,883</td>
<td>2,291*</td>
<td>59.0</td>
<td>NA</td>
</tr>
<tr>
<td>Grasselli 15</td>
<td>Lombardy, Italy</td>
<td>NA</td>
<td>1,300‡</td>
<td>1,150</td>
<td>88.5</td>
<td>NA</td>
</tr>
<tr>
<td>Zhou 18</td>
<td>Wuhan, China</td>
<td>191</td>
<td>50</td>
<td>32</td>
<td>64.0</td>
<td>16.8</td>
</tr>
<tr>
<td>Wang 3</td>
<td>Wuhan, China</td>
<td>NA</td>
<td>344</td>
<td>100</td>
<td>29.1</td>
<td>NA</td>
</tr>
<tr>
<td>Guan 19</td>
<td>China</td>
<td>1,099</td>
<td>55</td>
<td>25</td>
<td>45.5</td>
<td>2.3</td>
</tr>
</tbody>
</table>

*Definition of abbreviations: COVID-19 = coronavirus disease; ICNARC = Intensive Care National Audit & Research Centre; NA = not available.*
Mortality for patients who receive mechanical ventilation

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Total (n)</th>
<th>Died (n)</th>
<th>Survived to ICU Discharge (n)</th>
<th>Still Receiving Care (n)</th>
<th>Range of Possible Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Richardson (4)</td>
<td>New York City</td>
<td>1,151</td>
<td>282</td>
<td>38 (hospital)</td>
<td>831</td>
<td>24.5–96.7</td>
</tr>
<tr>
<td>ICNARC (14)</td>
<td>UK</td>
<td>2,291*</td>
<td>698†</td>
<td>355</td>
<td>1,238</td>
<td>30.5–84.5</td>
</tr>
<tr>
<td>Grasselli (15)†</td>
<td>Lombardy, Italy</td>
<td>1,581</td>
<td>405</td>
<td>256</td>
<td>920</td>
<td>25.6–83.8</td>
</tr>
</tbody>
</table>

Definition of abbreviation: ICNARC = Intensive Care National Audit & Research Centre.
Lower bound assumes everyone receiving care survives; upper bound assumes they all die.
*Mechanically ventilated within first 24 hours.
†Received advanced organ support; may include patients who received mechanical ventilation after the first 24 hours.
‡All patients in ICU, not just those mechanically ventilated.
Early Vs Late intubation

A fear of ventilator shortage with COVID-19 panicked politicians into demanding automakers to branch into ventilator manufacture.

Some experts have argued that mechanical ventilation should be employed early in order to prevent COVID-19 patients progressing from mild disease to more severe lung injury. This viewpoint has been expressed most forcefully by Marini and Gattinoni in a JAMA Editorial [1], where they attest that vigorous spontaneous inspiratory efforts can rapidly lead to patient self-induced lung injury (P-SIL).

P-SIL is thought to parallel ventilator-induced lung injury (VILI), an entity supported by decades of experimental and randomized trials [2]. In contrast, P-SIL has surfaced only in the past 4–5 years [3]. Two research studies are commonly cited by authors warning about P-SIL [4,5].

To induce hyperventilation, Masschaele et al. [6] infused saline into the brainstem of spontaneously breathing sheep. The authors claim that the consequent threefold increase in minute ventilation produced lung injury, and this was prevented by mechanical ventilation. Tidal volume (the focus of authors warning about P-SIL) [1, 3–5] increased from 128 to 235 mL. The proportional tidal volume in healthy humans would be 502 mL—much less than experienced by healthy pregnant women.

In a non-blinded, observational study, patients with acute respiratory failure who failed noninvasive ventilation had higher tidal volume than successfully managed patients. Carta et al. [7] concluded that high tidal volume predicted need for endotracheal intubation. Patients ultimately intubated were significantly sicker than non-intubated patients: more frequent immunosuppression (57.5% vs 6.7%), higher SAPS II (41 vs 30), and PaO2/FiO2 (122 v 177). Need for intubation was likely precipitated by severity of underlying illness, tidal-volume size (which was found to be a marginally significant predictor). Tidal volumes in these two studies do not constitute a sound scientific basis for occurrence of P-SIL in patients with COVID-19.

Based on the P-SIL hypothesis, Gattinoni and others advocate radical changes to ventilator management of patients with COVID-19. They claim that noninvasive options are of "questionable" value [5], "intubation should be prioritized" [4], and delayed intubation will cause P-SIL to worsen and induce more severe ARDS [1].

They view heightened respiratory drive in COVID-19 patients as maladaptive, and recommend deliberate weaning of respiratory drive in these patients [1]. They state that "near normal compliance...explains why so many patients present without dyspnea" [5]. If a COVID-19 patient is severely hypoxic, normal lung compliance will not prevent dyspnea. Concurrently some COVID-19 patients are free of dyspnea despite substantial hypoxemia (dubbed "silent-happy hypoxia") [8]. This may be because the level of hypoxemia per se is not sufficient to induce increased respiratory motor output, and accompanying Pco2 levels blunt the hypoxic response [2, 9].

To assess patient effort, Gattinoni and coworkers recommend inserting an esophageal balloon as a "CVSV" [9]. They specify that when esophageal pressure swings increase above 15 cmH2O, "the risk of lung injury and therefore intubation should be considered" [10].
Factors to consider

• Early vs delayed IMV
• "Happy hypoxic?“
• The idealized benefit of IMV
• The risks of IMV – VILI, sedation/paralytics, lines, tubes etc
• Ventilator induced lung injury (VILI) or patient self-induced lung injury (P-SILI)
• Alternatives to MV – High flow, Face mask oxygen

Intubation for COVID-19

- Most experienced team member available
- All intubations - rapid sequence with full paralytic and video laryngoscopy
- No awake intubations
- PAPR + N95+ goggles + “bunny suit” + shoe covers
- Prepare all drugs and equipment outside the room
- Avoid BMV, use HME filter, twist lock connections, inflate balloon just beyond vocal cords

Intubation for COVID-19

Strategies for mechanical ventilation

- Lowest TV, 4-8 ml/kg, lowest RR tolerated (permissive hypercapnia)
- Lowest level of sedation tolerated, dys-synchrony \( \rightarrow \) escapes low TV
- Paralytics and deep sedation if needed
- Individualized PEEP (not ARDS tables) – reserve higher PEEP for those with true lung stiffness
- Monitor oxygenation with arterial gases
- Tolerate hypoxia if no organ dysfunction

Tobin MJ. Basing respiratory management of coronavirus on physiological principles. Am J
Type H & L phenotypes of COVID-19

- The application of 5 cm of CPAP recruits significant amount of previously diseased lung tissue

PaO$_2$/FiO$_2$
95 mmHg

PaO$_2$/FiO$_2$
84 mmHg

Prone positioning

• PROSEVA 2013 trial, mortality benefit for minimum 12 hours per day of prone positioning (17% reduction in all cause mortality, with a NNT of 6)
• Recommended by ATS and SCCM guidelines
• Standard of care for ARDS
• Proning protocol and proning team
• Inclusion and exclusion criteria for prone positioning
• Watch -> chest tubes, vasopressors, and arrythmias
Figure 2: Decisional algorithm being used at Maimonides Medical Center

COVID+ by CT scan or symptomology

Increase O2 for SpO2 > 90%

Physician does not believe pt will tolerate non-invasive

Hypoxemia SpO2 < 90%

Nonbreather

Intubation – go to vent and sedation protocol

**HFNC preferred non-invasive strategy**

HFNC

Management
• FiO2 should always be set at 100%
• Initial LPM should be set at 20LPM
• LPM should be titrated up with a maximum of 50LPM as needed in order to achieve an SpO2>88%

NPPV

Management
**Should be performed in negative pressure room. If this is not possible, should be performed behind closed curtains with HEPA filter bedside.**
• FiO2 should always be set at 100%
• EPAP should be set at 5

On NRB w/ 5L NC

NRB w/ 5L NC

SpO2 < 85

PRIORITY 1 - Patient's at HIGH risk for requiring intubation

Prone should be encouraged in all patients and may be considered in PRIORITY 1 patients however Physician should be aware that prone appears to induce a non-sustainable improvement in SpO2. Prone should therefore be seen as "buying time" rather than "treatment." Regardless of SpO2 improvement, PRIORITY status should not change based on SpO2 improvement during prone.

Consider intubation:
- Hypoxicemic patient on maximal non-invasive oxygen with SpO2 < 85 – 88% w/ distress. (Presenting typically in the form of anxiety and tachypnea).
- Hypoxicemic patient on maximal non-invasive oxygen with sustained SpO2 < 85%

Post intubation Vent Settings
- FiO2 100%
- TV 6 - 8 cc/kg, RR < 20
- PEEP 5 - 10
- Target Sat > 80 % (higher the better)

Post intubation sedation
- Sedatives/Pain drip
- Paralytic drip x 24hrs
- Rocuronium 100mg 30 min – 1hr after intubation

IF POSSIBLE

PRONE

Patient should ideally have the following placed:
- NG tube
- Central line (L/L preferred site)
- Arterial line
- Foley

Vitals should look the same after intubation as before. If hypotensive, consider decreasing PEEP.
Preparation for the COVID surge

• Policies, policies and policies
  • Triage – hospital admission, ICU admission
  • Family communications, designation of SDM, code status discussions
  • Intubation, extubation checklists
  • Policies on limitations of care and futility, unilateral DNR
  • Code blue/Cardiac arrest

• Engineering/administrative changes
  • Closed and designated COVID units
  • Modify rounds
  • Coordinate entry/exit in rooms between providers
    • RT, nurse, physician cross share tasks
  • Re-evaluate need for insulin drips and hourly accuchecks
  • Placement of ventilators and IV pumps
Preparation for the COVID surge

• PPE management
  • Supplies and stockpile
  • Hospital policy by location/role
  • Availability and storage

• Rotation schedules for doctors/nurses
  • Avoid fatigue
  • Ensure adequate staffing
  • Ensure redundancy

• Miscellaneous
  • Transportation policies
  • Endoscopy, elective procedures and surgeries
  • Morgue capacity, transportation of the expired
  • Patient belongings
Thank you

Questions ?