





COVID-19 and Intensive Care

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ABSTRACT

COVID-19 caused by SARS-CoV2 has spread rapidly across the world, resulting in many patients in need of intensive care support. Severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis/septic shock, and multi-organ failure may occur during the disease course among many other complications. There still is not a definite cure, but supportive care is important to minimize complications. Patients in need of respiratory support and interventions should preferably be placed in negative pressure isolation rooms, with utmost care to decrease viral spread. Points to consider during oxygen therapy, non-invasive and invasive mechanical ventilation, and shock management of COVID-19 patients are discussed. Patients with mild hypoxia may be managed with conventional oxygen therapy, while others will benefit from high flow nasal oxygen therapy and mechanical ventilation. Although corticosteroids are not recommended for other viral pneumonia, there are recent reports suggesting that steroids may have a place in the treatment of COVID-19 patients with hypoxia. Shock may complicate the course of the disease and a search for the etiology of shock should be carefully planned. Thromboembolic events are common; prophylaxis and/or treatment of thromboembolic events should be managed according to the guidelines. Meanwhile, the results of ongoing randomized, controlled trials on antiviral and immunomodulatory agents are expected to offer better treatment options for COVID-19 patients in the near future.

Keywords: SARS-CoV2, respiratory failure, hypoxia, mechanical ventilation

COVID-19 caused by SARS-CoV2, first reported from Wuhan in December 2019, has spread rapidly across countries, causing hundreds of deaths all over the world. About 5% of the patients are critically ill, requiring admission to an intensive care unit (ICU) (1). Severe pneumonia, respiratory failure, acute respiratory distress syndrome (ARDS), sepsis/septic shock, and multi-organ failure may complicate the disease. Certain points merit attention while caring for these patients in the ICU.

Infection Control

High rates of infection among health care workers have been reported (2,3). Therefore, staff should be educated on droplet, respiratory, and contact isolation precautions and strict adherence should be ensured. Infection may occur directly via droplets, aerosols, or indirectly by touching contaminated surfaces before contact with mucosa. Aerosols, particles smaller than 5 microns, are a concern since they can stay in the air for longer periods and travel longer distances than droplets. Bronchoscopy,

endotracheal sampling/aspiration, nebulizer treatments, high flow nasal oxygen (HFNO) treatment, non-invasive mechanical ventilation (NIMV), bag-mask ventilation, and tracheostomy are procedures that may generate a high amount of aerosols (4,5). Surgical masks are not protective from aerosols.

Patients in need of aerosol-generating procedures should be cared for in isolated, negative pressure rooms if possible. A minimum number of individuals should be present in the room. The procedure must be performed by the most experienced members of the team. N95 masks, goggles, and coveralls should be worn by all.

ICU Admission Criteria

Worsening oxygenation, elevated inflammatory parameters, hyperferritinemia (>500 ng/mL), elevated d-dimer levels (>1000 ng/mL), and lymphopenia (<1000/mL) define high risk patients. Clinical deterioration with bilateral infiltration of the lungs, dyspnea, tachypnea > 30

breaths/min, peripheral oxygen saturation (spO_2) <93% or partial oxygen pressure (PaO_2) < 60 mm Hg under 5 lt/min oxygen with a nasal cannula, and $PaO_2 / FiO_2 < 300$ should suggest admission to an ICU.

Hypotension, hyperlactatemia, delayed capillary refill and mottling denoting hemodynamic instability, signs of multi-organ failure, and cardiac complications should also prompt ICU admission.

Oxygen Therapy

Oxygen therapy is indicated when spO_2 is < 90% and/ or PaO_2 is < 60 mm Hg, targeting an spO_2 level between 92-96%. Nasal cannula may be the initial choice in mild hypoxia but a simple face mask may be used if the target spO_2 cannot be attained with 6 lt/min oxygen flow. Oxygen flow rates with a face mask should be between 4 – 8 lt/min. A non-rebreather mask with a reservoir may be used to administer near 100% oxygen concentrations with a flow rate of 10-15 lt/min. However, it must be considered that oxygen at this concentration is toxic to the lungs, and may cause irreversible lung damage. Therefore, mechanical ventilation should be considered when the oxygen needs rise considerably.

High Flow Nasal Oxygen Therapy

HFNO is a non-invasive oxygen therapy device that allows applying humidified air flow up to 60 lt/min at an oxygen concentration of 21-100%. Adequate humidification, especially during high flow rates, is important to preserve the ciliary function of the respiratory epithelium. HFNO may be useful in selected patients with mild ARDS to avoid intubation as an alternative to NIMV (1,6). Delayed intubation is associated with increased mortality; the patients should be closely followed for their response and early detection of clinical deterioration. Failure is common in patients with moderate or severe ARDS ($PaO_2 / FiO_2 < 200$). Improvement in dyspnea, decreased respiratory rate, decreased tachycardia, and improvement in oxygenation are signs of a favorable response. Patients should be encouraged to stay in the prone position if possible.

With low flow rates, viral dissemination is similar to conventional oxygen therapy but dissemination is increased with increasing rates (7). HFNO should be applied in negative pressure isolation rooms, and surgical masks may be worn over the HFNO cannula.

Non-Invasive Mechanical Ventilation

NIMV is mechanical ventilation by a mask or a helmet instead of an endotracheal tube. In cases of mild ARDS, uncomplicated by organ failures, it may decrease intubation rates. However, in cases of moderate to severe ARDS, it may increase mortality if it delays intubation (8,9). NIMV generates aerosols and should be performed in negative pressure rooms (10). Helmets or well-fitting face masks may be used. Ventilators with dual limb circuits should be preferred. Viral filters should be placed at the inspiratory outlets, proximal to the expiratory valves of the ventilator and between the interface and Y-connector of the circuit to decrease any contamination in case of disconnection. Patients should be closely monitored. It is reported that recovery may be hastened if patients can tolerate prone positioning during NIMV. If no improvement is observed with NIMV or if clinical deterioration occurs, intubation should not be delayed.

Patients with copious secretions, altered consciousness, multiple organ failure, or hemodynamic instability are not suitable for NIMV and should be intubated for invasive mechanical ventilation (IMV).

Invasive Mechanical Ventilation

During the course of COVID-19, severe hypoxia not responding to non-invasive methods necessitates IMV. Intubation should be performed in a negative pressure room, by the most experienced team members with a videolaryngoscope (7). All team members should be wearing full PPE. A non-rebreather-mask with reservoir may be used for pre-oxygenation. Bag-mask ventilation should be avoided if possible; if mandatory, a viral filter is placed between the bag and mask. Rapid sequence intubation should be performed; adequate neuromuscular blockage should eliminate cough the reflex that may generate aerosols. Ventilation should start after the endotracheal cuff is inflated.

During IMV, tidal volumes should be adjusted to 6-8 ml/kg of predicted body weight (11). Lung mechanics should be closely monitored. Plateau pressures should be kept at <30 cm H_2O , driving pressures should be kept at <15 cm H_2O . In moderate to severe patients, higher PEEP levels (>10 cm H_2O) should be used. FiO_2 should be adjusted at the minimum possible to keep the spO_2 above target. Oxygen toxicity should be avoided. The respiratory rate should be adjusted to keep the pH above 7.20; in

severe cases, permissive hypercapnia may be practiced unless contraindicated.

For severe ARDS cases, neuromuscular blockage, recruitment maneuvers, inhaled nitric oxide, and extracorporeal membrane oxygenation may be utilized, according to patient characteristics. Yet, there is no evidence for these practices in COVID-19.

The closed system of the ventilator circuit should be maintained at all times, to minimize aerosol spread; closed suction systems should be utilized; metered dose inhalers should be preferred for inhalant therapies (12). T-tube trials for weaning should be avoided and spontaneous breathing trials should be conducted in pressure support modes. Respiratory isolation measures should be followed during extubation as well.

Prone Positioning

Prone positioning decreases edema in the dependent parts of the lung, recruits alveolar units, and improves the ventilation-perfusion mismatch, resulting in increased ventilation. Oxygenation and mortality rates have been reported to improve with early, daily proning for at least 16 hours in patients severe ARDS (13,14). During severe COVID-19, it has been observed that early proning, even before intubation, is associated with improved oxygenation and better clinical outcomes. Obesity should not be a contraindication (14).

Corticosteroids

For moderate-to-severe ARDS, corticosteroids have been reported to decrease the inflammatory response in the lungs, shorten the IMV duration, and increase survival (15). Previous studies on severe viral pneumonia have reported increased viral load, delayed viral clearance, decreased antibody response, and increased bacterial infection rates with steroids (16). Current guidelines suggest avoiding steroids for COVID-19 unless severe ARDS or another indication is present (11). For COVID-19 related severe ARDS, the present sepsis guidelines recommended 1-2 mg/kg/day methylprednisolone for 5-7 days.

Recently, a preliminary report of the randomized, controlled RECOVERY study suggested that 6 mg/day dexamethasone for up to 10 days for patients receiving oxygen therapy or IMV was associated with decreased 28-day mortality. This decrease was most significant for patients on IMV, less for patients on oxygen therapy. No

difference was present for patients who did not require oxygen.

Hemodynamic Support

Up to a third of COVID-19 patients have been reported to experience shock of various etiologies. During shock management, over-hydration may aggravate pulmonary edema and lung injury. This may further impair pulmonary functions especially in ARDS patients with diffuse alveolar epithelial and endothelial damage. Therefore, close monitoring to evaluate fluid responsiveness is of utmost importance. Balanced crystalloids solutions should be preferred over saline and colloids. Maintenance fluid therapy is not recommended. If vasopressors are needed, norepinephrine should be the treatment of choice and a mean arterial blood pressure of 60-65 mmHg should be targeted. The cause of shock should be searched for. Septic shock, especially by secondary bacterial infections, seems to be common. Myocarditis and other cardiovascular complications, including pulmonary thromboembolism, should be ruled out. Hemorrhagic shock may be a complication of anticoagulants.

Anticoagulant Therapy

Critically ill patients commonly have a tendency for thromboembolic events due to many factors including disseminated intravascular coagulation and immobilization. Prophylaxis with unfractionated heparin (UH) or low-molecular-weight-heparins (LMWH) is recommended. However, during the COVID-19 period, an increased tendency for major thromboembolic events and microvascular thrombosis has been reported, possibly due to direct endothelial involvement and inflammation. Microvascular thrombosis may also contribute to respiratory and other organ failure. Patients with elevated fibrinogen and d-dimer levels have a poor prognosis (17). Therefore, it is suggested that patients should be treated with UH or LMWH at prophylactic or therapeutic doses during the COVID-19 period and this should continue for up to 3 months depending on disease course.

Other Treatment Options

Many different antivirals, blood purification systems, immunomodulatory drugs, convalescent plasma, and mesenchymal stem cell therapy have been the subject of studies to treat COVID-19. However, no definitive cure has been found yet.

Many observations report that an hyperinflammatory syndrome and increased cytokine release may be the cause of deterioration in a group of patients during course of COVID-19. Consequently, immunomodulatory agents, one of which is tocilizumab, a monoclonal antibody against IL-6 receptors, are being investigated. Recently, some observational studies have reported favorable outcomes for patients on IMV (18). Randomized, controlled studies are expected to offer better treatment options in the near future.

CONCLUSION

Currently, there are a substantial number of COVID-19 patients in need of ICU care. They require close monitoring and attentive management by experienced teams, since multi-systemic involvement may occur. However, the resources are globally scant. Results of ongoing trials are urgently needed to prevent clinical deterioration of COVID-19 patients and their need for the ICU, and also to treat critically ill COVID-19 patients with respiratory and multi-organ failure.

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REFERENCES

- World Health Organization. Clinical management of severe acute respiratory infection (SARI) when covid-19 disease is suspected: Interim guidance. March 14 2020. (<https://www.who.int/emergencies/diseases/novelcoronavirus-2019>) (access date: 10.04.2020).
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; doi: 10.1001/jama.2020.2648 [Epub ahead of print]
- Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. *JAMA* 2020;323:1335.
- Turkoglu M. Personal protective equipment use for COVID-19 patients in intensive care unit. *J Crit Intensive Care* 2020; 11(Suppl. 1):1–3.
- Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for patients with confirmed 2019 novel coronavirus (2019-nCoV) or patients under investigation for 2019-nCoV in healthcare settings. <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/infection-control.html> (Accessed on April 15, 2020).
- Papazian L, Corley A, Hess D, Fraser JF, Frat JP, Guitton C, et al. Use of high-flow nasal cannula oxygenation in ICU adults: A narrative review. *Intensive Care Med* 2016;42:1336-49.
- Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: A systematic review. *Plos ONE* 2012;7:e35797.
- Cheung TM, Yam LY, So LK, Lau ACW, Poon E, Kong BMH, et al. Effectiveness of noninvasive positive pressure ventilation in the treatment of acute respiratory failure in severe acute respiratory syndrome. *Chest* 2004;126:845-50.
- Rodríguez A, Ferri C, Martin-Loeches I, Diaz E, Masclans JR, Gordo F, et al. Risk factors for noninvasive ventilation failure in critically ill subjects with confirmed influenza infection. *Respir Care* 2017;62:1307-15.
- Hui DS, Chow BK, Ng SS, Chu LCY, Hall SD, Gin T, et al. Exhaled air dispersion distances during noninvasive ventilation via different Respironics face masks. *Chest* 2019;136: 998–1005.
- Alhazzani W, Möller MH, Arabi YM, Loeb M, Gong NM, Fan E, et al. Surviving Sepsis Campaign: Guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Crit Care Med* 2020;48:e440-e469.
- Ocal S. Pulmonary rehabilitation. *J Crit Intensive Care* 2020; 11(Suppl. 1):16-7.
- Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013;368:2159-68.
- De Jong A, Molinari N, Sebbane M, Prades A, Futier E, Jung B, et al. Feasibility and effectiveness of prone position in morbidly obese patients with ARDS: A case-control clinical study. *Chest* 2013;143:1554-61.
- Villar J, Ferrando C, Martínez D, Ambrós A, Muñoz T, Soler JA, et al. Dexamethasone treatment for the acute respiratory distress syndrome: A multicentre, randomised controlled trial. *Lancet Respir Med* 2020;8:267-76.
- Arabi YM, Fowler R, Hayden FG. Critical care management of adults with community-acquired severe respiratory viral infection. *Intensive Care Med* 2020;46:315-28.
- Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Tromb Haemost* 2020;18:844-7.
- Toniati P, Piva S, Cattalini M, Gaffara E, Regola F, Castelli F, et al. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy. *Autoimmun Rev* 2020;19:102568.