Sonag University | Sohag Medical Journal | Faculty of Medicine

Overview of respiratory care for Covid-19 patients

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Abstract:

Coronavirus disease 2019 (SARS-CoV-2) is caused by Severe Acute Respiratory Syndrome-Corona Virus-2 (SARS-CoV-2) which is an encapsulated coronavirus single-stranded ribonucleic acid (RNA) and is highly contagious. Transmission is believed to be predominantly through droplet spread and direct patient contact rather than 'airborne spread.' There is still no specific antiviral treatment for COVID-19 infection except for supportive therapies for affected patients including respiratory care, especially in critical cases. It has become a clinical threat to the general population worldwide since the 2019 novel outbreak of coronavirus disease originated in Wuhan, China, in late 2019. Among people infected with the novel coronavirus (SARS-CoV-2), approximately 5–15% of patients need intensive care monitoring and ventilation support. In this article, we tried to provide a practical summary of the respiratory aid for COVID-19 patients. We conducted a review of the literature through revision of the available online data on PubMed and other online resources to examine best practice recommendations concerning respiratory support for COVID-19 patients with ARDS.

Keywords: Coronavirus, Respiratory, Intensive care, Ventilation.

Introduction:

SARS-CoV-2 is the causative virus of the 2019 (COVID-19) coronavirus pandemic. Transmission is primarily through live virus-droplet inhalation. COVID-19 represents unprecedented challenges to global healthcare. As of 1st June 2020, there have been 6,189,560 confirmed cases worldwide and it is estimated that 372,469 patients have died because of the infection (1). However, given the current limited worldwide ability to perform wide-spread testing, these figures may underestimate the true impact of the disease significantly. In certain series of cases, up to 12 percent of hospital patients need extra assistance beyond what can be given in a typical ward (2). This article aims to provide a simple practical advice for the respiratory care of critically ill patients with this disease as this pandemic represents great dilemma regarding the ICU management especially the respiratory and ventilatory support for those patients with many controversies, rapid updates, nonhomogeneous management guidelines and scanty of data available from the pandemic hotspots.

Diagnosis and clinical classification of COVID-19

The World Health Organization outlines the following Clinical syndromes associated with COVID-19: (3)

- ✓ **Mild illness:**
  Patients with an uncomplicated viral infection of the upper respiratory tract may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, discomfort, muscle pain, sore throat, dyspnea, nasal congestion, or headache; Very rarely. Diarrhea,

nausea, and vomiting can also be present in patients.

✓ **Pneumonia:**
Adults present with non-severe pneumonia with no additional oxygen needs while children present with cough, breathing difficulties or tachypnea with no signs of severe pneumonia. The cough may be productive, but it is less common in viral pneumonia.

✓ **Severe Pneumonia:**
- Adult with fever or suspected respiratory infection, plus one of the following: high respiratory rate > 30 breaths/min; severe respiratory distress; or room air $SpO_2 \leq 93\%$.
- Child: cough or breathing difficulties, plus at least one of the following: central cyanosis or $SpO_2 < 90$ percent; severe respiratory distress (e.g. fast breathing, grunting, severe chest indrawing) or signs of pneumonia with a general hazard (inability to breastfeed or drink, lethargy or unconsciousness, or fits). While the diagnosis is for clinical reasons, some pulmonary complications can be identified or excluded by chest imaging.

✓ **Acute respiratory distress syndrome (ARDS)**

Respiratory failure Starting 5-7 days after the appearance of the initial respiratory symptoms and is not fully explained by heart failure or fluid overload. Chest Radiograph, CT Scan, or Lung Ultrasound will show bilateral opacities not fully explained by pleural effusion, atelectasis, or nodules.

Based on PaO_2 / FiO_2 ratio, which is the ratio of partial arterial oxygen pressure to fractional inspired oxygen, ARDS can be classified into:

1. **Mild:** 200 mmHg < PaO_2 /$FiO_2 \leq$ 300 mmHg.
2. **Moderate:** 100 mmHg < PaO_2 /FiO_2 ≤ 200 mmHg
3. **Severe:** PaO_2 /$FiO_2 \leq$ 100 mmHg.

✓ **Sepsis**
- Adults with Life-threatening organ dysfunction caused by a dysregulated response of the host to a suspected or proven infection. organ dysfunction is defined as an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) score as disturbed mental status (any GCS < 15); rapid breathing (RR ≥ 22); low oxygen saturation; low urine output; high heart rate; low pulse; low blood pressure (SBP ≤ 100 mmHg) ; skin mottling; coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia.
- Children with Suspected or confirmed infection and ≥ 2 age-based systemic inflammatory response syndrome criteria, one of which must be elevated temperature or count of white blood cells.

✓ **Septic Shock:**

Adults: sepsis with serum lactate ≥ 2 mmol / L plus persistent hypotension (despite adequate volume resuscitation) which requires vasopressors to maintain MAP ≥ 65 mmHg.

Children: Any hypotension with two of the following: disturbed mental State; tachycardia or bradycardia; prolonged capillary refill or weak Pulse; tachypnea; mottled or cool skin or petechial or purpuric eruption; increased lactate; oliguria; hyperthermia or hypothermia.

Respiratory support for COVID patients:

Respiratory failure is a characteristic feature of severe COVID-19 infection. The majority of patients hospitalized need oxygen. Globally, there is a wide discrepancy in the availability and use of breathing aid for those who develop severe COVID-19 respiratory failure. (4).

Guidelines regarding the respiratory support for COVID-19 are not yet settled and advice has changed regarding whether to use techniques such as HFNO

and NIV. It was suggested early in the pandemic that both HFNO and NIV were contraindicated, due to the risk of SARS-CoV-2 aerosolization and the spread of infection associated with these techniques. More recently, both techniques have been used increasingly in many parts of the world (4).

Prone positioning

Proning has been shown to increase oxygenation and decrease mortality in mechanically ventilated patients with moderate to extreme ARDS as compared with supine positioning. Recently, the use of prone positioning has increased in patients receiving basic respiratory support in COVID-19. Importantly, prone positioning requires no expert or external equipment, and many non-sedated patients on face mask oxygen, HFNO, or NIV may also be able to set themselves prone. (5)

Suitable patients are advised to spend as much time in the prone position as possible. Mechanically ventilated patients who respond to the prone positioning should remain prone for up to 12-16 hours at a time. That should be repeated every day until the oxygenation improves. Awake patients may not tolerate remaining in the prone position this long time. Patients on basic respiratory support can be advised to mix supine positioning with a prone and left and right lateral positioning to reduce the time spent in the supine position (6).

Indications for awake proning:

Confirmed or suspected COVID-19 requiring fraction inspired oxygen (FiO_2) $\geq$ 0.28 to achieve SpO_2 94-95% (or SpO_2 88-92% if the risk of hypercapnia). (6)

Indications for proning in ventilated patients:

Confirmed or suspected COVID-19 and P_aO_2: FiO_2 ratio (P:F ratio) of < 150 mmHg. (6

Absolute contraindications for proning:

Need for immediate intubation, considerable hemodynamic compromise, mental agitation/alteration, chest injury / unstable spinal injury. (6)

Relative contraindications for proning:

Facial injuries, seizures, morbid obesity, pregnancy during the 2nd or 3rd trimester, anterior pressure sores, recent abdominal surgery. (6)

Non-invasive ventilatory support

1- High flow nasal oxygen (HFNO)

In non-COVID-19 acute hypoxic respiretory failure, like Acute Respiratory Distress Syndrome (ARDS), HFNO has been shown to minimize 90-day mortality relative to the face mask and NIV (7). Despite prior guidelines to combat the use of HFNO in COVID-19 patients, there has been a widespread change of opinion. For certain patient classes, HFNO is currently recommended by the National Institute of Health, the European Society of Intensive Care Medicine, and the World Health Organization as first-line non-invasive respiratory therapy. (8–10)

HFNO should be considered in patients who cannot or are not able to maintain sufficient oxygen saturation when consuming maximum oxygen through a reservoir facemask or 'non-re-breathing' mask However, an HFNO trial will not be suitable for all patients, and careful triage is required. Patients who are very hypoxic, or who have a very high work of breathing, are more likely to fail an HFNO therapy trial. Instead, these patients may need mechanical ventilation immediately. (11)

Globally, infection control measures to be taken while using HFNO therapy are significantly varied. Accepted practice ranges from the use in negative pressure rooms, standard side rooms, mixing of infected patients, and nursing suspected or confirmed cases, as long as they wear a surgical mask over their high-flow cannula. Health care personnel must always

wear appropriate personal protective equipment (PPE) for the aerosol-generating measures. (11)

There must be a rapid escalation of care, including the provision of quick sequence induction and transfer to intensive care. Assess response within 30-60 minutes of starting HFNO and unless there is a risk of hypercarbic type 2 respiratory failure, sampling of the arterial line and/or arterial blood gas analysis may not be needed, as long as continuous monitoring of SpO_2 is carried out. (11)

The initial settings suggested are Flow of 40 l / min and FiO_2 titrated to hypoxia severity (suggesting at least 0.6) (11)

The goal is SpO2 94-96 percent unless the possibility of type 2 respiratory failure (if IMV or BIPAP is taken into consideration), consider proning and check SpO_2 after every change of position. Patients who remain supine should be sit up 30-60 degrees. Lack of improveement or deterioration may indicate immediate intensive care review. (11)

2- Continuous positive airway pressure (CPAP)

While CPAP has been recommended in some countries as first-line non-inva-sive support for COVID-19 patients with hypoxia, this remains contro-versial. CPAP does not replace the need for IMV, but early use may delay or prevent IMV. (12)

Suggested initial settings are CPAP 10 cm H2O and FiO2 titrated to achieve target SpO_2 of 94-96 percent, except in the presence of acute or acute on top of chronic type 2 respiratory failure, in which case target SpO_2 is appropriate between 88-92 percent. (12)

3- **Bi-level positive airway pressure (BIPAP)**

BIPAP is usually not required in COVID-19 patients with previously normal lungs as compliance is usually retained in the initial stage of the disease. However, in patients who are awaiting intubation for high work of breathing, BIPAP can be considered as a bridging therapy. Otherwise, BIPAP should be reserved for those with acute-on-chronic ventilatory failure with documented respireatory acidosis (12).

Invasive mechanical ventilation

It has been proposed that COVID-19 patients have 2 distinct phenotypes (13). This theory, which remains controversial, may be useful in understanding why various patients with respiratory failure due to COVID-19 can respond to different treatments, as certain individuals do during their disease at different times. (13)

The two phenotypes were known as 'Type-L' (high compliance, low V/Q ratio, low lung weight, and low lung recruitability) and 'Type-H' (low compliance, high V/Q ratio, high lung weight, and high lung recruitability).

It was proposed that patients present with Type-L phenotype during the initial stages of COVID-19 disease and can then undergo a transformation into Type-H as the disease progresses (13).

It has been suggested that the transition from Type-L to Type-H may be caused by either COVID-19 pneumonia itself or by patient self-inflicted lung injury (P-SILI). The latter is believed to be caused by involuntary breaths of high tidal volume (Vt). Type-H is similar to Adult Respiratory Distress Syndrome (ARDS). (13)

Invasive Ventilation strategies

Initial mechanical ventilation approaches for COVID-19 patients reflected the usual strategies employed in ARDS. Some suggested, however, that this approach using high levels of positive end-expiratory pressure (PEEP) could be harmful during the early phase of the disease (Type-L phenotype) (14,15).

Type-L patients have compliant lungs, and it has been proposed that higher Vt values of up to 8-9 ml/kg may be acceptable in these patients, mainly to mini-

mize the incidence of hypercapnia and lower Vt-associated absorption atelectasis, although this remains highly controversial and counteracts ARDS core management. These settings along with lower PEEP rates (8-10 cm H_2O) may reduce the ventilator-induced lung injury (VILI) and progression towards the type-H phenotype (15)

Patients who have undergone a transition to Type-H phenotype are more like classic ARDS patients and require lower Vt (5-6 ml/kg) and higher PEEP (up to 15 cm H_2O) levels (15).

Step 1: Initial ventilator settings

Volume controlled mode (avoid spontaneous breaths in the early course of the disease to avoid patient self-inflicted lung injury), Fio_2 1.0 (although this may be able to be quickly reduced), Vt 6 ml/kg ideal body weight and PEEP 8-10 cmH_2O (16,17)

Suggested targets for initiating invasive mechanical ventilation include; SpO_2 90-94 percent, plateau pressure (Pplat) < 30 cmH_2O, driving pressure < 15 cmH_2O and PH > 7.3, however, permissive hypercapnia may be needed to limit ventilator-induced lung injury and it is usually well tolerated if the patient is hemodynamically stable down to a pH of 7.1 - 7.15 (18)

Step 2: Strategies to optimize oxygenation

Wean FiO_2 to maintain the initial SpO_2 target at around 92-96 percent (14). Oxygen saturation targets may be further lowered in the presence of extreme oxygenation problems. Consider assessing compliance: (15)

o If > 50 ml/cm H_2O consider lower PEEP strategy (<10 cm H_2O) and a Vt of up to 8 ml/kg (Type-L phenotype), although higher Vt remains controversial.

o If < 50 ml/cm H_2O consider higher PEEP strategy (up to 15 cm H_2O) and a lower Vt of up to 6 ml/kg (Type-H phenotype):

- If driving pressure > 14 cm H_2O reduce Vt until ,14 cm H_2O (minimum Vt 4ml/kg) (9, 23)
- If Pao_2: Fio_2 ratio < 200 mm Hg:

1. Consider muscle relaxants (bolus preferred)
2. Consider higher PEEP strategy (monitor for barotrauma)
3. Consider prone positioning for 12-16 hours
4. If proned, asynchronous or Pplat >30 cm H2O consider muscle relaxant infusion for 24 hours

Step 3: Rescue therapies

If Pao_2: Fio_2 ratio does not improve, the following strategies should be considered for both groups: (19)

- Prone positioning, if not done already
- Sedation (infusion of ketamine, midazolam, dexmedetomidine or combination of them tailored for each case) plus neuromuscular blockade infusion for 24hrs, especially if prone, dyssynchronous, or high inspiratory pressures. However, there is conflicting trial data for the use of neuromuscular blockade; the 2010 ACURASYS trial (ARDS et Curarisation Systematique=systematic early use of meuromuscular blocking agents in ARDS Patients) demonstrated a 90-day mortality benefit with the use of cisatracurium but the more recent ROSE trial (Reevaluation of Systemic Early Neuromuscular Blockade) did not demonstrate a mortality benefit (19,20).
- Referral for extracorporeal membrane oxygenation, if available.
- Adjuvant therapies such as prostacyclin or nitric oxide may be
- considered, although evidence in non-COVID-19 ARDS suggests there is no mortality benefit with routine use of these agents. Either inhaled nitric oxide or prostacyclin (epoprostenol) may improve V/Q matching and both may also offload a failing right

ventricle, as may intravenous prostacyclin. (9)

- Consider airway pressure release ventilation (APRV) if familiar with this mode (although there is no proven survival benefit associated with this mode of ventilation) as it may improve oxygenation and reduce the number of ventilated days (21)

Weaning from mechanical ventilation

Trying spontaneous breathing too early raises oxygen demand, increases the risk of pulmonary edema, and puts the patient at the hazard of patient self-inflicted lung injury (P-SILI) due to excessive -ve intrathoracic pressure. decreasing ventilatory support must be done with caution and spontaneous breathing trials should only be tried near the end of the weaning trial (15). A trial of weaning with a view to extubation should be started once patients have met the following criteria and have a rapid shallow breathing index of < 100-105 while on a spontaneous ventilation mode: (22)

- Cooperative cognitive state whilst off sedation
- Adequate cough
- Absence of excessive secretions
- $SpO_2 \geq 90\%$ on $FiO_2 \leq 0.4$
- Pressure support ≤ 10 cm H_2O
- PEEP ≤ 8 cm H_2O
- RR < 35/minute
- Vt > 5 ml/kg
- Vital capacity > 10 ml/kg
- Maximal inspiratory pressure of $\leq$ -20-25 cm H_2O

In the first 24-48 hours (23), failed extubation rates of up to 60 percent in COVID-19 patients were reported. An incremental incidence of clinically signifycant airway edema is one contributing factor. The following steps have been proposed to minimize the risk of a failed extubation (14):

- Test regularly for audible cuff leakage when the cuff is momentarily deflated before any planned extubation. Do not proceed if no cuff leak. The oropharynx should be suctioned prior to cuff deflation to minimize the incidence of micro-aspiration.
- Carry out chest physiotherapy and tracheal suction as necessary.
- Consider administration of IV dexamethasone (4mg every 6 hours) in the 24 hours prior to extubation
- give nebulized adrenaline (5 ml of 1:1000) when post-extubation stridor is suspected.

Patients with proven COVID-19 should wear a surgical facemask on top of an oxygen mask or nasal cannula following extubation. Current evidence suggests that unless they have had 2 negative PCR tests for coronavirus, 24 hours apart, they remain an infection risk (10). This remainns an area of controversy and many centers are continuing to mix these patients until discharge from hospital.

Steroids as an emerging therapy:

The RECOVERY (Randomized Evaluation of COVid-19 Therapy) trial was established in March 2020 as a randomized trial to test a range of possible treatments for COVID-19, including dexamethasone. More than 11,500 patients have been enrolled from over 175 NHS hospitals in the UK. (24)

A total of 2104 patients were randomized to receive dexamethasone 6 mg once per day (either oral or by IV) for 10 days and were compared with 4321 patients randomized to usual care alone. Among the patients who received usual care alone, 28-day mortality was highest in those who required ventilation (41%), intermediate in those patients who required oxygen only (25%), and lowest among those who did not require any respiratory intervention (13%). Dexamethasone decreased deaths by one-third in ventilated patients (p=0.0003) and by one fifth in

other patients receiving oxygen only (p=0.0021). There was no benefit among those patients who did not require respiratory support (p=0.14). Based on these results, 1 death would be prevented by treatment of around 8 ventilated patients and 1 death would be prevented by treatment of around 25 patients requiring oxygen alone. (24)

Conclusion:

Respiratory care and ventilation of COVID-19 ICU patients is challenging due to the heterogeneous pathology of the lung that requires an individualized lung-protective ventilation strategy to improve outcomes. Further research is needed to understand the exact pathological changes in the lung of covid-19 patients, the role of anticoagulant and steroidal drugs to improve the outcome of ventilated patients and the possible role of using extracorporeal techniques in the patient outcomes.

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