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5.1 Treatment Principles for the Critical COVID-19 Patients Admitted to ICU

Zhaohui Fu

Early identification of critical COVID-19 patients who meet one of the following conditions:

1. Suffering from respiratory failure that requires mechanical ventilation.
2. Suffering from shock.
3. Suffering from a combination of other organ dysfunctions requiring ICU monitoring and management.

5.1.1 Treatment of Critical Patients

5.1.1.1 Treatment Principles

On the basis of symptomatic treatment, active life support shall be applied to prevent organ dysfunctions. Treat underlying diseases, and actively prevent and treat complications.

5.1.1.2 Respiratory Support

For patients who fail to respond to common oxygen therapy, oxygenation with high-flow nasal cannula or noninvasive ventilator-based ventilation may be considered. Changes in the patient’s respiratory status should be closely observed and tracheal intubation and invasive ventilation should be considered if the patient does not experience significant improvement within 1–2 h. Since some critical patients with severe hypoxia may not have significant symptoms of respiratory distress, careful assessment is required. The dynamic changes in HR, RR, BP, SPO2, blood gas analysis, etc. should be closely monitored, and attention may be paid to whether patients are using accessory respiratory muscles for breathing. If the patient’s condition does not improve, or with altered mental...
status, hemodynamic instability, failure to remove airway secretions, intolerance to noninvasive ventilation, etc., tracheal intubation and invasive ventilation should be considered as early as possible.

A “lung-protective strategy” for invasive mechanical ventilation, i.e., the administration of a lower tidal volume (predicted body weight 4–8 mL/kg) and a lower inspiratory pressure (plateau pressure <30 cm H₂O), should be applied to reduce ventilator-associated lung injury. High PEEP can be applied appropriately in case of ensuring a plateau pressure ≤35 cm H₂O. Human–machine dysynchrony may occur for many patients. Adequate sedation, analgesia, and muscle relaxant therapy may be considered. Closed suction tubing can be used, and fiber optic bronchoscopy will be performed in accordance with the patient’s airway secretions.

For patients with severe ARDS, lung recruitment is recommended. Prone position ventilation should be performed for more than 12 h/day. For patients with poor mechanical ventilation in the prone position, if conditions allowed, extracorporeal membrane oxygenation (ECMO) should be considered as soon as possible. ECMO indications: (1) In case of FiO₂ > 90%, oxygenation index less than 80 mmHg, with a duration of more than 3–4 h; (2) airway plateau pressure ≥35 cm H₂O. For patients with only respiratory failure, VV-ECMO mode will be preferred; if circulatory support is required, VA-ECMO mode shall be selected when the underlying disease has been controlled, cardiopulmonary function shows signs of recovery, and withdrawal tests can be initiated.

5.1.1.3 Circulatory Support
On the basis of adequate fluid resuscitation, microcirculation shall be improved, vasoactive drugs shall be used, and changes in patient’s blood pressure, heart rate, and urine volume as well as lactate and base excess in their arterial blood gas analysis shall be closely monitored. Noninvasive or invasive hemodynamic monitoring shall be performed, such as ultrasonic Doppler, echocardiography, invasive blood pressure, or PiCCO monitoring, when necessary. Identify the type of shock in patients to guide fluid replacement therapy.

5.1.1.4 Renal Failure and Renal Replacement Therapy
The cause of renal impairment in critical patients should be figured out actively. In the treatment of patients with renal failure, attention should be paid to fluid balance, acid–base balance, and electrolyte balance. For severe patients, CRRT can be considered for treatment. Indications include (1) hyperkalemia, (2) acidosis, (3) pulmonary edema or water overload, and (4) fluid management in case of multiple organ dysfunctions.

5.1.1.5 Nutritional Support
Patients admitted to the ICU should undergo nutritional risk screening using the Nutritional Risk Scale. ICU patients are most at risk of malnutrition, so nutritional support should be applied as early as possible. If the patient is able to eat, eating by mouth is preferred. If not, EN should be performed as early as possible (within 48 h). If EN cannot be administered, PN is recommended (3–7 days). For
patients with enteral nutritional intolerance, Erythromycin and other gastrointestinal motility drugs can be considered. In case of the poor effects of gastrointestinal motility drugs, jejunal feeding can be considered. PN should be considered in the absence of any effective attempt to improve EN tolerance, and regimen should be individualized with all-in-one formula as preferred. In the process of enteral nutrition support, gastrointestinal function such as gastric residual volume should be monitored, and attention should be paid to whether the patient has gastrointestinal symptoms such as diarrhea, nausea, and vomiting, and changes in blood glucose and electrolytes should be monitored. Patients with long-term parenteral nutrition support should be monitored for changes in blood glucose, electrolytes, liver, and renal function.

5.1.1.6 Convalescent Plasma Therapy
It applies to patients with rapid disease progression, severe, and critical types of illness.

5.1.1.7 Blood-Purifying Therapy
The blood purification system includes plasma exchange, adsorption, perfusion, blood/plasma filtration, etc., which can remove inflammatory factors and block the “cytokine storm,” thus mitigating the damage of inflammatory response to the body. It can be used for the early and mid-term treatment of cytokine storm in severe and critical patients.

5.1.1.8 Immunotherapy
For patients with extensive involvement and severe patients, and those with elevated IL-6 levels, tocilizumab treatment can be used. The first dose is 4–8 mg/kg (the recommended dose is 400 mg, diluted to 100 mL with 0.9% normal saline), infusion for more than 1 h; for patients with poor response to the first dose, an additional dose can be administered after 12 h (same dosage as the previous one). At the most maximum of 800 mg be aware of allergic reactions. It is contraindicated for patients with active infections such as tuberculosis.

5.1.1.9 Other Therapeutic Measures
For patients with progressive deterioration of oxygenation parameters, rapid imaging progression, and hyperactive body inflammation, glucocorticoids can be used in a short period of time (3–5 days) as appropriate, with the recommended dose not exceeding the equivalent of 1–2 mg/kg/day. It should be noted that larger doses of glucocorticoids will delay the clearance of coronavirus due to immunosuppressive effect; Xue Bi Jing (100 mL/time, twice daily) can be intravenously administered for treatment; intestinal microecological regulators can be used to maintain intestinal microecological balance and prevent secondary bacterial infection. Intravenous infusion of immunoglobulin can be considered for children with severe and critical symptoms as appropriate. Pregnant women with severe or critical COVID-19 should actively terminate their pregnancy, and cesarean section is preferred.
5.2 Anti-shock Therapy

Zhaohui Fu

For COVID-19 patients, shock is as one of the diagnostic criteria for critical illness, and also a sign of critical condition. With sudden increase of heart rate for more than 20% from baseline or the decrease of blood pressure greater than 20% from baseline, and accompanied by poor skin perfusion and decreased urine volume, the patient should be closely observed for septic shock, gastrointestinal bleeding, or heart failure. Meanwhile, we should quickly identify the type of shock in patients at an early stage.

The latest autopsy pathological changes in COVID-19 patients demonstrated visible degeneration and necrosis of myocardial cells in their heart, and infiltration of a few monocytes, lymphocytes, and/or neutrophils in the interstitium. Laboratory tests may reveal an increase in indicators such as TNI and CKMB, all of which suggest that the virus may cause myocardial damage. We found that some patients may be present with severe viral myocarditis or even cardiogenic shock during treatment. Patients with a combination of underlying diseases such as coronary heart disease, hypertension, and diabetes, may suffer from acute myocardial infarction. It resulted in more complex clinical pictures of such patients. Therefore, patients should undergo dynamic monitoring with ECG, myocardial enzyme spectrum, high-sensitivity troponin, B-type natriuretic peptide for identification, and, if necessary, coronary angiography can be performed to confirm the diagnosis. Bedside B-ultrasound, PICCO, etc. should be performed at an early stage for the assessment of changes in the patient’s cardiac function. Patients with cardiogenic shocks, such as showing decreased CI, pulmonary congestion, and shock should be actively treated with anti-shock management. If the patient is induced by acute myocardial infarction, antiplatelet, and PCI treatment should be considered as early as possible. If the patient suffers from myocardial damage caused by COVID-19 viruses, drugs can be considered for nourishing the myocardium, among which dopamine, dobutamine, and other drugs can increase myocardial contractility, and in severe cases, treatments including IABP, VA-ECMO, etc. may also be considered.

Hypovolemic shock can be caused by inadequate fluid intake at the early stage, strict fluid restriction due to severe ARDS, and negative balance in COVID-19 patients. Autopsy pathological changes in COVID-19 patients have suggested different degrees of degeneration, necrosis, and shedding of the mucosal epithelium of the esophagus, stomach, and intestine, so gastrointestinal bleeding is also one of their common complications. Hypovolemic shock can also be frequently observed in patients with gastrointestinal bleeding. Dynamically monitoring the blood routine coagulation function, blood gas analysis, etc. should be performed. Monitoring CVP, PICCO with bedside B-ultrasound and other identification and monitoring and management of patient volume may be considered. Active fluid resuscitation, transfusion of blood products, etc. can be pursued to correct shock. If gastrointestinal bleeding is difficult to be controlled by medical treatment, digestive endoscopic hemostasis, or even surgical treatment can be considered.
COVID-19 patients are prone to sepsis and septic shock. According to the latest diagnostic criteria for sepsis 3.0, sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response against infection. The clinical diagnostic criterion for sepsis is based on SOFA score ≥2 with coinfection. Septic shock is a severe form of sepsis, and the clinical diagnostic criteria are that patients with sepsis have persistent hypotension after adequate fluid resuscitation and require vasopressors to maintain mean arterial pressure above 65 mmHg and blood lactate above 2 mmol/L. Septic shock can be quickly identified by the means of qSOFA score, etc. Treatment of septic shock should begin with adequate fluid resuscitation (fluid resuscitation with crystalloids is preferred), improvement of microcirculation, and usage of vasoactive agents (norepinephrine is preferred). Epinephrine is recommended when more vasoconstrictors are needed to maintain adequate blood pressure. Changes in patient’s blood pressure, heart rate, and urine output, as well as lactate and base excess on arterial blood gas analysis should be closely monitored, and if necessary, noninvasive or invasive hemodynamic monitoring such as Doppler echocardiography, echocardiography, as well as invasive blood pressure or continuous cardiac output (PiCCO) monitoring should be performed. During treatment, attention should be paid to fluid balance strategies to avoid overdose and underdose.

Precautions for the treatment of septic shock: in the process of fluid resuscitation for patients with septic shock, lactate and lactate clearance rate can be used as indicators to determine the prognosis; crystalloids are the preferred resuscitation fluid for septic shock, and 30 mL/kg (body weight) of crystalloids should be rapidly infused within 1–2 h; hydroxyethyl starch is not recommended for fluid resuscitation; albumin can be considered for fluid resuscitation; the initial goal of vasoconstrictor drug therapy is for MAP close to 65 mmHg. Shock in patients at the early stage may be considered to be caused by viruses, and antiviral drugs can be considered and antibacterial drugs are selected based on PCT and WBC and etiology of the patients. Patients at the later stage are prone to bacterial or even fungal infections, and a comprehensive strategy may be considered. Sputum and blood microbiological tests should be performed as early as possible. If the effect of antibiotics is poor before drug sensitivity results have been obtained, the drug-resistant bacteria should be covered based on the situation of drug-resistant bacteria in our hospital.

COVID-19 patients showing shock symptoms are the signal for critical illness. The clinical picture of patients varies during treatment, so quick identification and active treatment are required. During the treatment, patients may experience ARDS aggravation, AKI, etc., and mechanical ventilation or even CRRT should be considered based on the condition. For patients with suboptimal shock correction, noninvasive or invasive hemodynamic monitoring such as Doppler echocardiography, echocardiography, as well as invasive blood pressure or continuous cardiac output (PiCCO) monitoring should be performed as early as possible. This will help us identify the type of shock at early stage to provide guidance on fluid resuscitation and treatment, which is important in managing the fluid balance of patients.
5.3 **Tracheal Intubation**

Weimin Xiao

5.3.1 **Emergency Plan and Technical Process of Urgent Tracheal Intubation for COVID-19 Patients**

Indications for urgent intubation for confirmed/clinically diagnosed/suspected cases in fever clinics and isolation ward areas:

1. It is manifested as severe hypoxemia without improvement or even deterioration of the condition under high-flow nasal cannula oxygen therapy or mechanical ventilation (the indications of BIPAP ventilator are patients with blood oxygen saturation less than 93%, no improvement of shortness of breath R > 30 beats/min, and conscious and cooperative patients under oxygen inhalation of 3–5 L/min).
2. Those who cannot clear respiratory secretions by themselves and need repeated suctioning due to significant amount of respiratory secretions.
3. Patients who are unable to wear a mask or nasal cannula due to facial trauma.
4. Patients with cardiorespiratory arrest.

5.3.2 **Ward Preparations for Intubated Patients**

Personnel preparation: Ask the doctor in charge and/or the medical personnel and nurses who are familiar with the usage and maintenance of ventilator as well as the operation of sputum suctioning for assistance.

Material Preparation:

1. Patients should fast for more than 6 h.
2. Sign the Informed Consent.
3. Open the venous access (with indwelling needles, 20G or above) and three-way valve, and connect to 0.9% normal saline.
4. Monitor vital signs (ECG, oxygen saturation, and blood pressure).
5. Connect the invasive ventilator with power supply, oxygen, screw pipe and membrane lung, and adjust the parameters of the respirator.
6. Reserve oxygen pillows full of oxygen for replacement.
7. Connect suction devices (negative pressure suction head, suction apparatus, connecting tube, and closed suction tube).
8. Prepare doctor’s prescription in advance and prepare sedatives.


5.3.3  Precautions for Tracheal Intubation by Anesthesiologists

1. Reconfirm the indications of tracheal intubation, and know the patient’s age, gender, weight, and complications upon notice via telephone.
2. Check the ventilator to set parameters properly, make sure the venous access is opened and evaluate the airway condition.
3. To reduce the risk of exposure, it is recommended that a trained and experienced anesthesiologist complete all the operations alone.
4. In order to reduce the cough caused by tracheal intubation and the spread of pathogens, moderate sedation, and intubation with adequate muscle relaxants are recommended.
5. For patients with unpredictable difficult airway and unsuccessful tracheal intubation for three times, laryngeal masks will be placed instead.

5.3.4  Protection Measures During Tracheal Intubation

Take Level-III medical protection measures:

Ensure good personal protection according to hospital requirements. For details, please see the manual “User Instructions for COVID-19 Protective Equipment”.

Protocol for donning PPE: Disinfect both hands → put on a surgical cap → put on a medical protective mask → put on goggles/face shield/medical mask with eye shield → put on isolation gown/protective suit → put on shoe covers → put on gloves.

Protocol for removing PPE: Remove shoe covers → remove gloves → disinfect hands → remove isolation gown/protective suit → disinfect both hands → remove goggles/face shield → disinfect hands → remove medical protective mask → disinfect both hands → remove disposable round cap → disinfect hands/wash hands → replace medical protective mask and disposable working cap.

Avoid vibrating while removing PPE: After the protective suit is removed, roll it up from the inner surface and place it in the yellow garbage bin. The protective gear shall be discarded into the double-layer yellow garbage bags and placed in designated areas.

Those who go to the infected area or intubate for the suspected COVID-19 cases shall be properly disinfected before reentering the operating room. It is strictly prohibited to leave the contaminated area without removing personal protective equipment and take any used protective suit back to the operating room.

5.3.5  Pre-intubation Preparations

Antifogging: Antifogging is of paramount importance, otherwise rapid and accurate tracheal intubation will be impossible. It is recommended to perform antifogging before arriving at the fever clinics or isolation ward areas. Treat as follows:

1. Spray goggles with antifogging agent. Doctors wearing glasses should spray their glasses for antifogging at the same time.
2. Application of povidone-iodine: Pour the iodophor into the goggles, shake it from side to side, dump the excess iodophor after it lies flat, and let the goggles dry before use.

3. Apply hand sanitizer or detergent evenly to goggles with gauze and allow them to dry before use.

   Narcotic drugs: Carry rapid onset general anesthesia-inducing drugs, such as Propofol, Etomidate, Fentanyl, and Rocuronium.

   First aid drugs: Prepare ephedrine, atropine, epinephrine, salbutamol, aminophylline, etc.

   Tracheal intubating appliances: Separately set up disposable visual laryngoscope lenses (discarded after use), primary tracheal tube bags, and appropriate models of tracheal tubes and laryngeal masks. After intubation, the visual laryngoscope stylet and video equipment will be disinfected in the contaminated area by UV light and then placed in a specific location of Intensive Care Unit (isolated storage).

5.3.6 Intubation Process

Before tracheal intubation, the patient monitoring equipment (ECG, blood pressure, and pulse oxygen saturation), intubation equipment (visual laryngoscope, oropharyngeal airway, tracheal tube, intubation stylet), and auxiliary respiratory equipment (respiratory balloon, mask) must be rechecked, various instrument circuits (at the head side of the patient), oxygen supply equipment and sputum suction equipment should be sorted out, and rescue drugs should be extracted for future use.

Preoxygenation before induction: Preoxygenation with 100% FiO₂ for 5 min through mask with oxygen storage bag, breathing mask, BIPAP ventilator, etc. [1]. High-flow preoxygenation can be administered through a mask when the patient is awake; oxygen flow can be increased in the case of BIPAP ventilator, and pressure-assisted ventilation should be avoided as much as possible before unconsciousness occurs to the patient. Patients with severe COVID-19, especially young children, obese, or pregnant patients, may see a rapid decrease in pulse oxygen saturation during intubation.

   Anesthesia induction process (at least one nurse or doctor in the isolation ward area is needed to participate during the whole process):

1. Patients with unknown history at fever clinic will be treated under the condition of nonfasting.

2. For patients in the intensive care unit, airway assessment is not possible due to wearing the BIPAP ventilator on arrival to the ward. It is recommended to not remove their breathing masks for airway assessment and treat them under the condition of difficult airway. First, use Propofol 0.5–1 mg/kg [2], and observe the change in the patient’s oxygen saturation under the condition of increased sedation (confrontations between insufficient sedation and noninvasive ventilator are common in the ward). When the saturation rises, use Propofol (60–80 mg)
again in combination of Rocuronium 0.9–1.2 mg/kg [2] and Fentanyl 2–4 μg/kg, while ensuring that BIPAP ventilator should not be withdrawn at this point.

Rapid intubation: Make sure the muscle relaxant works after 60–90 s of administration, and then quickly remove the respiratory mask of oxygen therapy or BIPAP ventilator and place the visual laryngoscope (preferred) [3] or common laryngoscope (disposable) to complete the intubation as fast as possible. It is recommended that the anesthesiologist perform the intubation alone, and, if necessary, some nurses can assist according to instructions from the anesthesiologist (nurses can help to deliver the catheter, pull out the stylet, and deliver pad, syringe, adhesive plaster, etc.), to ensure the successful completion of tracheal intubation.

Determination of depth of tracheal tube: The depth of tracheal tube for patients with severe pulmonary lesions cannot be determined through auscultatory breathing sound. It is recommended to observe the degree of thoracic fluctuation, respiratory waveform of ventilator, and respiratory parameters for comprehensive judgment. If conditions permit, end-tidal carbon dioxide or fiber optic microscopy can be used to determine the position of the tracheal tube [4], or use bedside ultrasonography to indirectly determine the position of the tracheal tube by checking whether it is mistakenly inserted into the esophagus. Auscultation is not recommended to determine the depth of tracheal tube, and bedside chest radiography can be applied after vital signs are stable [1].

For patients with oral secretions, if there is no respiratory tract obstruction, it is recommended to complete tracheal intubation followed by closed airway suctioning. If repeated intubation is not successful and the patient’s blood oxygen saturation is extremely low, it is recommended to quickly place the laryngeal mask for mechanical ventilation. After the oxygenation is improved, tracheal intubation will be reattempted.

5.3.7 Post-intubation Management

Improve Relevant Doctor’s Prescription and Intubation Records.

Routine sedation is recommended to avoid collapse or even prolapse of tracheal tubes due to biting from restless patients. To avoid secondary intubation caused by prolapse of tracheal tube, if necessary, muscle relaxants can be used to eliminate spontaneous breathing, and a nursing doctor’s advice on tracheal intubation should be prepared with the use of 0.5% erythromycin ointment to protect the cornea.

Lung protective ventilation strategy, i.e., mechanical ventilation with low tidal volume (4–8 mL/kg, ideal body weight) and low inspiratory pressure (plateau pressure <30 cm H2O) to reduce ventilator-associated lung injury, and arterial blood gas can be checked for adjustment of respiratory parameters [5].
5.3.8  Post-intubation Sedation and Analgesia
Plan for Patients in Wards

Recommended regimen of sedation for intubated patients on ventilators:

1. Phase 1: Basic Sedation (overlay of one or two regimens as appropriate)
   (a) Pump infusion of Propofol 0.5~3.0 mg/(kg·h), increase or decrease as appropriate [6].
   (b) Pump infusion of Dexmedetomidine 0.2~1.4 𝜇g/(kg·h), increase or decrease as appropriate [6, 7].
   (c) Pump infusion of Midazolam 0.02~0.1 mg/(kg·h), increase or decrease as appropriate [7].

2. Phase 2: Sedation + Analgesia (choose one as appropriate)
   (a) Pump infusion of Sufentanil 0.1~1 𝜇g/(kg·h), increase or decrease as appropriate.
   (b) Pump infusion of Remifentanil 0.05~2.0 𝜇g/(kg·min), increase or decrease as appropriate.

3. Phase 3: Sedation + Analgesia + Muscle Relaxation
   (a) Pump infusion of Rocuronium 0.01~0.012 mg/(kg·min), or single intravenous injection of Rocuronium 0.1~0.2 mg/kg.

5.4  TracheotomY

Xiaomeng Zhang

For severe and critical COVID-19 patients, tracheal intubation and mechanical ventilation are major treatments to maintain their vital signs. However, tracheotomy should be considered if prolonged tracheal intubation could not effectively promote the drainage and suctioning of sputum, and it may seriously affect the airway patency of the patient and can cause ventilator withdrawal.

During tracheotomy, the splashing of airway secretions caused by opening of airway-related wound, cough reflex, and ventilator ventilation may spray the virus-carrying secretions upon medical personnel and form the massive aerosol into the surgical environment, thus greatly increasing the risk of nosocomial dissemination [8]. Therefore, the primary task during tracheotomy is to protect the medical staff and the surgical environment from nosocomial infection.

Usually, percutaneous dilation tracheotomy should be preferred. It is a minimally invasive surgical method with the advantages of less time-consuming, less splashing, and operable at bedside [9]. However, some patients are not suitable for percutaneous dilation tracheotomy due to their neck conditions. At this point, traditional tracheotomy is an inevitable choice, though it is more dangerous than percutaneous tracheotomy.
5.4.1 Preoperative Evaluation

For patients undergoing elective tracheotomy, oro-tracheal intubation and mechanical ventilation are usually performed. Custodians, anesthesiologists, and otolaryngologists should conduct a comprehensive pre-surgery assessment to choose the appropriate timing and mode of tracheotomy. Whether early tracheotomy after mechanical ventilation with intubation facilitates early withdrawal of ventilator is still under academic controversy [10]. However, it is a consensus among all disciplines that the removal of tracheal intubation through the mouth can increase the comfort of the patient. Sedatives can be discontinued or reduced as soon as possible, and the replacement of tracheal intubation with tracheotomy, would reduce respiratory dead space and work of breathing. Therefore, upon comprehensive multidisciplinary assessment, elective tracheotomy may be generally considered when extubation cannot be performed after more than 7 days of oro-tracheal intubation and conventional mechanical ventilation, or in a short period of time. For those who are not suitable for percutaneous dilation tracheotomy mainly due to short neck, thyroid hyperplasia, cervical scar contracture, etc., traditional tracheotomy may be considered.

5.4.2 Mode of Anesthesia

Since most of the COVID-19 patients are scheduled for elective tracheotomy, it is recommended to perform tracheotomy under general anesthesia after tracheal intubation from a safe prospective.

For very few COVID-19 patients with upper airway obstruction who require emergency tracheotomy, surgery should be performed after tracheal intubation under general anesthesia. If it has to be done under local anesthesia, it is necessary to prepare for intubation under general anesthesia at the same time.

5.4.3 Preoperative Preparation

Preparation of personal protective equipment: It shall be carried out according to Level III protection criteria, including protective suits, N95 masks, goggles, foot covers, gloves, and positive pressure ventilation head covers.

Preparation of surgical environment and instruments: in consideration of the limited vision and operation of the operator under Level III protection criteria, except for the percutaneous dilation tracheotomy, all traditional tracheotomy should be carried out in the operating room with good lighting, suction devices, energy surgical instruments such as an electric knife or bipolar electrocoagulation in place, so as to reduce bleeding and obtain a clear operation vision.

Preparation of operating personnel: a group of three operators is recommended, among which one is the main surgeon, one the assistant, and the third can work as a back-up person to replace the one with discomfort at any time.
Preparation of anesthesia personnel: Preoperative assessment before general anesthesia and preparation for tracheal intubation under general anesthesia, control of anesthesia machine during surgery, replacement of intubation by mouth with ventilation through tracheostomy tube, etc.

5.4.4 Surgical Indications

Secretion retention caused by severe COVID-19 in the lower respiratory tract.
COVID-19 complicated with other diseases (such as stroke, postcraniac surgery, thoracoabdominal trauma, and myasthenia gravis) resulting in weak cough or inability to cough, who require long-term orotracheal intubation after evaluation.
Those with upper airway obstruction combined with novel coronavirus infection: severe laryngeal obstruction caused by laryngeal inflammation, tumors, trauma, or foreign bodies.

5.4.5 Relative Surgical Contraindications

Critical COVID-19 patients are often associated with severe coagulation abnormalities and thrombocytopenia. Operation should be carried out after the correction and improvement of these conditions.
Surgery can be performed after correction and improvement of the severe anemia.

5.4.6 Absolute Surgical Contraindications

1. Patients with tension pneumothorax
2. Hypovolemic shock
3. Patients with heart failure, especially right heart failure
4. Patients with bullae, pneumothorax, or pneumomediastinum without drainage
5. Patients with massive hemoptysis
6. Patients with recent acute myocardial infarction

5.4.7 Surgical Precautions

Follow the procedures of the tracheotomy with the same surgical risks and precautions. For traditional tracheotomy in COVID-19 patients, the surgeon should communicate and cooperate with the anesthesiologist, paying special attention to avoid splashing of airway secretions during tracheotomy, so as to avoid increasing the exposure risk for medical personnel and aerosol formation in the surgical environment. Specific measures may include ventilation through machine and totally stopping spontaneous respiration during surgery, avoiding pinching the balloon when incising the anterior wall of trachea, and transient cessation of mechanical ventilation from the timing of trachea incision to cannula insertion.


5.4.8 Surgical Complications

Postoperative bleeding; wound infection; subcutaneous emphysema; pneumothorax and mediastinal emphysema; cannula prolapse; respiratory arrest; tracheoesophageal fistula; laryngotraechal stenosis; difficult extubation; rare complications, including innominate artery and common carotid artery injury, recurrent laryngeal nerve paralysis.

5.5 ECMO Support

Zhaohui Fu

According to the pathological characteristics of diffuse alveolar injury caused by acute inflammation of COVID-19, for severe patients with respiratory failure, if the protective ventilation strategy and prone position cannot effectively improve oxygenation and eliminate carbon dioxide, early ECMO treatment should be pursued in case of no contraindications to prevent the increase of transpulmonary pressure due to respiratory distress and inappropriate mechanical ventilation, avoid further aggravation of lung injury, reduce pulmonary and systemic inflammatory response, and prevent secondary extrapulmonary tissue and organ injury caused by severe long-term hypoxia, so as to help patients survive the acute phase, and create conditions and buy time for the recovery of lungs.

Precautions for the application of ECMO in COVID-19: Timing and mode of intervention, anticoagulation and bleeding, coordination with mechanical ventilation, early rehabilitation training, withdrawal criteria, and treatment of complications.

5.5.1 Timing of ECMO Intervention

When protective mechanical ventilation with low tidal volume is used, positive end-expiratory pressure (PEEP) \( \geq 10 \) cm H\(_2\)O should be pursued combined with recruitment maneuver, prone position ventilation, neuromuscular block, and sedation. ECMO treatment is recommended when the following conditions occur with pure oxygen inhalation:

1. \( \text{PaO}_2/\text{FiO}_2 < 100 \) mmHg, or alveolar–arterial oxygen pressure difference \([\text{P} (A-a) \text{O}_2]\) > 600 mmHg.
2. Ventilation frequency \(<35\) breaths/min, pH < 7.2.
3. Plateau pressure >30 cm H\(_2\)O.
4. Age <65 years old.
5. Duration of mechanical ventilation \(<7\) days.
6. No contraindications: Irreversible primary disease; severe brain dysfunction; anticoagulant contraindications; advanced age >80 years; BMI > 45 kg/m\(^2\); high
ventilatory support level [airway plateau pressure $>30$ cm H$_2$O, FiO$_2$ $>0.8$] applied for more than 7~10 days. However, ECMO has no absolute contraindications. It is crucial to weigh the pros and cons and communication with the patient’s family for decision making.

7. The condition is potentially reversible.

### 5.5.2 Establishment of ECMO

Since the risk of blood splashing during the establishment of ECMO for COVID-19 patients is high, and due to the operational inconveniences possibly caused by multiple protections, in order to establish ECMO tubing as quick and accurate as possible and minimize infection, the following suggestions for the operation and protection during the establishment of ECMO are proposed:

1. Prepare 800 mL of suspended red blood cells, 400 mL of plasma, and 40 g of 20% human albumin in case to correct hypovolemia, coagulation function, and platelet count before catheterization.
2. The goggles must undergo sufficient antifogging treatment, so as to avoid affecting the visual field during operation.
3. Patients need adequate sedation and analgesia to prevent accidental body movement during operation, which will result in unnecessary tissue damage and prolonged operation time.
4. If possible, Level III protection can be applied.
5. Bedside ultrasound must be used to assess vascular conditions, cardiopulmonary function, and hemodynamic status before puncture.
6. Use ultrasound to measure the inner diameter of target puncture vessel, and correctly select the model of catheter. The inner diameter of catheter should not exceed 2/3 of that of the vessel.
7. Catheterization should be guided in real time using ultrasound localization.
8. Prepare for incision and catheterization. For patients with poor vascular conditions and failed puncture, multiple attempts should not be made to prevent severe vascular injury and massive hemorrhage.
9. After catheterization, the position of the drainage tube should be assessed ultrasonically before securing the catheter. The femoral drainage tube should be placed at the entrance of the vein into the right atrium.

### 5.5.3 Mode Selection

V-V mode should be applied for patients with simple respiratory failure, and V-A mode should not be preferred for possible circulatory problems;

For patients with respiratory failure who have cardiogenic shock due to a combination of severe cardiovascular dysfunctions (PaO$_2$/FiO$_2$ $<100$ mmHg), V-A-V mode should be selected, and maintain $V/A = 0.5/0.5$ by limiting flow; since
COVID-19 patients have severe pulmonary lesions and may have progressive aggravation of pulmonary conditions during ECMO, it is not recommended to use VA-ECMO to provide respiratory and circulatory support at the same time.

For COVID-19 patients without severe respiratory failure who have cardiogenic shock due to a combination of severe cardiovascular events, V-A mode should be selected for ECMO support, but mechanical ventilation will also be needed and awake ECMO should be avoided.

Given that COVID-19 patients treated with ECMO suffer from multiple organ dysfunctions, and medical and nursing personnel are in extreme shortage, ECMO treatments when patients’ conscious is clear are not recommended.

5.5.4 Flow Setting and Target of Oxygen Supply

The initial flow shall be >80% of CO (cardiac output).

SPO₂ > 90% and FiO₂ < 0.5 should be maintained during the maintenance.

Initial airflow regulation in V-V mode: blood flow: airflow = 1:1, basic target: PaCO₂ < 45 mmHg;

Be alert to the dysfunction of membrane lung caused by the accumulation of condensate due to long-term low airflow. It is necessary to regularly and intermittently increase the airflow to reduce the accumulation of condensate.

HCT should be maintained at 40–45% to ensure oxygen supply.

In the initial stage, sedation and analgesia or even muscle relaxant can be administered to avoid fever and tachycardia as well as reduce oxygen consumption.

Assess volume status to ensure normal cardiac output.

5.5.5 Setting of Ventilation Target

After ECMO operation, FiO₂ < 0.5 can be pursued, respiratory rate can be reduced by 4–10 breaths/min, and appropriate PEEP of 10–15 cm H₂O can be applied. According to respiratory mechanics monitoring, super protective mechanical ventilation (VT < 4 mL/kg) should be applied to make driving pressure <10 cm H₂O and plateau pressure <25 cm H₂O.

Prone position ventilation, lasting >12 h/day, can be administered during ECMO to promote lung recruitment. Be alert to unplanned extubation, catheter displacement, tube entanglement, pressure sore, etc. Reassess the position of catheter ultrasonically after prone position ventilation ends.

5.5.6 Anticoagulation and Bleeding Prevention

Before catheterization, for patients without active bleeding or visceral bleeding and platelets >80 × 109/L, the first loading dose of 20–30 U/kg is recommended.
For patients with a combination of bleeding risk or platelet <50 × 10⁹/L, component transfusion should be performed before catheterization to increase platelet count to be above 80 × 10⁹/L and correct FiO₂—4 g/L; coagulation PT should not be prolonged longer than 3–5 s against normal value; AT III should be maintained above 80%.

Coagulation function or ACT should be monitored every 4 h. The anticoagulation dose target can be maintained as APTT (activated prothrombin time) 60–80 s, or ACT 160–200 s, with reference to the trend of D-dimer; if possible, thromboelastography should be monitored intermittently.

In case of ECMO with heparin-free anticoagulation, for the purpose of getting active bleeding or fatal bleeding under control, where ECMO support cannot be discontinued, the all-heparin coated circuit and catheter with blood flow >3 L/min may be considered for heparin-free operation with recommended operation time <24 h, and equipment and consumables for replacement should be prepared in advance; anticoagulation should be gradually restored once active bleeding ceases or coagulation improves.

During heparin anticoagulation, if APTT cannot be up to standard and coagulation occurs, antithrombin III (ATIII) activity should be monitored. If activity reduces, fresh frozen plasma should be supplemented to restore heparin sensitivity.

As for heparin-induced thrombocytopenia (HIT), immune-mediated production of heparin platelet factor 4 (PF4) antibodies is present in patients, which results in abnormal platelet aggregation and thrombosis. Argatroban may be used as a substitute.

Attention should be paid to bleeding or exudation in the catheterization site, alimentary tract, invasive operation site, and intracranial area. The anticoagulation intensity can be reduced or anticoagulation can be suspended altogether depending on the severity of the bleeding event; if anticoagulation is discontinued, attention should be paid to the possibility of thrombosis in the catheter and membrane lungs, and a readily available ECMO system should be prepared at the bedside for replacement. Antifibrinolytic therapy can be used for treating surgical bleeding.

Thromboelastography should be monitored carefully to obtain a complete picture of coagulation and fibril volume.

Avoid unnecessary invasive procedures as much as possible to reduce bleeding.

### 5.5.7 Catheter-Related Bloodstream Infections

The majority of COVID-19 patients require prolonged VV-ECMO support, with prevention of blood flow in related catheters being a top priority. If possible, treatment should be carried out in a single room with special care by designated medical personnel. In patients with ECMO support for more than 1 week, PCT and CRP should be closely monitored, and attention should be paid to the sudden increase of body temperature or no increase in body temperature. In patients with ECMO support for over 2 weeks, regular blood cultures and G tests are recommended, so as to monitor bloodstream infections. During the process of ECMO withdrawal, blood
cultures, and cultures from intravascular catheter tips should be obtained. In addition to Gram-positive bacteria, Gram-negative bacteria should not be ignored in the bloodstream infections of ECMO patients either, most of which are multiple or pan-resistant bacterial infections, such as CRAB and CRE. During administration of antibiotics, attention should be paid to the lipid solubility of the drug, protein binding rate and the patient’s heart, liver and renal function, as well as serum albumin level, while adjusting the dosage and monitoring the drug concentration if possible.

5.5.8 ECMO Withdrawal

When the etiology is eliminated or condition improves, tidal volume recovery and CO₂ removal capacity are improved under the same support conditions, the ventilator should be maintained as follows before ECMO withdrawal:

1. Inhaled oxygen concentration <50%.
2. Tidal volume is 6–8 mL/kg, airway plateau pressure <25 cm H₂O, PEEP ≤ 10 cm H₂O.

Under the above conditions, blood flow of ECMO shall be lowered to 2 L/min without changing ECMO oxygen concentration, and observe it for 24 h. If vital signs are stable, experimental withdrawal could be considered. When lowering the flow, pay attention to strengthen anticoagulation so as to avoid thrombosis.

Experimental withdrawal: Blood flow of VV-ECMO and anticoagulation will remain unchanged with airflow of ECMO being turned off; changes in SaO₂, PaCO₂, airway pressure, respiratory rate, tidal volume, etc. will be monitored; duration of monitoring: 2–4 h. In case of SaO₂ > 95% and PaCO₂ < 50 mmHg, ECMO withdrawal may be considered.

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