

## Expert consensus on the diagnosis and treatment of severe and critical coronavirus disease 2019

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This consensus focuses on severe and critical coronavirus disease 2019 (COVID-19) mainly based on the consideration that mortality of severe and critical cases is higher than mild and moderate cases of COVID-19. Severe patients usually developed dyspnea and/or hypoxemia in a short period of time, and in some cases progressively developed respiratory failure, septic shock, coagulation disorders, and multi-organ dysfunction.<sup>[1-3]</sup> To better standardize and guide the diagnosis and treatment of severe and critical COVID-19 patients and improve the treatment success rate, the frontline medical experts across China first

identified the problems relevant to the diagnosis and treatment of severe and critical COVID-19, then defined the clinical problems using the population, interventions, comparisons, and outcomes framework to guide the literature search. The databases searched included PubMed, Web of Science, and Embase. The keywords searched included severe acute respiratory syndrome-

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coronavirus-2 (SARS-CoV-2), novel coronavirus, nCoV, COVID-19, critically ill, severely ill, diagnosis, treatment, novel coronavirus pneumonia, severe and critical, and management. The keywords were searched in combination with free terms. The time period searched was from the date the databases were established to June 2022. All search results were pooled, including systematic reviews, meta-analyses, randomized, controlled studies, cohort studies, case reports, and guidelines. Publications not in English or Chinese and publications where full text was not available and the authors could not be reached were excluded. Based on a comprehensive review (analysis, consolidation, and summarization) of the treatment protocols, management consensuses, and relevant literature on COVID-19 and the experience gained from the diagnosis and treatment of severe and critical COVID-19 patients during the fight against the pandemic in China, a draft of this consensus was produced. The draft was subsequently discussed at face-to-face and online video expert workshops, underwent several rounds of revision (including repeated searching and updating of references), and finally formulated the current statement based on a consensus reached using the Delphi method. This consensus comprises 49 recommendations. The expert consensus involves etiology, pathology, pathophysiology, clinical features, classification, diagnostic criteria, early warning, clinical monitoring and treatment, traditional Chinese medicine, rehabilitation therapy, patients transfer, protection of health care workers, and vaccine. This expert consensus is expected to provide valuable suggestions for the treatment of severe and critical COVID-19 [Supplementary files, <http://links.lww.com/CM9/B253>].

The strength of the recommendations was graded using the grading of recommendations assessment, development, and evaluation approach. The recommendations were graded into three levels: strong recommendation, optional recommendation, and expert opinion, as shown in Table 1.

**Recommendation 1:** The experts suggest that patients aged >65 years, immunocompromised, unvaccinated, or with comorbidities could be at higher risk of developing severe COVID-19 after infection with Delta and Omicron variants. (Expert opinion)

**Recommendation 2:** Nucleic acid amplification testing for COVID-19 nucleic acid detection should probably be used as the first-choice method for the diagnosis of COVID-19. (Grade 2+, weak recommendation)

**Recommendation 3:** SARS-CoV-2-specific immunoglobulin (Ig) M and IgG antibodies assay should probably be used as an auxiliary method for the rapid diagnosis of COVID-19. (Grade 2+, weak recommendation)

**Recommendation 4:** SARS-CoV-2-specific antigen assays should probably not be used as a method for the rapid diagnosis of COVID-19. (Grade 2-, weak recommendation)

**Recommendation 5:** Nirmatrelvir plus ritonavir should be recommended for use within 3 days after the onset of symptoms for COVID-19 patients at risk of progression to severe COVID-19. (Grade 1+, strong recommendation)

**Recommendation 6:** The following antiviral drugs should not be selected for the treatment of severe COVID-19: remdesivir, lopinavir/ritonavir, favipiravir, and arbidol. (Grade 1-, strong recommendation)

**Recommendation 7:** Interferons should probably not be used as standard care for severe COVID-19. (Grade 2-, weak recommendation)

**Recommendation 8:** Chloroquine/hydroxychloroquine should not be used as standard care for severe COVID-19. (Grade 1-, strong recommendation)

**Recommendation 9:** Neutralizing antibodies should probably be used for the treatment of patients with early severe or advanced COVID-19. (Grade 2+, weak recommendation)

**Recommendation 10:** Convalescent plasma is not used as standard care for COVID-19 (Grade 1-, strong recommendation); however, severe COVID-19 patients should probably benefit from early infusion of high-titer convalescent plasma. (Grade 2+, weak recommendation)

**Recommendation 11:** Corticosteroids should probably not be used as standard care for patients with COVID-19

**Table 1: Strength of recommendation grading using the GRADE system.**

Evidence	Recommendation	Grade
High level of evidence	Strong recommendation	Grade 1+
Moderate level of evidence	“ . . . should be done . . . ” Weak recommendation	Grade 2+
Low level of evidence	“ . . . should probably be done . . . ” Recommendation in the form of an expert opinion	Expert opinion
Moderate level of evidence	“The experts suggest . . . ” Weak recommendation	Grade 2-
High level of evidence	“ . . . should probably not be done . . . ” Strong recommendation	Grade 1-
	“ . . . should not be done . . . ”	

GRADE: Grading of recommendations assessment, development, and evaluation.

(Grade 2–, weak recommendation); however, low-dose, short-course use of dexamethasone should be used for the treatment of patients with severe and critical COVID-19. (Grade 1+, strong recommendation)

**Recommendation 12:** Interleukin-6 receptor monoclonal antibodies should probably be used for the treatment of severe or critical patients under specific conditions. (Grade 2+, weak recommendation)

**Recommendation 13:** High-flow nasal cannula (HFNC) oxygen therapy should probably be selected as the first treatment choice for patients with oxygenation index ( $\text{PaO}_2/\text{FiO}_2$ ) = 200–300 mmHg. (Grade 2+, weak recommendation)

**Recommendation 14:** Close monitoring of patients undergoing HFNC therapy is necessary to prevent delayed intubation, and the respiratory rate-oxygenation index (defined as  $[\text{SpO}_2/\text{FiO}_2]/\text{respiratory rate}$ ) should probably be a potential predictor of HFNC success. (Grade 2+, weak recommendation)

**Recommendation 15:** Non-invasive ventilation (NIV) support should probably be tried in COVID-19 patients with a  $\text{PaO}_2/\text{FiO}_2 \leq 200$  mmHg. (Grade 2+, weak recommendation)

**Recommendation 16:** The experts suggest that invasive mechanical ventilation (IMV) with tracheal intubation is used in patients with  $\text{PaO}_2/\text{FiO}_2 < 150$  mmHg, consciousness disorder, hemodynamic instability, or respiratory distress or hypoxemia after receiving NIV or HFNC. (Expert opinion)

**Recommendation 17:** The experts suggest that rapid sequence induction and intubation in patients with COVID-19 is performed after pre-oxygenation. (Expert opinion)

**Recommendation 18:** Timely tracheotomy should probably be used for critical COVID-19 patients when failure of timely extubation is expected. (Grade 2+, weak recommendation)

**Recommendation 19:** Low-tidal-volume ventilation should probably be used for COVID-19 patients with acute respiratory distress syndrome (ARDS) undergoing IMV. (Grade 2+, weak recommendation)

**Recommendation 20:** For COVID-19 patients with ARDS undergoing IMV, plateau pressure should probably be set  $< 30$  cmH<sub>2</sub>O and the driving pressure  $< 15$  cmH<sub>2</sub>O. (Grade 2+, weak recommendation)

**Recommendation 21:** For COVID-19 patients with ARDS undergoing IMV, positive end-expiratory pressure (PEEP) should probably be initially set according to the ARDS-net low PEEP/ $\text{FiO}_2$  table and subsequently titrated according to the patient's respiratory system compliance, oxygenation, and dead space. (Grade 2+, weak recommendation)

**Recommendation 22:** Recruitment maneuver should probably not be used as standard care for COVID-19

patients with ARDS undergoing IMV. (Grade 2–, weak recommendation)

**Recommendation 23:** The experts suggest that bedside bronchoscopy could improve sputum suction in mechanically ventilated patients with severe COVID-19. (Expert opinion)

**Recommendation 24:** Awake prone positioning should probably be used for non-intubated severe COVID-19 patients with persistent hypoxemia. (Grade 2+, weak recommendation)

**Recommendation 25:** For invasively ventilated patients with critical COVID-19, prone positioning no less than 16 h daily should probably be used. (Grade 2+, weak recommendation)

**Recommendation 26:** For critical COVID-19 patients with refractory hypoxemia and/or hypercapnia after fully optimized lung-protective ventilation and prone positioning, ECMO should probably be used as early as possible at experienced centers. (Grade 2+, weak recommendation)

**Recommendation 27:** Close monitoring and evaluation of patients with severe COVID-19 undergoing HFNC oxygen therapy and NIV are indispensable, and a light sedation protocol should probably be used for less-tolerable patients. (Grade 2+, weak recommendation)

**Recommendation 28:** For mechanically ventilated patients with early COVID-19 and moderate-to-severe ARDS, adequate analgesia and deep sedation should probably be used. (Grade 2+, weak recommendation)

**Recommendation 29:** For COVID-19 patients with moderate-to-severe ARDS ( $\text{PaO}_2/\text{FiO}_2 \leq 150$  mmHg) who have respiratory distress and tidal volume  $\geq 8$  mL/kg predicted body weight after appropriate sedation and analgesia, neuromuscular blockers should probably be used based on the patient's conditions. (Grade 2+, weak recommendation)

**Recommendation 30:** For invasively ventilated COVID-19 patients with moderate-to-severe ARDS who have entered the convalescent period, the experts suggest a light sedation strategy is used to prevent delayed ventilator removal. (Expert opinion)

**Recommendation 31:** The experts suggest delirium screening and evaluation is used as standard care for patients with severe and critical COVID-19. (Expert opinion)

**Recommendation 32:** Close monitoring of COVID-19 patients for hypoxia and inflammatory response-induced myocardial injury should probably be performed. (Grade 2+, weak recommendation)

**Recommendation 33:** Considering that acute right ventricular impairment is not uncommon in patients with COVID-19, optimization of right ventricle-pulmonary artery coupling should probably be used to improve cardiac efficiency. (Grade 2+, weak recommendation)

**Recommendation 34:** For COVID-19 patients with abnormal pulmonary blood flow distribution, optimization of the mechanical ventilation strategy should probably be used to improve abnormal pulmonary blood distribution-induced dead space ventilation. (Grade 2+, weak recommendation)

**Recommendation 35:** Screening the risk of venous thromboembolism in patients with severe and critical COVID-19 and dynamically evaluating its evolutions should probably be performed. (Grade 2+, weak recommendation)

**Recommendation 36:** Anticoagulation interventions using low-molecular-weight heparins or unfractionated heparins should probably be used for severe and critical COVID-19 patients without contraindications to anticoagulation. (Grade 2+, weak recommendation)

**Recommendation 37:** Prophylactic antimicrobial agents should probably not be used as standard care for patients with COVID-19 unless definitive evidence of bacterial or fungal secondary infections is available. (Grade 2–, weak recommendation)

**Recommendation 38:** The experts suggest that renal replacement therapy (RRT) is initiated in a timely manner for COVID-19 patients with AKI and indications of RRT. (Expert opinion)

**Recommendation 39:** Blood purification therapy should probably not be used as standard care for clearing inflammatory mediators and cytokines in COVID-19 patients. (Grade 2–, weak recommendation)

**Recommendation 40:** Early nutritional risk assessment and therapy should probably be performed for patients with severe and critical COVID-19. (Grade 2+, weak recommendation)

**Recommendation 41:** The experts suggest a target calorie intake of 20 to 25 kcal/kg (actual body weight if BMI <30 kg/m<sup>2</sup>; adjusted body weight for obese patients) is used for the early stage (first week) of intensive care unit (ICU) stay, with calorie intake to be increased appropriately in later stages based on the patient's clinical status. The daily protein intake is 1.2 to 1.5 g/kg. For patients with a 25-hydroxyvitamin D level <50 nmol/L, 500,000 IU complement vitamin D3 is suggested to be given within 1 week. (Expert opinion)

**Recommendation 42:** The experts suggest that enteral nutrition (EN) is administered to severe and critical COVID-19 patients within 24 to 48 h of ICU admission, and parenteral nutrition is administered to ICU patients intolerable to all-calorie tube feeding of EN. (Expert opinion)

**Recommendation 43:** Early mobilization in patients with severe COVID-19 is safe and effective, and early initiation of rehabilitation therapy should probably be used in patients with stable clinical status and indications of early mobilization. (Grade 2+, weak recommendation)

**Recommendation 44:** Patients with severe and critical COVID-19 should probably receive psychological rehabilitation therapy during hospitalization and after discharge. (Grade 2+, weak recommendation)

**Recommendation 45:** The experts suggest that diagnostic and therapeutic operations are performed at bedside as far as possible to avoid unnecessary transfer. If the situation does warrant a transfer, it can be performed after an adequate risk assessment, formulation of a transfer program, and preparation of an emergency response plan for potential risks. In addition, life-threatening medical conditions need to be corrected as far as possible before a transfer. (Expert opinion)

**Recommendation 46:** The experts suggest necessary monitoring and therapeutic measures should be taken during transport, and the original monitoring and therapeutic measures should be maintained as far as possible; negative-pressure transfer devices should be used, such as negative-pressure transfer vehicles and beds; healthcare workers should use third-level protection. (Expert opinion)

**Recommendation 47:** The experts suggest that ICUs hosting patients with severe COVID-19 have a “three zones, two lines, three passages” layout. (Expert opinion)

**Recommendation 48:** The experts suggest that ICU healthcare workers involved in the treatment of COVID-19 assess the risk of the medical operations and use appropriate personal protective equipment. Third-level protection is used when performing high-risk operations such as tracheal intubation, tracheotomy, and tracheoscopy. (Expert opinion)

**Recommendation 49:** COVID-19 vaccination should probably be used to reduce the proportion of breakthrough infections that progress to severe and critical illness. (Grade 2+, weak recommendation).

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### Conflicts of interest

None.

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