# Chinese expert consensus on the diagnosis and treatment of severely and critically ill patients with coronavirus disease 2019

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The coronavirus disease 2019 (COVID-19) threatens the health of humans worldwide, and at the time of this writing, there is no specifically targeted effective drug for COVID-19. The major initial symptoms of patients with COVID-19 are fever, dry cough, and fatigue, although some patients mainly experience vomiting, diarrhea, and other gastrointestinal symptoms. Other severe symptoms, namely chest tightness, dyspnea, and respiratory distress, usually appear one week later, with some patients rapidly developing acute respiratory distress syndrome (ARDS), septic shock, and possibly even death. A retrospective study of critically ill patients with COVID-19 has recently reported that 67.3% of patients presented with ARDS, 28.9% with acute kidney injury, 23.1% with heart injury, and 28.9% with abnormality in liver function. In addition, the 28-day mortality rate was up to 61.5%.<sup>[1]</sup>

COVID-19 is a new disease that is poorly understood by humans; therefore, we draw lessons from the successful experiences in fighting against severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome, and conduct in-depth discussions with clinical experts who were working in frontlines in the battle against COVID-19. Finally, we reached consensuses on diagnosis, treatment principles (including antiviral therapy, glucocorticoid therapy, antibiotic therapy, organ function support, and other special treatments), prevention of complications, discharge, and follow-up of severe and critical COVID-19 patients [Supplementary Material, http://links.lww.com/CM9/A404].

The main suggestions are as follows:

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#### **Diagnosis**

Suggestion: Refer to "Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)". [2]

#### **Treatment**

In addition to symptomatic treatment, clinicians should prevent and treat complications, treat underlying conditions, prevent secondary infections, and provide organ function support in time.

#### Antiviral treatment

Suggestion: There is no specific effective antiviral drug for COVID-19.

Not suggested: Use of neuraminidase inhibitors (oseltamivir, palamivir, zanamivir, etc) and ganciclovir.

### Glucocorticoid therapy

Not suggested: The administration of systemic gluco-corticoids to severely and critically ill patients with COVID-19.<sup>[3]</sup>

Suggestion: Methylprednisolone (0.5–2.0 mg  $\cdot$  kg<sup>-1</sup>  $\cdot$  d<sup>-1</sup>) should be given as early as possible for 3 to 5 days to patients with rapidly progressing conditions and complicated by moderate-to-severe ARDS (partial pressure of oxygen [PaO<sub>2</sub>]/fraction of inspired oxygen [FiO<sub>2</sub>] <150 mmHg).

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#### Antibiotic treatment

Not suggested: The administration of antimicrobial drugs, especially combined with other broad-spectrum antimicrobial drug.

Suggestion: Second-generation cephalosporins can be used in short term to prevent bacterial infections for patients receiving glucocorticoid therapy. Besides, third-generation cephalosporins, combined with enzyme inhibitors, can be used empirically in those patients with bacterial coinfections.

#### Respiratory support therapy

- (1) Suggestion: Oxygen therapy is suggested for severely and critically ill patients with COVID-19 immediately.
- (2) Suggestion: Patients with severe acute hypoxic respiratory failure or mild-to-moderate ARDS (150 mmHg < PaO₂/FiO₂ ≤ 300 mmHg) should receive high-flow nasal oxygen (HFNO) as the first choice or non-invasive ventilation (NIV) as the second choice.
- (3) Suggestion: Patients with moderate-to-severe ARDS (PaO<sub>2</sub>/FiO<sub>2</sub> <150 mmHg) or failure in HFNO or NIV should receive invasive mechanical ventilation as the first choice.

The strategy of lung protective ventilation with low tidal volumes and extracorporeal membrane oxygenation (ECMO) therapy should be considered if partial pressure of carbon dioxide is still >50 mmHg and pH < 7.25 after increasing respiratory rate to 35 breaths/min with enough sedatives.

Positive end expiratory pressure (PEEP) titration is suggested to set the optimal PEEP level.

Prone position ventilation should be applied more than 12 h per day for patients with moderate-to-severe ARDS  $(PaO_2/FiO_2 < 150 \text{ mmHg})$  as early as possible.

For patients receiving invasive mechanical ventilation, the treatment of sedatives and analgesics is recommended but not as a routine treatment.

The closed suction pipe is suggested. The disconnection of ventilator requires clamping its pipe.

ECMO can be as a remedy for patients with severe ARDS.

#### Circulatory support therapy

- (1) Suggestion: Conservative fluid therapy is suggested for patients with ARDS who are sufficiently perfused.
- (2) Suggestion: The sepsis-3 definition should be referred to identify septic shock. [4]
- (3) Suggestion: Patients with septic shock accompanied by hypotension or lactate ≥4 mmol/L should be supplemented with isotonic crystalloid solution rapidly within 1 h.
- (4) Suggestion: With sufficient rescue fluid resuscitation, vasoactive drugs should be administered to maintain

the target mean arterial pressure ≥65 mmHg. Norepinephrine is the first choice for vasoactive drug therapy, and it can be combined with epinephrine, vasopressin, and dobutamine.

#### Renal support therapy

Suggestion: For patients with excessive inflammatory reactions, the use of *in vitro* blood purification techniques should be considered as early as possible.<sup>[2]</sup>

#### Liver support therapy

Suggestion: Patients with liver failure should receive artificial liver support.

## Cardiac protective therapy

Suggestion: COVID-19 patients accompanied with acute myocardial injury can be prescribed drugs nourishing the myocardium.

# Nutritional support and other treatments

- (1) Suggestion: Patients should receive enteral nutrition promptly, even during the use of prone position ventilation or ECMO, and intestinal micro-ecological therapy should be given as early as possible.
- (2) Suggestion: Human convalescent plasma containing SARS-CoV-2 antibodies can be used for patients with rapid disease progressing, or severely and critically ill patients.
- (3) Suggestion: Thymosin  $\alpha 1$  can be administered to patients with low lymphocyte counts and disordered cellular immune system. The treatment of gamma globulin has to be used with caution.
- (4) Suggestion: Ventilator-associated pneumonia, deep vein thrombosis, catheter-related bloodstream infections, stress ulcers, and intensive care unit-related complications should be prevented.
- (5) Suggestion: Chinese patent medicine suitable for severely and critically ill patients should be chosen, referring to "Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)". [2]
- (6) Suggestion: Psychological support and psychiatric consultation should be noted.

# **Discharge**

Refer to "Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)". [2]

#### Follow-up

Patients should be followed up at 1, 3, 6, and 12 months after discharge, and pulmonary function should be monitored.

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#### **Conflicts of interest**

None.

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