Mechanical Ventilation Management in COVID-19 Patients

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ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), was first reported in Wuhan, Hubei, China, and has spread to more than 200 other countries around the world. COVID-19 can be complicated by severe pneumonia, ARDS, sepsis, and septic shock in severe cases. About 80% of cases are mild or moderate, 13.8% have severe disease, and 6.1% fall into a critical condition. Positive responses in COVID-19 patients with respiratory failure are usually seen right after the initiation of NIV and HFNC. If there is no substantial improvement in gas exchange and respiratory rate within a few hours, invasive mechanical ventilation should be started without delay. Delayed intubation increases COVID-19 ARDS mortality.

Keywords: COVID-19, intubation, mechanical ventilation

ABSTRAK

Coronavirus disease 2019 (COVID-19), yang disebabkan oleh *Severe Acute Respiratory Syndrome-Coronavirus-2* (SARS-CoV-2), pertama kali dilaporkan di Wuhan, Hubei, China, dan telah menyebar ke lebih dari 200 negara lain di seluruh dunia. Manifestasi klinis pasien COVID-19 sebagian besar tidak bergejala (asimtomatik), namun dapat diperumit dengan pneumonia berat, ARDS, sepsis, hingga syok septik. Sekitar 80% kasus biasanya ringan atau sedang, 13,8% mengalami gejala berat, dan 6,1% pasien mengalami kondisi kritis. Respons positif biasanya terlihat segera setelah dimulainya NIV dan HFNC. Jika tidak ada perbaikan substansial dalam pertukaran gas dan laju pernapasan dalam beberapa jam, ventilasi mekanik invasif harus dimulai segera. Intubasi yang tertunda meningkatkan mortalitas ARDS. **Wibowo Frischa, Harjanto Bernadus Realino. Tata Laksana Ventilasi Mekanik Pasien COVID-19.**

Kata kunci: COVID-19, intubasi, ventilasi mekanik

INTRODUCTION AND BACKGROUND

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The average incubation period for SARS-CoV-2 is five days (range 2 to 14 days), and symptoms develop within 12 days after infection (range 8 to 16 days).[1,2] SARS-CoV-2 virus primarily affects the respiratory system, although other organ systems are also involved. Symptoms associated with lower respiratory tract infections such as fever, dry cough, and dyspnea were reported in an initial case series from Wuhan, China. In addition, headache, dizziness, general weakness, vomiting, and diarrhea may also be experienced.[3] The infection may progress to severe illness with shortness of breath and other pneumonia-associated respiratory symptoms in about 75% of patients. Symptoms of pneumonia mainly occur in the second or third week of symptomatic infection. Prominent signs of viral pneumonia include decreased oxygen saturation, deviation of blood gases, changes in lung imaging (chest X-ray and other imaging techniques), which shows the presence of ground glass, uneven consolidation, alveolar exudate, and interlobular involvement. Lymphopenia is frequently a common finding, and the other inflammatory markers (such as C-reactive protein and proinflammatory cytokines) are also elevated.[4–6]

Patients should be monitored regularly through peripheral oxygen saturation levels. Oxygen supplementation can be provided by using a nasal cannula or venturi mask to maintain oxygen saturation between 90%, and 96%.[7] It is critical to determine whether intubation is required in treating severe COVID-19 patients. Clinicians must weigh the risk between early intubation against the risk of sudden respiratory arrest and emergency intubation, which puts medical staff at greater risk of infection. Excessive breathing effort, hypoxemia resistance to oxygen supplementation, and encephalopathy suggest a high risk of respiratory arrest and need endotracheal intubation and urgent mechanical ventilation.[7–9]

REVIEW

Ventilation Management

The primary goal of acute respiratory distress syndrome (ARDS) management is to treat hypoxemia and identify and treat the underlying cause.

Intubation performed too soon or too late put the patient at risk.[10,11] High-flow nasal cannula (HFNC) can provide warmed and humidified oxygen at a flow rate of up to 60 L/min. This modality of oxygen delivery may reduce

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the need for intubation and mechanical ventilation for patients with acute hypoxemic respiratory failure. The success of HFNC can be predicted by the ROX index, which is a score that has been validated in the treatment of pneumonia and ARDS. ROX index is described as the oxygen saturation ratio to the fraction of inspired oxygen [SPO2/FiO2] and respiratory rate. The fraction of inspired oxygen to respiratory rate is a viable predictor of the need for intubation in patients receiving high-flow nasal cannula therapy. These clinical scores were initially applied based on clinical data at 2 hours, 6 hours, and 12 hours after the HFNC application. Most previous studies related to the use of HFNC in COVID-19 patients focused on utilizing the ROX index to identify patients at risk for subsequent endotracheal intubation.[12,13] HFNC is indicated for patients with SpO2≤92% and/or RR≥25/min under nasal tube oxygen inhalation 10 L/min or mask oxygen supply. The initial HFNC sets the gas flow rate to 30 L/min and the FiO2 of 1.0, then adjust the flow rate and FiO2 to maintain the pulse oxygen saturation (SpO2) at 92%-96% and adjust dynamically based on the blood gas analysis results. During HFNC treatment, how to judge the therapeutic effect and the need to be converted to invasive mechanical ventilation (IMV) have always been a concern. In particular, studies have found that delayed intubation in HFNC may lead to increased mortality. Therefore, the most critical issue in HFNC treatment is determining the poor therapeutic effect early and timely change the ventilator support mode.[13,14]

Up to 50% non-invasive ventilation (NIV) usage in patients with moderate and severe ARDS fail and is associated with a 50% mortality rate in those with severe ARDS. The severity of the disease and prolonged hypoxemia indicate the failure of NIV; PaO2/FiO2 150 mmHg is a sign of increased mortality risk. In addition, a high tidal volume (>9.5 mL/kgBW) during the first 4 hours predicts the failure of NIV use, and the patient may deteriorate rapidly. Patients with HFNC or NIV require adequate monitoring in the ICU. Intubation and use of invasive mechanical ventilation should be started immediately and should not be delayed in a rapidly worsening condition.[8,16]

ARDS pathogenesis involves alveolar damage and increased capillary permeability, inflammatory response, and pulmonary edema, with hypoxic vasoconstriction leading to intrapulmonary shunting and severe hypoxemia.[17] The ensuing ventilation-perfusion (V/Q) mismatch directs lung recruitment maneuvers to minimize ventilatory-induced lung injuries (VILIs) and improve oxygen delivery to the lungs. Most lungs lack adequate ventilation in the supine position due to the weight of the ventral lungs, heart, and abdominal viscera.[17,18] As ARDS progresses, the edematous lung reduces ventilation in the dorsal regions of the lungs even more. Gravitational pressures on the lung vasculature increase perfusion to poorly ventilated lung fields. As a result, areas that still have perfusion but are poorly ventilated exacerbate the V/Q mismatch and subsequent hypoxemia.[19]

Prone position can improve oxygenation in severe COVID-19 patients; prospective cohort data described its usefulness in unintubated patients with severe hypoxemia.[20] The main mechanisms of prone position in the improvement of ARDS are dorsal lung regions recruitment, increasing end-expiratory lung volume, increasing chest wall elastane, decreasing alveolar shunt, and improving tidal volume.[21] Patients who remain in the prone position for extended periods have a lower mortality rate;[21] correct selection of patients and proper treatment protocol for prone positioning are the key to its effectiveness. Patients in the prone position should have their positions changed every 2 hours. Their sides should be switched.[21] Contraindications for the prone position include, but may not be limited to, extreme obesity, pregnancy, unstable spine, seizures, elevated intracranial pressure, maxillofacial surgery, and hemodynamic instability.[19] However, it is unclear whether the prone position can prevent intubation in severe COVID-19 patients. In patients in deteriorating conditions, this position should be avoided.[20]

Endotracheal Intubation

Endotracheal intubation is a clinical procedure involving a flexible tube insertion into the trachea to secure the airway and provide ventilation support. Some conditions, such as patients with decreased consciousness, major surgery, decreased oxygen saturation levels (hypoxia), airway obstruction (laryngospasm), or respiratory disorders, i.e., acute respiratory distress syndrome (ARDS), may require intubation.[22,23] Endotracheal intubation is a high-risk intervention in patients with suspected and confirmed SARS-CoV-2.[24] Preparation and implementation, especially to maintain cleanliness, need to follow specific protocols; intubation should be elective and well planned; the number of people around must be kept to a minimum. The use of intubation boxes to cover patients during the procedure has been controversial but may be a reasonable option to reduce aerosol spreading of the SARS-CoV-2 virus. It may depend on the design of the aerosol box, and healthcare workers may still be exposed during the post-intubation period, especially after box removal.[25,26] Aerosol packs may increase intubation times and expose patients to hypoxia risk. Without an aerosol box, all anesthetists obtained first-pass success.[26] The time was relatively shorter when intubation was performed by more experienced proceduralists using video laryngoscopy.[27] An

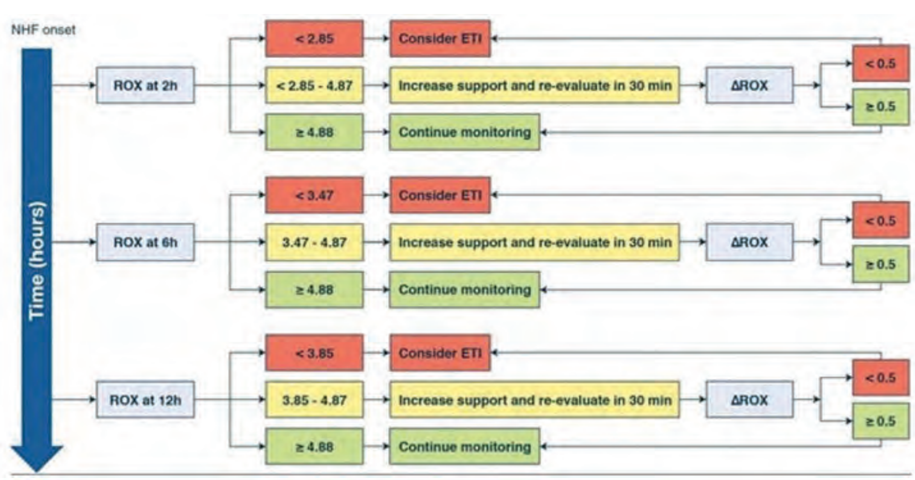

Figure 1. ROX index management for HFNC[15]

alternative approach to our primary outcome would have been to measure intubation success as defined by an arbitrary time cut-off, such as 60 s. It has been suggested that the box should be removed if difficulty is encountered.[26–28]

According to a recent study, using the aerosol box resulted in higher airborne particle exposure than not using the device, which persisted after the device was removed, as measured by a particle counter near the laryngoscopist's head. Clouds of aerosolized particles were seen escaping through the arm openings of their aerosol box towards the laryngoscopist. The difference in contamination level between using an aerosol box and not using an aerosol box could be offset by proper doffing of personal protective equipment (PPE). Clinicians should decide whether to use the aerosol box with caution, balancing between risks and benefits, particularly in difficult airway situations. When performing aerosol-generating procedures, strict adherence to proper PPE donning and doffing and good hand hygiene should be maintained.[29]

Several factors influence intubation in COVID-19 patients. When intubated, elderly and male patients and those with a history of previous comorbidities such as hypertension and diabetes are more at risk of mortality.[30,31] CT-thorax findings and respiratory rate are important prognostic factors determining disease severity.[32] Increased levels of ferritin, d-dimer, and lipase in hypoxic conditions correlated with the need for intubation and ICU care. Pulmonary embolism and cardiac tamponade are two complications of COVID-19 patients admitted to the ICU. The ROX index is a non-invasive predictor and is good enough to determine the need for intubation in COVID-19 patients.[23,33,34]

In complex airway management, the upper airway nerve block method may be proper for tracheal stenosis patients who are rigid bronchoscopy candidates. It is also suggested that video laryngoscopy, as opposed to direct laryngoscopy, can better visualize tracheal intubation in congenital heart disease. It does, however, take time and a well-trained expert. A flexible laryngeal mask airway is preferable to an endotracheal tube in children with tongue trauma because it reduces extubation time, recovery time, and hemodynamic changes to airway control.[23]

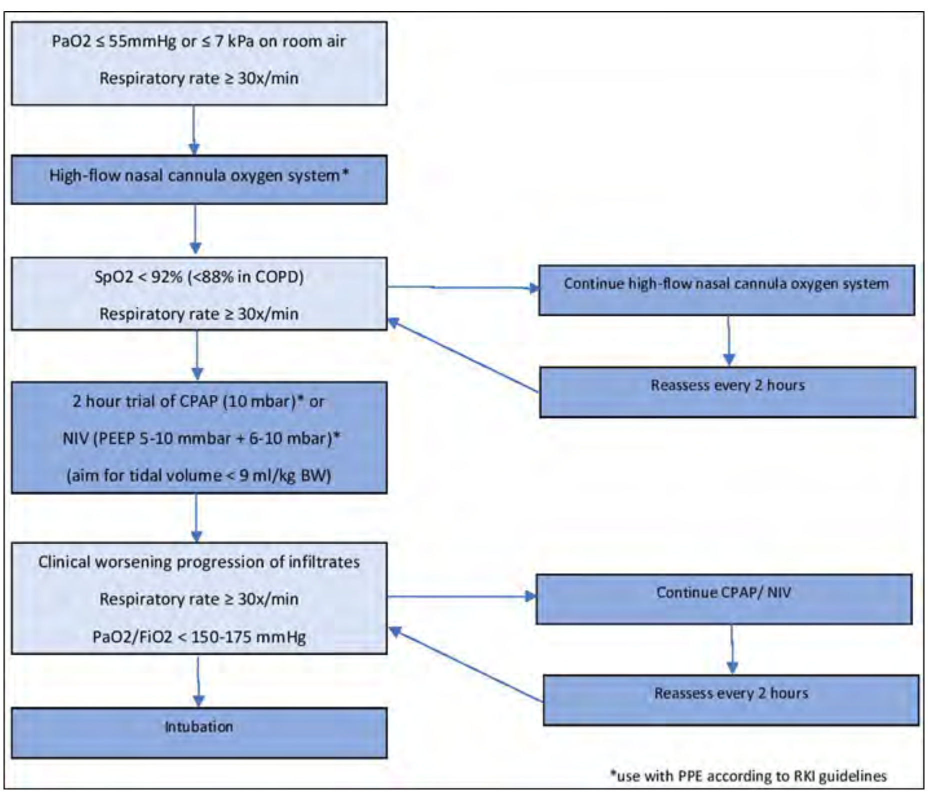

Figure 2. Ventilation management algorithm[16]

Endotracheal Intubation Procedure

After receiving strict tertiary protection (N95 mask, protective clothing, goggles, protective face shield), the doctor who performs the intubation enters the isolation ward. Prepare rescue kits for COVID-19 patients, equipped with different types of disposable tracheal catheters, and video laryngoscope handles, disposable laryngoscopes, closed suction tubes, disposable masks, and breathing sacs. Give oxygen before induction through a mask at a high flow rate for more than 5 minutes, and avoid positive pressure ventilation. Prior to intubation, propofol was administered 1–2 mg/kg (etomidate 0.1–0.2 mg/kg in patients with hemodynamic instability), 2% lidocaine hydrochloride 0.5–1 mg/kg, rocuronium 0.5-1 mg/kg. After the patient's breathing completely disappeared, a video laryngoscope was quickly placed and completed intubation. The location depth of the tube was comprehensively judged based on the bilateral thoracic undulations, breathing waveform, and breathing parameters of the anesthesia machine. Then the ventilator was used for ventilation treatment. Disposable intubation supplies that come into contact with the patient's airways should be disposed of in designated double-layer medical waste bags. A hydrogen peroxide disinfection wipe was used to wipe down the handle of the visual laryngoscope several times. The outer packaging of the COVID-19 patient-specific rescue kit was repeatedly disinfected with 75% medical alcohol. Before leaving the isolation ward, the intubation doctor should remove the outer protective clothing, bathe, and change clothes in the cleaning area. Pay attention to hand hygiene at every step.[35]

Invasive Mechanical Ventilation

In COVID-19 patients, the following conditions warrant the use of invasive mechanical ventilation:[36,37]

- Severe respiratory distress with acute respiratory failure
- Exacerbation of hypoxia associated with increased respiratory rate
- Increased respiratory work with the use of respiratory accessory muscles
- Inability to maintain SpO2 >90% with high-flow oxygen flow rates exceeding 50 L/min (HFNC or maximal oxygen supplementation)
- Hypoxia resulting in impaired consciousness and failure to maintain an

airway patent

- Patients with multiorgan failure, persistent hemodynamic instability requiring vasopressor support, or multiple comorbidities such as diabetes, cardiovascular disease, hypertension, advanced age, malignancy, or chronic respiratory disease.
- Arterial pH of 7.3 with $PaCO_2$ greater than 50 mmHg
- PaO_2/FiO_2 <200
- Increased respiratory rate associated with asynchronous thoracoabdominal movements or paradoxical breathing
- Patients with HFNC have a low ROX index (4.88). The ROX index is the ratio of SpO_2/FiO_2 to respiratory rate and has been used to predict the need for intubation in patients receiving HFNC oxygen therapy. ROX index 4.88 after HFNC initiation was associated with a lower risk of intubation.

The optimal time to intubate COVID-19 patients is still unclear. Mechanical ventilation should still be considered in COVID-19 patients with moderate to severe ARDS symptoms (PaO_2/FiO_2<200) to avoid P-SILI (patient self-induced lung injury) and virus transmission to health workers.[38] In COVID-19 patients, increased efforts have been associated with higher inspiratory pressures and volumes and increased transpulmonary pressure, which may progress to barotrauma (pneumothorax and pneumomediastinum). Recent studies emphasized that expiratory efforts may also cause P-SILI. The pleural pressure increases during excessive expiratory muscle activity, leading to markedly reduced transpulmonary pressure and collapse of most dependent lung regions and peripheral airways. Thus, both high inspiratory and expiratory efforts may promote P-SILI, especially in lung diseases, which feature inhomogeneous distribution, such as in COVID-19.[39] Endotracheal intubation and invasive mechanical ventilation are priorities in ARDS patients whose conditions are worsened despite HFNC oxygen supplementation. Because of the increased inhaled tidal volume, ARDS patients who are not intubated and breathe spontaneously have a higher risk of P-SILI. In spontaneous breathing and non-intubated patients, esophageal pressure measurement with a manometer can be used to estimate the time of intubation.[38]

COVID-19 patients with acute respiratory disease syndrome (CARDS) who need mechanical ventilation have a high mortality rate (67%).[40] In ARDS patients, the use of inappropriate ventilation strategies can result in VILI (ventilator-induced lung injury), which includes barotrauma (high airway pressure), volutrauma, atelectrauma, biotrauma, myotrauma (diaphragmatic injury), and oxytrauma.[40]

Conventional Approaches to Minimizing VILI

In ARDS, the primary goal of mechanical ventilation is to provide adequate gas exchange while minimizing organ injury. Tidal volume, plateau airway pressure, driving pressure, respiratory rate, inspiratory flow, and excessive positive end-expiratory pressure (PEEP) all impact on the severity of VILI, even though it is unclear which parameter is the most important in affecting the severity of VILI.[41]

There are two types of COVID-19 pneumonia, and the treatment methods for ventilatory management vary. Type L is characterized by low elastance, high compliance, and low lung weight as estimated by lung CT scan, low lung recruit ability, low ventilation-to perfusion (V/Q) ratio, and a low response to PEEP. Type H is characterized by high elastance, low compliance, high lung weight, high lung recruit ability, high right-to-left shunt, higher lung weight, and high PEEP response. The later type of pneumonia has features like typical ARDS.[37,42,43]

Patients with type L CARDS and good lung compliance should be given a higher tidal volume (7-8 mL/kg ideal body weight). A tidal volume of 8 mL/kg produces a plateau pressure of 21 cm H_2O and a driving pressure of 11 cm H_2O in a 70 kg man with respiratory system compliance of 50 mL/cm H_2O and a PEEP of 10 cm H_2O, both well below the currently accepted thresholds. This setting is accustomed for VILI protection (30 and 15 cm of H_2O, respectively). Higher VT aid in preventing reabsorption of atelectasis and hypercapnia, which is caused by hypoventilation with lower tidal volume.[43]

The use of high PEEP (PEEP >10 cm H_2O) is not recommended due to the heterogeneity of COVID-19 patients' lungs (with the simultaneous presence of severely affected areas and unaffected areas). However, the European guidelines for the management of sepsis in critically ill COVID-19 patients and the intensive care and critical care guidelines recommend giving PEEP more significant than 10 cm H_2O to treat ARDS caused by SARS-CoV-2. The PEEP should be titrated by assessing their lung compliance. Suppose the lung compliance is elevated or normal and accompanied by hypoxemia, which is commonly found in the L-phenotype. In that case, PEEP less than 10 cm H_2O is recommended to avoid overdistention of normal healthy alveoli. Suppose compliance is low, as it is more common in the H-phenotype of COVID-19 pneumonia and is also seen in ARDS. In that case, PEEP should be applied just above the lower inflection point in the pressure-volume loop on the ventilator to recruit the collapsed alveoli, prevent atelectasis, and increase oxygenation. Alveolar over-distention in the pressure-volume loop should be monitored by looking for a "beaking" pattern that can be corrected by lowering the tidal volume or PEEP.[23]

The plateau pressure should be less than 30 cm H_2O. When there is no airflow, the pressure in the alveoli remains constant. This pressure is slightly lower than the peak pressure and is calculated by adding a 0.5 to 1-second inspiration pause in volume control mode, which indicates the pressure-time scalar. The formula for calculating driving pressure is driving pressure = (plate pressure – PEEP). The pressure given should be less than 15 cm H_2O and can be achieved by either decreasing tidal volume (risk of hypercapnia) or increasing PEEP (risk of overdistention of the alveoli). As a result, PEEP and tidal volume must be carefully titrated to keep the driving pressure low. Compliance is a measure of the elastic lung tissue's ease of distensibility. The easier the lungs expand or stretch, the more compliant they are. In an adult, the total compliance of the two lungs is typically around 200 mL/cm of H_2O. Low compliance is common in ARDS patients with stiff lungs. Airway occlusion pressure (P0.1) is defined as the pressure generated in the airways during the first 100 msec of an inspiratory effort against a blocked airway. P0.1 is generally around 1 cm H_2O in spontaneous breathing patients. Values above 3.5 cm H_2O were associated with the increased effort in mechanically ventilated patients.

Therefore, the airway occlusive pressure in CARDS patients should be kept below 3.5 cm H_2O to avoid VILI and diaphragmatic injury (myotrauma).[23]

Prognosis of Patients on Mechanical Ventilation

Several studies have shown that elderly patients contribute to most COVID-19 death. The mortality rate in patients aged 70 and over is 84.3%.[44] However; the mortality rate is only 32.6% of patients less than 70 years and 22% of those aged less than 50 years old. Based on the multivariate logistic regression model, there was a 7% increase in the death probability for each increase in years of age.[44] This association between advanced age and the likelihood of death is consistent with other studies. There are several reasons for the high mortality rate, including more patients with comorbidities, poor baseline functional status, and variations in the aggressiveness of treatment goals.[44]

Extubation and Weaning

A retrospective study showed one-third of COVID-19-extubated patients required reintubation, which was associated with a higher mortality rate.[45] Needs of reintubation should be considered in older patients, patients who are paralyzed, required high PEEP before extubation, needed more respiratory support after extubation and had nonpulmonary organ failure.[45]

Weaning or readiness for extubation should follow standard practice by performing a spontaneous breathing experiment (SBT). There are some variations in weaning; some specialists typically use low-pressure support ventilation (PSV) parameter instead of a higher PEEP to overcome endotracheal tube resistance during the trial, while others leave SBT for a longer period (e.g., two to four hours, as opposed to the usual two hours). This is based on the observation that COVID-19 patients are intubated for a longer period than non-COVID-19 patients, as well as anecdotal evidence of high secretions and airway edema; all of these factors increase the risk of post-extubation respiratory failure and reintubation.[45]

CONCLUSION

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It primarily affects the respiratory system. The use of mechanical ventilation should still be considered in COVID-19 patients with moderate to severe ARDS. Endotracheal intubation and invasive mechanical ventilation are prioritized for ARDS patients who experience worsening symptoms regardless of HFNC oxygen supplementation. The use of inappropriate ventilation strategies in ARDS patients may induce VILI (ventilator-induced lung injury), which includes barotrauma (high airway pressure), volutrauma, atelectrauma, biotrauma, myotrauma (diaphragmatic injury), and oxytrauma. The primary focus of mechanical ventilation in ARDS is to provide adequate gas exchange while limiting organ injury. Tidal volume, plateau airway pressure, driving pressure, respiratory rate, inspiratory flow, and excessive positive end-expiratory pressure (PEEP) all affect the severity of VILI. However, it is unclear which of these parameters is most important in reducing injury. The prognosis of successful mechanical ventilation in COVID-19 patients is influenced by several factors, including age and a history of comorbidities. Needs of reintubation should be considered in older patients, paralyzed patients, requiring high PEEP before extubation, requiring more respiratory support after extubation, and had nonpulmonary organ failure.

REFERENCES

1. Weissleder R, Lee H, Ko J, Pittet MJ. COVID-19 diagnostics in context. Sci Translat Med. 2020;12(546):eabc1931. doi:10.1126/scitranslmed.abc1931
2. Tang LY, Wang J. Anesthesia and COVID-19: What we should know and what we should do. Seminars in Cardiothoracic and Vascular Anesthesia 2020;24(2):127-37. doi:10.1177/1089253220921590
3. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. Clin Immunol. 2020;215:108427. doi:10.1016/j.clim.2020.108427
4. Velavan TP, Meyer CG. The COVID-19 epidemic. Trop Med Internat Health 2020;25(3):278-80. doi:10.1111/tmi.13383
5. Susilo A, Rumende C, Pitoyo C, Santoso WD, Yulianti M, Herikurniawan H, et al. Coronavirus disease 2019: Tinjauan literatur terkini. J Peny Dalam Indon. 2020;7(1):45-67.
6. WHO. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected [Internet]. 2020 [cited 2022 February 11]. Available from: https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf?sfvrsn=bc7da517_2
7. Alhazzani W, Møller MH, Arabi YM, Loeb M, Ng Gong M, Fan E, et al. Surviving sepsis campaign: Guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Intensive Care Med. 2020;46(5):854-87. doi:10.1007/s00134-020-06022-5
8. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med. 2020;383(25):2451-60. doi:10.1056/NEJMcp2009575
9. Shang Y, Pan C, Yang X, Zhong M, Shang X, Wu Z, et al. Management of critically ill patients with COVID-19 in ICU: Statement from front-line intensive care experts in Wuhan, China. Ann Intensive Care 2020;10(1):73. doi:10.1186/s13613-020-00689-1
10. Thompson BT, Chambers RC, Liu KD. Acute respiratory distress syndrome. N Engl J Med. 2017;377(6):562-72. doi:10.1056/NEJMra1608077
11. Windisch W, Weber-Carstens S, Kluge S, Rossaint R, Welte T, Karagiannidis C. Invasive and non-invasive ventilation in patients with COVID-19. Dtsch Arztebl Int. 2020;117(31-32):528-33. doi:10.3238/arztebl.2020.0528
12. 12. Rochwerg B, Granton D, Wang DX, Helviz Y, Einav S, Frat JP, et al. High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: A systematic review and meta-analysis. Intensive Care Med. 2019;45(5):563-72. doi:10.1007/s00134-019-05590-5
13. Chandel A, Patolia S, Brown AW, Collins AC, Sahjwani D, Khangoora V, et al. High-flow nasal cannula therapy in COVID-19: Using the ROX index to predict success. Respiratory Care 2021;66(6):909-19. doi:10.4187/respcare.08631
14. Hu M, Zhou Q, Zheng R, Li X, Ling J, Chen Y, et al. Application of high-flow nasal cannula in hypoxemic patients with COVID-19: A retrospective cohort study. BMC Pulmonary Med. 2020;20(1):324. doi:10.1186/s12890-020-01354-w
15. Mauri T, Carlesso E, Spinelli E, Turrini C, Corte FD, Russo R, et al. Increasing support by nasal high flow acutely modifies the ROX index in hypoxemic patients: A physiologic study. J Critical Care 2019;53:183-5. doi:10.1016/j.jcrc.2019.06.020

16. Kluge S, Janssens U, Welte T, Weber-Carstens S, Schälte G, Salzberger B, et al. Recommendations for treatment of critically ill patients with COVID-19. Der Anaesthesist. 2021;70(S1):19-29. doi:10.1007/s00101-020-00879-3
17. Scholten EL, Beitler JR, Prisk GK, Malhotra A. Treatment of ARDS with prone positioning. Chest 2017;151(1):215-24. doi:10.1016/j.chest.2016.06.032
18. Mitchell DA, Seckel MA. Acute respiratory distress syndrome and prone positioning. AACN Advanced Critical Care 2018;29(4):415-25. doi:10.4037/aacnacc2018161
19. Flynn Makic MB. Prone position of patients with COVID-19 and acute respiratory distress syndrome. J PeriAnesthesia Nursing 2020;35(4):437-8. doi:10.1016/j.jopan.2020.05.008
20. Coppo A, Bellani G, Winterton D, Di Pierro M, Soria A, Faverio P, et al. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): A prospective cohort study. Lancet Respir Med. 2020;8(8):765-74. doi:10.1016/S2213-2600(20)30268-X
21. Ghelichkhani P, Esmaeili M. Prone position in management of COVID-19 patients; A commentary. Arch Acad Emergency Med. 2020;8(1):48.
22. Mohammadi M, Varpaei HA, Amini M. Intubation prognosis in COVID-19 patients and associated factors: A cross-sectional study. Am J BiomedlSci Res [Internet]. 2020. Available from: https://www.researchgate.net/publication/347178027_Intubation_prognosis_in_COVID-19_patients_and_associated_factors_a_cross-sectional_study
23. Mohammadi M, Khafaee Pour Khamseh A, Varpaei HA. Invasive airway "intubation" in COVID-19 patients; Statistics, causes, and recommendations: A review article. Anesthesiology and Pain Med. 2021;11(3):e115868. doi:10.5812/aapm.115868
24. Cook TM, El-Boghdadly K, McGuire B, McNarry AF, Patel A, Higgs A. Consensus guidelines for managing the airway in patients with COVID-19. Anaesthesia 2020;75(6):785-99. doi:10.1111/anae.15054
25. Dalli J, Khan MF, Marsh B, Nolan K, Cahill RA. Evaluating intubation boxes for airway management. Br J Anaesthesia 2020;125(3):293-95. doi:10.1016/j.bja.2020.05.006
26. Begley JL, Lavery KE, Nickson CP, Brewster DJ. The aerosol box for intubation in coronavirus disease 2019 patients: An in-situ simulation crossover study. Anaesthesia 2020;75(8):1014-21. doi:10.1111/anae.15115
27. Sorbello M, Rosenblatt W, Hofmeyr R, Greif R, Urdaneta F. Aerosol boxes and barrier enclosures for airway management in COVID-19 patients: A scoping review and narrative synthesis. Br J Anaesthesia. 2020;125(6):880-94. doi:10.1016/j.bja.2020.08.038
28. Lim ZJ, Ponnapa Reddy M, Karalapillai D, Shekar K, Subramaniam A. Impact of an aerosol box on time to tracheal intubation: systematic review and meta-analysis. Br J Anaesthesia 2021;126(3):122-5. doi:10.1016/j.bja.2020.11.036
29. Noor Azhar M, Bustam A, Poh K, Zahedi AZA, Nazri MZAM, Ariffin MAA, et al. COVID-19 aerosol box as protection from droplet and aerosol contaminations in healthcare workers performing airway intubation: A randomized cross-over simulation study. Emergency Med J. 2021;38(2):111-7. doi:10.1136/emermed-2020-210514
30. Kafan S, TadbirVajargah K, Sheikhvatan M, Tabrizi G, Salimzadeh A, Montazeri M, et al. Predicting risk score for mechanical ventilation in hospitalized adult patients suffering from COVID-19. Anesthesiology and Pain Med. 2021;11(2):e112424. doi:10.5812/aapm.112424
31. Zheng H, Li S, Sun R, Yang H, Chi X, Chen M, et al. Clinical experience with emergency endotracheal intubation in COVID-19 patients in the intensive care units: A single-centered, retrospective, descriptive study. Am J Translational Res. 2020;12(10):6655-64.
32. Rahimzadeh P, Faiz HR, Farahmandrad R, Hassanlouei B, Habibi A, Emami SH, et al. Clinical features and prognosis of invasive ventilation in hospitalized patients with COVID-19: A retrospective study. Anesthesiol Pain Med. 2020;10(6):e108773. doi:10.5812/aapm.108773
33. Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al. An index combining respiratory rate and oxygenation to predict outcome of nasal high-flow therapy. Am J Respir Critical Care Med. 2019;199(11):1368-76. doi:10.1164/rccm.201803-0589OC
34. Prakash J, Bhattacharya PK, Yadav AK, Kumar A, Tudu LC, Prasad K. ROX index as a good predictor of high flow nasal cannula failure in COVID-19 patients with acute hypoxemic respiratory failure: A systematic review and meta-analysis. J Critical Care 2021;66:102-8. doi:10.1016/j.jcrc.2021.08.012
35. Huang J, Zeng J, Xie M, Huang X, Wei X, Pan L. How to perform tracheal intubation for COVID-19 patients safely and effectively: Experience AND tips from Sichuan, China. J Clin Anesthesia 2020;64:109800. doi:10.1016/j.jclinane.2020.109800
36. Whittle JS, Pavlov I, Sacchetti AD, Atwood C, Rosenberg MS. Respiratory support for adult patients with COVID-19. J Am Coll Emergency Physicians Open 2020;1(2):95-101. doi:10.1002/emp2.12071
37. Singh V, Sasidharan S, Naseer A, Singh-Dhillon H, Manalikuzhiyil B, Singh S, et al. Invasive mechanical ventilation of COVID-19 ARDS patients. Revista Peruana de Investigaciónen Salud. 2021;5(2):113-26. doi:10.35839/repis.5.2.930
38. Gattinoni L, Giosa L, Bonifazi M, Pasticci I, Busana M, Macri M, et al. Targeting transpulmonary pressure to prevent ventilator-induced lung injury. Expert Rev Respiratory Med. 2019;13(8):737-46. doi:10.1080/17476348.2019.1638767
39. Battaglini D, Robba C, Ball L, Silva PL, Cruz FF, Pelosi P, et al. Noninvasive respiratory support and patient self-inflicted lung injury in COVID-19: A narrative review. Br J Anaesthesia 2021;127(3):353-64. doi:10.1016/j.bja.2021.05.024
40. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. JAMA. 2020;323(16):1612. doi:10.1001/jama.2020.4326
41. Abrams D, Schmidt M, Pham T, Beitler JR, Fan E, Goligher EC, et al. Mechanical ventilation for acute respiratory distress syndrome during extracorporeal life support. Research and practice. Am J Respiratory Critical Care Med. 2020;201(5):514-25. doi:10.1164/rccm.201907-1283CI
42. Gattinoni L, Quintel M, Marini JJ. "Less is more" in mechanical ventilation. Intensive Care Med. 2020;46(4):780-2. doi:10.1007/s00134-020-05981-z
43. Marini JJ, Gattinoni L. Management of COVID-19 respiratory distress. JAMA. 2020;323(22):2329. doi:10.1001/jama.2020.6825
44. King CS, Sahjwani D, Brown AW, Feroz S, Cameron P, Osborn E, et al. Outcomes of mechanically ventilated patients with COVID-19 associated respiratory failure. PLOS ONE 2020;15(11):e0242651. doi:10.1371/journal.pone.0242651
45. Ionescu F, Zimmer MS, Petrescu I, Castillo E, Bozyk P, Abbas A, et al. Extubation failure in critically ill COVID-19 patients: Risk factors and impact on in-hospital mortality. J Intensive Care Med. 2021;36(9):1018-24. doi:10.1177/08850666211020281