Strategies to support the COVID-19 response in LMICs

A virtual seminar series
Management of Critically Ill Patients

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www.globalncd.org
1. Review COVID-19 epidemiology and clinical course
2. Unique features of COVID-19
3. Ventilatory Strategies
4. Lessons Learned and Best Practices
Clinical Course

Survivors

- Fever
- Cough
- Dyspnoea
- ICU admission
- Systematic corticosteroid
- SARS-CoV-2 RNA positive

Days after illness onset
- Day 1
- Day 2
- Day 3
- Day 4
- Day 5
- Day 6
- Day 7
- Day 8
- Day 9
- Day 10
- Day 11
- Day 12
- Day 13
- Day 14
- Day 15
- Day 16
- Day 17
- Day 18
- Day 19
- Day 20
- Day 21
- Day 22

Non-survivors

- Fever
- Cough
- Dyspnoea
- ICU admission
- Invasive ventilation
- Systematic corticosteroid
- SARS-CoV-2 RNA positive

Days after illness onset
- Day 1
- Day 2
- Day 3
- Day 4
- Day 5
- Day 6
- Day 7
- Day 8
- Day 9
- Day 10
- Day 11
- Day 12
- Day 13
- Day 14
- Day 15
- Day 16
- Day 17
- Day 18
- Day 19
- Day 20

Events:
- Sepsis
- ARDS
- Acute kidney injury
- Secondary infection
- Death
Severity

• Most people with COVID-19 develop mild or uncomplicated illness
• Approximately 14% develop severe disease requiring hospitalization and oxygen support
• 5% require admission to an intensive care unit
• In severe cases, COVID-19 can be complicated by
  • Acute respiratory disease syndrome (ARDS)
  • Sepsis and septic shock
  • Multiorgan failure, including acute kidney injury and cardiac injury
Severe COVID-19 pneumonia

- Most common and severe complication of COVID-19 pneumonia is hypoxemic respiratory failure
- Arterial hypoxemia is dominant feature and exceeds abnormalities in respiratory system compliance
- Increased A-a gradient from V/Q mismatch or intra-pulmonary shunt
Outcomes Among US Patients

The graph shows the number of hospitalizations, ICU admissions, and deaths across different age groups in the US. The age groups are 0-19, 20-44, 45-54, 55-64, 65-74, 75-84, and ≥85 years. The vertical axis represents the number of hospitalizations, ICU admissions, and deaths, while the horizontal axis represents the age groups in years.
COVID-19 death rates by underlying conditions

Chinese CDC documented underlying conditions, if any, for fewer than half of the 44,600 confirmed cases it studied.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Death rate</th>
<th>Confirmed cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>10.5%</td>
<td>873</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7.3</td>
<td>1,102</td>
</tr>
<tr>
<td>Chronic respiratory disease</td>
<td>6.3</td>
<td>511</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6</td>
<td>2,683</td>
</tr>
<tr>
<td>Cancer</td>
<td>5.6</td>
<td>107</td>
</tr>
<tr>
<td>None</td>
<td>0.9</td>
<td>15,536</td>
</tr>
</tbody>
</table>
Pathophysicsiology
COVID severe pneumonia phenotypes

1) Hypoxemia and Low Compliance – Classic ARDS. Will likely need higher PEEP for oxygenation

2) Hypoxemia with High Compliance - Seeing more of this type of patients
   • Higher PEEP may be harmful
Silent Hypoxemia

Patients present without respiratory symptoms to acute respiratory failure requiring emergent intubation

“Silent Hypoxemia” – Occasionally some patients may develop hypoxemia and respiratory failure without dyspnea (especially elderly. This can lead to some unusual presentations
Management Implications
Misconceptions

• Early intubation necessary to manage hypoxemia

• Higher levels of sedation are necessary for management

• Management of COVID-19 hypoxemia requires high levels of PEEP
What SpO₂ to target?

• WHO recommends SpO₂ > 94% for COVID patients
• Our experience so far
  • Pragmatic approach of keeping SpO₂ > 88-92% using non-invasive oxygen delivery strategies while watching the work of breathing and clinical status
  • Lead to lower intubations
Non-invasive oxygen delivery strategies

• Nasal cannula (1-10 L/min)
• Partial Non-Rebreather
• Non-Rebreather
• High-flow nasal cannula
• Non-invasive mechanical ventilation (CPAP, BiPAP)
  • Use cautiously given risk of aerosolization of virus
• Awake, non-ventilated proning
  • No clinical trials supporting use
Awake non-intubated proning

Authors’ response
Lin Ding and Hangyong He

First of all, which etiology of acute respiratory distress syndrome (ARDS) should be the most appropriate group treated with prone position (PP) combined with high-flow nasal cannula (HFNC)? In our study, the majority of ARDS were caused by infectious disease. And we totally agree that PP combined with HFNC should be tried in noninfectious ARDS patients, which was reported in previous studies and case series. However, as reported by Perez-Nieto et al., the use of prone positioning of the patients with complex chest trauma and post status of thoracic surgery is sparse and relatively controversial. Thus, its safety should be evaluated in these noninfectious ARDS population with special protocol.

Another question is whether it is safe and effective enough for patients with noninfectious ARDS with $\text{PaO}_2/\text{FiO}_2 < 100$. PP is a respiratory support technique but not for treating the causative disease which induced ARDS. Thus, as reported in the case series of Perez-Nieto et al., some group of noninfectious ARDS caused by autoimmune diseases (such as lupus pneumonitis) may need a longer duration of disease resolving than infectious disease and may present with deterioration even under PP and HFNC therapy. And patients with $\text{PaO}_2/\text{FiO}_2 < 100$ may face a delayed intubation and worse outcome. Therefore, the safety and efficacy of PP combined with HFNC in noninfectious diseases which cause severe ARDS in patients with $\text{PaO}_2/\text{FiO}_2 < 100$ also need evaluation.

Acknowledgements
We would like to thank Dr. Octavio Lescas, Dr. Raymundo Flores, and Dr. Eder Zamarron for his contribution to the treatment of the patients.

Table 1
Clinical characteristics and outcomes of patients

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Cause of ARDS</th>
<th>Ventilatory support</th>
<th>Baseline $\text{PaO}_2/\text{FiO}_2$ (P/F) (mmHg)</th>
<th>Baseline S/F</th>
<th>P/F after prone position with HFNC or NIV</th>
<th>S/F after prone position with HFNC or NIV</th>
<th>Beginning of prone position and HFNC or NIV</th>
<th>Intubation</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>33</td>
<td>Closed thorax trauma</td>
<td>HFNC</td>
<td>– 195</td>
<td>–213</td>
<td>&lt; 24 h</td>
<td>No</td>
<td>Survive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>19</td>
<td>Lupus pneumonitis</td>
<td>HFNC</td>
<td>91 133</td>
<td>150</td>
<td>165</td>
<td>&lt; 24 h</td>
<td>No</td>
<td>Survive</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>56</td>
<td>Open thorax trauma</td>
<td>HFNC</td>
<td>80 98</td>
<td>101</td>
<td>128</td>
<td>48 h</td>
<td>Yes</td>
<td>Survive</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>36</td>
<td>Bone marrow transplant</td>
<td>NIV</td>
<td>67 87</td>
<td>96</td>
<td>155</td>
<td>72 h</td>
<td>Yes</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>45</td>
<td>Bilateral atelectasis</td>
<td>NIV</td>
<td>89 150</td>
<td>–</td>
<td>250</td>
<td>72 h</td>
<td>No</td>
<td>Survive</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>24</td>
<td>Near drowning</td>
<td>HFNC</td>
<td>75 93</td>
<td>131</td>
<td>188</td>
<td>&lt; 24 h</td>
<td>No</td>
<td>Survive</td>
<td></td>
</tr>
</tbody>
</table>

ARDS acute respiratory distress syndrome, S/F oxygen saturation ratio by pulse oximetry between inspired oxygen fraction, HFNC high-flow nasal cannula, NIV noninvasive ventilation

Fig. 1 Patients with ARDS with high flow oxygen cannula and prone position

- Can increase $\text{SpO}_2$ as well as $\text{PaO}_2$
- Patients report symptom improvement
- Careful patient selection of awake patients who can protect their airway
Time to Intubation

• Early practice was to intubate patients early in the course of the disease

• Experience around the world now suggests to delay intubation as much as possible without compromising patient safety

• Use your arsenal of non-invasive oxygen delivery systems
Intubation strategies

- Most experienced provider using airborne precautions.
- Pre-oxygenate with 100% FiO₂ for 5 minutes, via a face mask with reservoir bag or HFNC.
- Rapid sequence intubation
- Use of Fiberoptic or Video Assisted Intubation to maximize the distance between patient and Provider
Ventilator management

- Keep tidal volumes and airway pressures low to avoid lung injury
- Use volume A/C mode to dial a specific $V_T$ and monitor airway pressures
- Avoid spontaneous modes of ventilation as they may lead to $V_T > 8$ mL/kg
- Titrate $V_T$ and FiO2/PEEP according to ARDS Network Protocol
- Start at 8 mL/kg PBW and aim for $V_T$'s 4-6 mL/kg PBW
- Keep airway pressures low by lowering $V_T$ (plateau pressures < 30 cm H$_2$O)
- Consider neuromuscular blockers early if dysynchrony
- Use high FiO$_2$/low PEEP tables to keep arterial PaO$_2$'s 55-80 mmHg.
- Prone positioning if FiO$_2$ $\geq$ 0.6 and PEEP $\geq$ 10 cm H$_2$O.
Be careful with high PEEP
Watch this space

BRONCHOSPASM

BLOOD CLOTS

SEDATION
To Summarize

• Fear of the unknown: Do not practice critical care medicine differently
  • Avoid early intubation, use high flow nasal cannula
  • Consider CPAP if adequate PPE/negative pressure rooms (SARS experience)
  • Humidify/heat ventilator circuits early to avoid excessive secretions
  • Use lung protective ventilation modes, low $V_T$s; avoid spontaneous modes
  • Avoid high PEEP, as it may lead to barotrauma / VILI

• Early proning beneficial in intubated patients
Practice evidence-based medicine

• Avoid therapies that are not supported by rigorous RCTs
  • Do not use hydroxychloroquine
  • Do not use remdesivir or other IL-6 inhibitors
  • Pending clinical trials
Less is more in ICU
Treatment options

• No therapy is known to be effective
• Supportive care
Drugs under investigation

- Hydroxychloroquine
- Remdesivir
- Lopinavir/Ritonavir
- Ribavirin
- Faviparir
- Umifenovir
- IL6 inhibitors or other immunomodulatory agents