

Critical care for severe coronavirus disease 2019: a population-based study from a province with low case-fatality rate in China

Xue-Lian Liao¹, Hong Chen², Zhen Li³, Bo Wang^{1,2}, Zhong-Wei Zhang¹, Wei-Min Li⁴, Zong-An Liang^{2,4}, Jin Tang⁵, Jian Wang⁵, Rui Shi^{6,7}, Xiao-Dong Jin¹, Yan Kang¹, SUNRISE Group

¹Department of Critical Care Medicine, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China;

²Department of Critical Care Medicine, Public Health Clinical Centre of Chengdu, Chengdu, Sichuan 610066, China;

³Clinical Research Centre, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Shanghai 201204, China;

⁴Department of Respiratory and Critical Care Medicine, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China;

⁵Department of Critical Care Medicine, Guang'an People's Hospital, Guang'an, Sichuan 638001, China;

⁶Department of Orthopaedics, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China;

⁷Department of Infectious Disease, Ganzi Hospital of West China Hospital, Ganzi Tibetan Autonomous Prefecture People's Hospital, Ganzi, Sichuan 626000, China.

The coronavirus disease 2019 (COVID-19) pandemic has affected over twenty million people worldwide since its outbreak,^[1] in which approximately 19% are expected to progress to severe or critical disease, constituting the high-risk group for death.^[2] The reported case-fatality rates among the severe COVID-19 varied a lot across different regions from zero to 61.5%^[1,3] and the reason behind remained unclear. Very limited data concerning management of severe cases were reported from low case-fatality areas. In this study, we described the clinical features, multi-strategy management, and respiratory support resources usage for the severe COVID-19 in Sichuan province, where the 28-day case-fatality rate was 0.6% in all patients and 3.7% in severe cases, which was much lower compared with that reported in most of the studies worldwide.

Using data from Sichuan Provincial Department of Health, the multicentre cohort study (StUdy of 2019 Novel coRonavirus pneumonia Infected critically ill patients in Sichuan provincE, SUNRISE, ChiCTR2000029758) was performed.^[4] All 21 hospitals designated for patients with severe COVID-19 in the province were included. Data were prospectively collected for patients who were still in the hospital after study enrolment, and otherwise retrospectively collected, between January 16 and March 15 [Supplementary Figure 1, <http://links.lww.com/CM9/A369>]. All microbiologically confirmed COVID-19 patients who met any of the five following criteria^[2] were

included as severe cases: (1) dyspnoea or respiratory frequency ≥ 30 breaths/min; (2) pulse oxygen saturation (SpO_2) $\leq 93\%$ without oxygen therapy in resting state; (3) partial pressure of oxygen/fraction of inspired oxygen (P/F) ratio ≤ 300 mmHg; (4) lung infiltrates $> 50\%$ within 24 to 48 h; (5) respiratory failure, septic shock, and/or multiple organ dysfunction. The day of enrolment of each patient with severe COVID-19 was considered day 1 (D1). Each patient was followed up from D1 until discharge, death, or the end of the study. Clinical outcomes by D28, including rapid recovery (RR), prolonged recovery (PR), and no recovery (NR), were defined as follows: (1) RR: patient fully meeting the discharge criteria before D28, with normal body temperature ≥ 3 days, obvious improvement in respiratory symptoms and pulmonary imaging, and twice-negative nucleic acid tests (sampling interval being at least 24 h) on respiratory samples; (2) PR: patient partially meeting the discharge criteria on D28 and still requiring hospitalization but without advanced respiratory support; (3) NR: death or the patient still in need of advanced respiratory support on D28. The study protocol was approved by the Ethics Committee of the West China Hospital and the participating hospitals (No. 2020-131). Informed consent was obtained from the patient or the patient's legally authorized representative.

Eighty-one out of 539 patients were identified as severe cases. The median (interquartile range [IQR]) durations

Xue-Lian Liao, Hong Chen, and Zhen Li contributed equally to this work.

Correspondence to: Dr. Xiao-Dong Jin, Department of Critical Care Medicine, West China Hospital, Sichuan University, 37 Guo Xue Xiang Street, Chengdu, Sichuan 610041, China
E-Mail: zh_jxd@163.com

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from the onset of symptoms to the first hospitalization and the diagnosis of severe condition were 3 (1–6) and 9 (6–11) days, respectively. Among the five severe diagnostic criteria,^[2] P/F ≤300 mmHg, SpO₂ ≤93% without oxygen therapy in resting state, and dyspnoea were the most commonly reported, accounting for 87.7% (71/81), 66.7% (54/81), and 27.2% (22/81), respectively. The median age (IQR) of the patients was 50 (39–65) years, 37.0% (30/81) were female, and 50.6% (41/81) were with a body mass index ≥24 kg/m². The elderly (age ≥65 years) accounted for 28.4% (23/81) of the patients and chronic comorbidities were observed in 43 (53.1%) patients. All patients were followed up to the end of the study. Fifty-three (65.4%) were discharged before D28 and regarded as RR. Eighteen (22.2%) patients were regarded as PR, including 13 still in need of conventional oxygen therapy (COT) and five awaiting negative results of reverse transcription-polymerase chain reaction on D28. Ten patients (12.3%) were in the NR group, including three deaths and seven still in need of advanced respiratory support including high flow nasal cannula (HFNC), non-invasive (NIV) or invasive mechanical ventilation (IV) [Supplementary Table 1, <http://links.lww.com/CM9/A369>].

Among the 18 designated hospitals receiving severe cases, only two had standard intensive care unit (ICU) wards, while 16 had provisional ICUs which were transformed from general wards for infectious disease and equipped with ICU team and equipment needed. All 81 severe cases were centralized to the 18 ICUs, among whom 51 (63.0%) were treated in 16 provisional ICUs. Seventy (86.4%) patients were transferred from non-designated hospitals or designated hospitals for non-severe cases, and only 11 (13.6%) were admitted directly. In total, 77 patients

(95.1%) were admitted to ICUs by D1 [Supplementary Figure 2, <http://links.lww.com/CM9/A369>].

Respiratory support was the most commonly used organ support method for patients with severe COVID-19. On D1, 76 patients (93.8%) received respiratory support, including 55 (67.9%) with COT, 13 (16.0%) with NIV, and 8 (9.9%) with HFNC. No patient was intubated or given extracorporeal membrane oxygenation (ECMO) [Supplementary Figure 3, <http://links.lww.com/CM9/A369>]. During the study period, 79 (97.5%) patients used COT, 31 (38.3%) used HFNC, 22 (27.2%) used NIV, 10 (12.3%) used IV, and 1 (1.2%) used ECMO. Thirty-four patients (42.0%) used only COT among which 79.4% (27/34) were discharged before D28. In the 25 patients who started with COT and needed escalation to advanced respiratory support methods, 12 (48.0%) were discharged by D28. In total, all forms of respiratory support were used 1579 person-day, of which COT took up 62.7% (990 person-day), HFNC 19.3% (305 person-day), NIV 9.4% (149 person-day), IV 8.5% (134 person-day), and ECMO 0.1% (one person-day). The peak needs of respiratory support, which developed on February 5, had a significant lag of 9 days behind the peak of newly diagnosed patients in Sichuan, lasted for 20 days and paralleled with hospitalization needs for severely ill patients [Figure 1].

Early identification of severe COVID-19 is a prerequisite for timely interventions for severe COVID-19. For the diagnosis of severe cases, different criteria were used in the previous studies while some did not report clear criteria. In this study, using the criteria for severe cases proposed by the National Health Commission of the People’s Republic

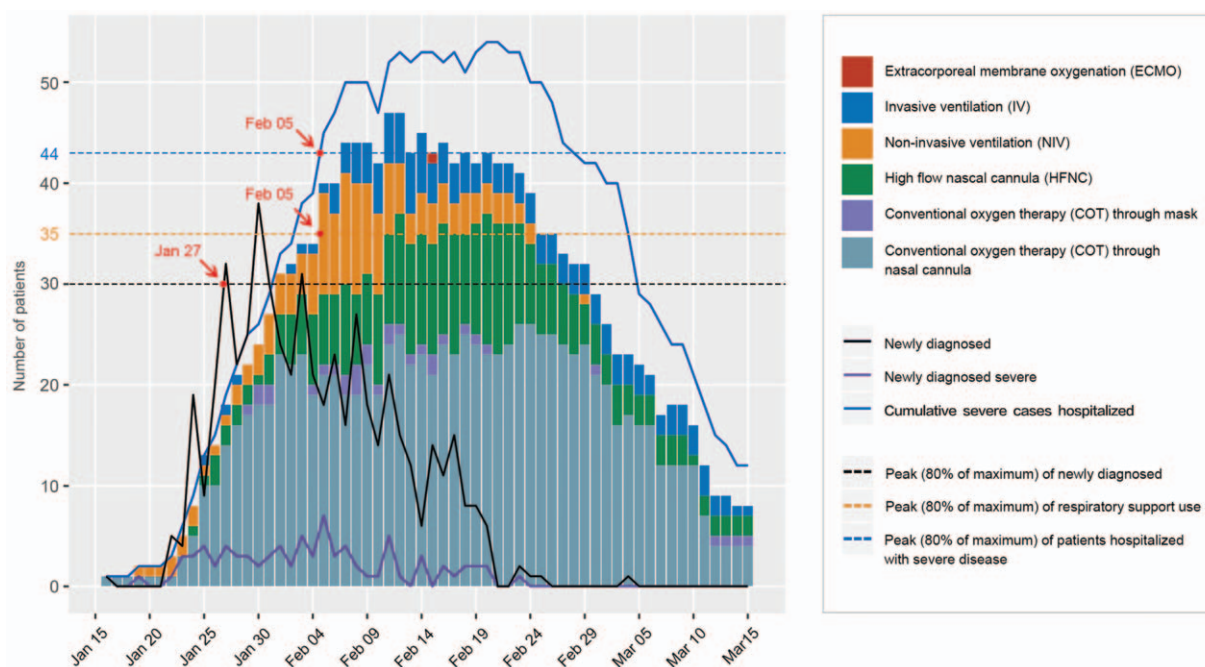


Figure 1: Daily respiratory support needs for patients with severe COVID-19. The bar plot shows, for each calendar day, counts of the respiratory support used for patients with severe COVID-19. Daily number of newly diagnosed patients with COVID-19 disease in Sichuan, newly diagnosed severe cases, and cumulative severe cases hospitalized are shown in lines. COVID-19: Coronavirus disease 2019.

of China, none of the severe cases needed mechanical ventilation or ECMO on the day of diagnosis. In particular, our data showed that, on the day of diagnosis of severe COVID-19, up to 72.8% did not present symptoms of dyspnoea and only 33.3% had an SpO₂ no less than 93%. Using only dyspnoea or SpO₂ as the diagnostic criteria would fail to identify a large number of severe cases of COVID-19 in the early stage and miss the opportunity of intervening in time. P/F ratio was more likely a sensitive indicator for early identification of severe COVID-19, as 87.7% severe cases were identified by using this criterion. With early identification of the severe illness, 93.8% patients in this study received various respiratory support by D1, with a median P/F ratio of 204 mmHg. In the previous studies, the reported median P/F ratio on ICU admission was much lower (103.8–169.0 mmHg).^[3,5] Similar to the patients in Sichuan, the patients outside Wuhan were less severe than those in Wuhan in China. The use of sensitive diagnostic criteria might be crucial for improving prognosis of patients with old age or comorbidity, for whom symptoms may be more atypical and the progression of the disease may be faster than others.

The shortage of advanced support equipment such as ventilators is a challenging issue. As there's no definite effective drug to treat COVID-19, appropriate respiratory therapy is essential for severe cases. According to data reported in studies from Wuhan and a study from the US, IV was administered in 38.9% to 71% of severely ill patients.^[5,6] However, in our study, IV was used in only 12.3% of the patients and the case-fatality rate was much lower than that in these studies. This difference may be explained, at least in part, by the timing of intervention. It is reasonable to hypothesize that hypoxemia may participate in multiple organ injury if the hypoxic compensatory period was missed or the patients were not treated timely. Given that the COVID-19 pandemic is spreading rapidly, this finding is of particular interest for treating newly diagnosed severe cases and for regions facing a shortage of ventilators.

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Conflicts of interest

None.

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