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The clinical course of critically ill COVID-19 patients receiving invasive mechanical ventilation with subsequent terminal weaning

Primary data from 11 cases

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Abstract

The coronavirus disease (COVID-19) outbreak was first reported in December 2019 in Wuhan, China. Specific information about critically ill COVID-19 patients receiving invasive mechanical ventilation (IMV) is rare.

To describe the clinical course and complications of critically ill patients with COVID-19 who received IMV and were successfully weaned from it.

This retrospective study included patients admitted to 3 intensive care units (ICUs) and 1 sub-ICU of Renmin Hospital of Wuhan University and Wuhan Jin Yin-tan Hospital between December 24, 2019, and March 12, 2020. Eleven patients who had been diagnosed with critically ill COVID-19 according to the World Health Organization interim guidance, received invasive ventilation, and were finally successfully weaned from it, were enrolled in our study. Their presenting symptoms, comorbidity conditions, laboratory values, ICU course, ventilator parameters, treatments, and relative complications were recorded.

Of 108 critically ill COVID-19 patients who received invasive ventilation, 11 patients who underwent tracheal extubation or terminal weaning were included. The mean age of the 11 patients was 52.8 years (range, 38–70 years), 8 (72.7%) were male, and 2 were health care workers. The median time from onset of symptoms to dyspnea was 6.6 days (range, 3–13 days), and the median duration of IMV was 15.7 days (range, 6–29 days). All 11 patients presented with acute severe hypoxemic respiratory failure and received IMV, and 1 patient switched to extracorporeal membrane oxygenation assistance. A lung-protective strategy with lower tidal volume ventilation and proper driving pressure is the main strategy of IMV. All patients had extrapulmonary manifestations, including acute kidney injury, hepatic dysfunction, myocardial damage, and/or lymphopenia. Hospital-acquired infections occurred in 7 (63.6%) patients.

Critical COVID-19 illness is characterized by acute hypoxemic respiratory failure and subsequent dysfunction of other organs with a high mortality rate. Correct ventilation strategies and other clinical strategies to improve oxygenation based on the skilled trained group and the availability of equipment are the key methods to rescue lives.

Abbreviations: AKI = acute kidney injury, ALSS = artificial liver support system, ARDS = acute respiratory distress syndrome, COVID-19 = coronavirus disease, ECMO = extracorporeal membrane oxygenation, HFNC = high-flow nasal cannula, ICU = intensive care unit, IMV = invasive mechanical ventilation, NIPPV = non-invasive positive-pressure ventilation, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Keywords: coronavirus disease, critically ill, intensive care unit, invasive mechanical ventilation

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YL, WX, and YM contributed equally to this work.

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All relevant data are within the study and its supporting information files.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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1. Introduction

The pandemic of the coronavirus disease (COVID-19) started in Wuhan in December 2019 and outbroke across the world.[1–4] As of March 23, 2020, more than 350,000 patients with COVID-19 have been reported, and more than 15,000 deaths have been confirmed globally. On January 3, 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in bronchoalveolar lavage fluid samples from a patient and was confirmed as the cause of COVID-19. SARS-CoV-2 belongs to the coronavirus family and is classified into the beta-coronavirus 2b lineage. The clinical spectrum of COVID-19 ranges from mild to critical. The main presenting symptoms were fever, cough, dyspnea, weakness, and sore throat. The mortality of critically ill patients with COVID-19 who are diagnosed with SARS is considerable, particularly in critically ill patients receiving invasive mechanical ventilation (IMV).[3,5] However, specific information characterizing invasive ventilated critical patients remains unknown.

We described and analyzed the clinical, laboratory, and radiological characteristics and treatment of 11 critically ill patients with COVID-19 who received tracheal intubation and IMV, and were finally successfully weaned. These patients were recruited from 3 intensive care units (ICUs) and a sub-ICU of Renmin Hospital of Wuhan University and Wuhan Jin Yin-tan Hospital. Eleven patients presented with acute severe hypoxemic respiratory failure and received IMV, and 1 patient switched to extracorporeal membrane oxygenation (ECMO) assistance. The median duration of IMV was 15.7 days (range, 6–29 days). A lung-protective strategy with lower tidal volume ventilation and proper driving pressure is the main strategy of IMV. All patients had extrapulmonary manifestations, including acute kidney injury (AKI), hepatic dysfunction, myocardial damage, and/or lymphopenia. We anticipate that the findings will inform the global medical fraternity of the clinical features of the critical type of COVID-19 with IMV.

2. Methods

2.1. Design

During the COVID-19 outbreak, the number of critically ill patients exceeded the capacity of ICUs. Therefore, some temporary ICUs and sub-ICUs were established at the Renmin Hospital of Wuhan University and Jin Yin-tan Hospital. We conducted a retrospective study focusing on patients from December 24, 2019, to March 12, 2020, who had been diagnosed with COVID-19 according to World Health Organization interim guidance, were critically ill, requiring invasive ventilation, and were successfully weaned off and extubated. These patients were recruited from 3 intensive care units (ICUs) and a sub-ICU of Renmin Hospital of Wuhan University and Wuhan Jin Yin-tan Hospital. Laboratory confirmation of COVID-19 was performed using throat swab samples. Positivity for either of the 2 target genes, including open reading frame lab and nucleocapsid protein (N), was tested using the real-time polymerase chain reaction (RT-PCR) assay, and the patients were confirmed to be SARS-CoV-2 positive.[6]

Critically ill patients were defined as those admitted to the ICU, requiring mechanical ventilation or with fraction of inspired oxygen (FiO_2) being a minimum of 60% or more.[7,8] This study was approved by the National Health Commission of China and the Ethics Commission of Renmin Hospital of Wuhan University, and Jin Yin-tan Hospital. Written informed consent was waived by the ethics committee of the designated hospital for the emergence of infectious diseases.

2.2. Data collection

We reviewed the clinical electronic medical records, nursing records, laboratory test results, and radiological examinations of the enrolled patients. Two authors independently extracted and collected data with consensus regarding all terms by using a case record from a modified version of the International Severe Acute Respiratory and Emerging Infection Consortium case report forms.[9] If the data were not identical, both investigators checked the data again to reach an agreement.

Data on demographic characteristics, contact history with a COVID-19-confirmed patient, underlying comorbidity conditions, symptoms from onset hospital admission, and radiographic findings were collected from the medical records. On the day of oral tracheal intubation, we evaluated the severity of the illness in patients using the sequential organ failure assessment.[10] On days 1, 2, 3, 7, and 14 of intubation (IV-D1, IV-D2, IV-D3, IV-D7, IV-D14), laboratory values (leukocyte count, lymphocyte count, platelet count, alanine aminotransferase [ALT] level, total bilirubin [TBIL] level, lactate dehydrogenase [LDH] level, creatinine concentration, high-sensitivity cardiac troponin I [hscTNI] level, N-terminal pro-brain natriuretic peptide [NT-proBNP] level, and procalcitonin [PCT] level); ventilator variables (mode of ventilation, tidal volume, positive end-expiratorypressure, respiratory rate, and FiO_2); and arterial blood gas analysisparameters (pH, the partial pressure of CO_2, oxygenation index value, and lactate concentration) were documented. Leukopenia was defined as a leukocyte count of $<3.5 \times 10^9$ cells/L and lymphopenia as a lymphocyte count of $<1.1 \times 10^9$ cells/L. We also recorded the time course of the patient's illness, treatment received, and microbiological test results, along with the following outcomes: duration from disease onset to confirmation, dyspnea, intubation, and duration of mechanical ventilation.

3. Results

By March 12, 2020, 108 critically ill SARS-CoV-2 pneumonia patients with IMV were treated in 4 wards in the 2 hospitals. Of these, 11 patients who were weaned from the ventilator were included in this study and all of them had shown onset symptoms in January (Fig. 1). Among them, 4 patients were treated in an ICU (ICU1) and 1 patient in a sub-ICU of Renmin Hospital of Wuhan University, while 6 patients were treated in 2 ICUs of Jin Yin-tan Hospital (ICU2+3). The clinical characteristics of the enrolled 11 patients are shown in Table 1 and Supplementary Tables 1–2; http://links.lww.com/MD/G45 and http://links.lww.com/MD/G46. All patients were residents of Wuhan city, and 2 of them were healthcare workers. The mean age was 52.8 years (range, 38–70 years), and 8 (72.7%) patients were men. Four (36.4%) patients had a history of exposure to patients with confirmed COVID-19, and 3 (27.3%) patients had a healthcare-associated infection.

The main presenting symptoms were fever (10/11), cough (10/11), and dyspnea (8/11). In contrast, symptoms of upper respiratory tract infections were infrequent (Table 1 and Supplementary Table 1; http://links.lww.com/MD/G45). The median time from onset of symptoms to hospitalization was 6.2 days (range, 0–15 days), the median time from dyspnea to

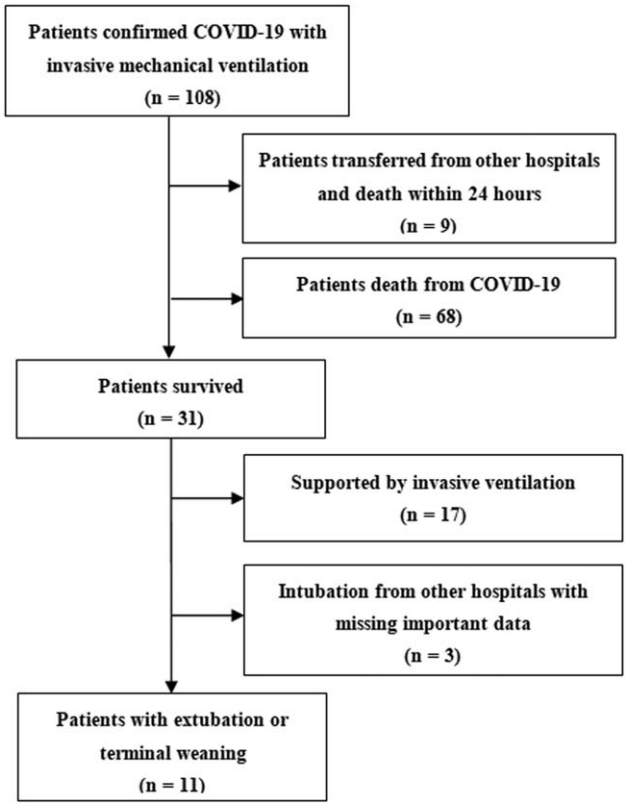

Figure 1. Study flow diagram.

Table 1

Characteristics of critically ill COVID-19 patients with extubation and terminal weaning.

Variable	Value (n = 11)
Median age (range), y	52.8 (38–70)
Men, n (%)	8 (72.7)
Median body mass index (range), kg/m^2	25.3 (23.4–27.3)
Median time from onset of symptoms to hospitalization (range), d	6.2 (0–15)
Median time from onset of symptoms to dyspnea (range), d	6.6 (3–13)
Median time from dyspnea to intubation (range), d	11.5 (3–19)
Median duration of invasive mechanical ventilation (range), d	15.7 (6–29)
Health care worker, n (%)	2 (18.2)
Health care–associated infection, n (%)	3 (27.3)
Smokers, n (%)	4 (36.4)
Presenting symptoms, n (%)	
Fever (temperature ≥38°C)	10 (90.9)
Cough	10 (90.9)
Sputum production	5 (45.5)
dyspnea	8 (72.7)
Weakness	4 (36.4)
myalgia	2 (18.2)
Sore throat	1 (9.1)
Diarrhoea	1 (9.1)
Hemoptysis	1 (9.1)
Comorbidity conditions, n (%)	
Hypertension	6 (54.5)
DM	1 (9.1)
Sinus tachycardia	1 (9.1)
NAFL	1 (9.1)
Puerperant	1 (9.1)

DM = diabetes mellitus, NAFL = non-alcoholic fatty liver.

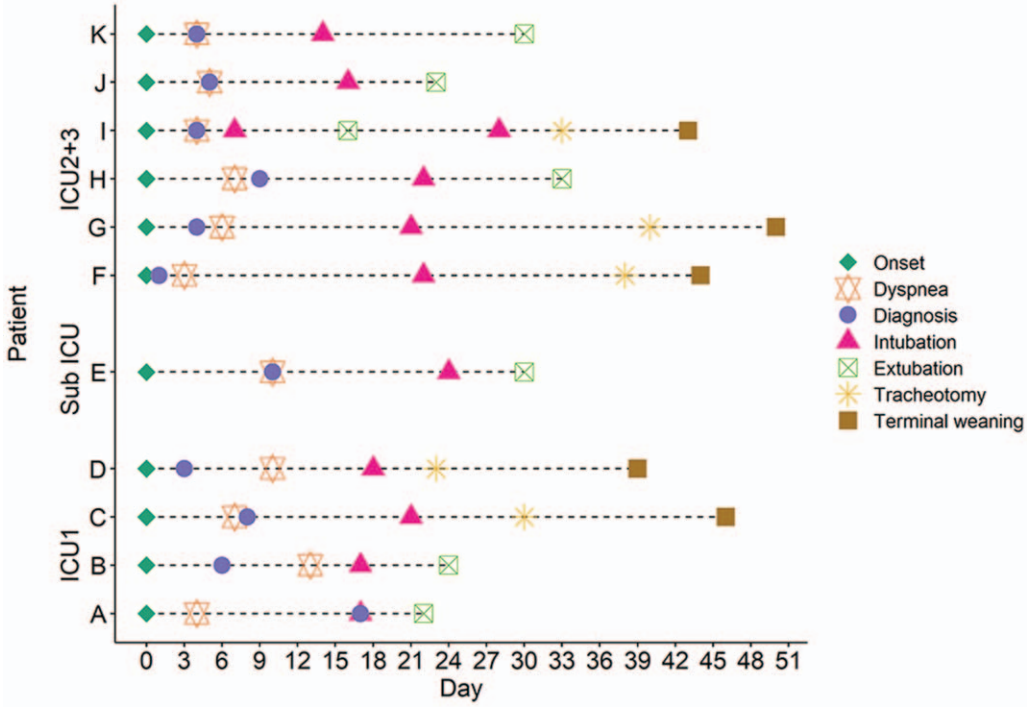

Figure 2. Timeline of the clinical course of the study patients.

Table 2

Physiologic and laboratory variables of patients on days 1, 2, 3, 7, 14, of invasive mechanical ventilation (IMV).

Variable	IMV-D1 (n=11)	IMV-D2 (n=11)	IMV-D3 (n=11)	IMV-D7 (n=9)	IMV-D14 (n=5)
Median FiO2 (range)	1.00 (1.00)	0.80 (0.6–1.0)	0.62 (0.45–0.90)	0.46 (0.35–0.75)	0.44 (0.35–0.55)
Median tidal volume (range), ml/kg	6.4 (5.0–7.0)	6.3 (6.0–7.0)	6.1 (5.0–7.0)	5.7 (2.0[♯]–7.0)	6.0 (2.0[♯]–7.0)
Median PEEP (range), cm H2O	12.7 (10–16)	11.0 (7–14)	10.2 (8–12)	9.2 (5–12)	7.4 (5–10)
Median respiratory rate (range), breaths/min	20.8 (20–25)	23.8 (20–30)	21.0 (12–30)	18.0 (10–28)	20.5 (20–22)
Mode of ventilation, n (%)					
Volume control assist-control ventilation	8 (72.7)	9 (81.8)	8 (72.7)	6 (66.7)	2 (40.0)
Synchronized intermittent mandatory ventilation	2 (18.2)	1 (9.1)	1 (9.1)	1 (11.1)	0 (0)
Pressure-regulated volume control ventilation	1 (9.1)	1 (9.1)	2 (18.2)	1 (11.1)	0 (0)
Pressure support ventilation	0 (0)	0 (0)	0 (0)	1 (11.1)	3 (60.0)
Median arterial blood gas values (range)					
pH	7.41 (7.32–7.50)	7.3 (7.12–7.36)	7.38 (7.24–7.49)	7.39 (7.22–7.53)	7.36 (7.29–7.51)
PaCO2, mm Hg	40.9 (30–54)	64.9 (49–102)	58.8 (48–93)	62.8 (49–79)	54.2 (43–75)
Median oxygenation index value (range)	47.8 (38–52)	115.7 (66–184)	158.9 (84–288)	140.2 (97–202)	260.7 (180–391)
Median lactate level (range), mmol/L	2.4 (1.2–5.6)	1.7 (0.7–3.1)	1.6 (1–2.7)	1.4 (0.8–2.5)	1.4 (0.6–2.3)
Median leukocyte count (range), $\times 10^9$ cells/L[a]	14.88 (5.63–41.25)	16.44 (7.24–33.49)	11.29 (5.18–13.19)	12.01 (6.29–22.79)	14.22 (9.34–24.53)
Median lymphocyte count (range), $\times 10^9$ cells/L[b]	0.77 (0.27–1.31	0.75 (0.3–1.48)	0.93 (0.23–1.99)	1.00 (0.38–205)	0.84 (0.46–1.51)
Median platelet count (range), $\times 10^9$ cells/L[c]	247 (114–487)	235 (83–548)	203 (88–425)	186 (128–318)	199 (113–372)
Median ALT level (range), U/L[d]	42 (20–75)	104 (15–540)	183 (7–1325)	165 (12–1111)	48 (19–95)
Median TBIL level (range), μmol/L[e]	16.8 (4.3–29.7)	10.3 (5.6–18.1)	12.4 (7.0–20.5)[*]	14.8 (8.2–21.9)	19.6 (10.7–32.7)
Median LDH level (range), U/L[f]	572 (345–1002)	595 (343–1502)	795 (290–3498)[†]	466 (311–690)[*]	396 (158–580)[*]
Median creatinine concentration (range), mmol/L[g]	58.8 (34–76.1)	105.2 (37.7–303.8)	96.7 (38.7–334.5)	73.6 (36.6–191.2)	80.3 (31.8–131.3)
Median hscTNI concentration (range), ng/ml[h]	0.025 (0.003–0.125)	0.732 (0.002–3.713)[*]	0.544 (0.009–2.676)[*]	0.080 (0.002–0.422)	0.066 (0.003–0.119)
Median NT-proBNP concentration (range), pg/ml[i]	773.3 (10–5307)[*]	1876.4 (11.8–6043)[‡]	587.6 (12.5–2967)[*]	685.8 (9.6–3980)[†]	553.5 (9.5–1751)[*]
Median CRP level (range), mg/L[j]	106.8 (21–200)[*]	80.0 (31.4–154.9)[‡]	53.8 (6–200)[†]	64.5 (3.6–200)[‡]	32.0 (5.8–68.3)[*]
Median PCT level (range), ng/ml[k]	0.56 (0.05–4.1)[*]	2.69 (0.05–16.65)[*]	1.26 (0.04–7.70)[*]	0.99 (0.05–2.41)	1.53 (0.05–3.63)[*]
Median SOFA score (range)	7 (4–9)	6 (3–9)	5 (3–10)	4 (3–9)	4 (3–9)

[♯] Patient G received ECMO therapy meanwhile.

[*] Missing 1 value.

[†] Missing 2 values.

[‡] Missing 3–5 values.

ALT = nine aminotransferase, AST = aspartate aminotransferase, hscTNI = high-sensitivity cardiac troponin I, LDH = lactate dehydrogenase, NT-proBNP = N-terminal pro-brain natriuretic peptide, PCT = procalcitonin, PEEP = positive end-expiratory pressure, SOFA = Sequential Organ Failure Assessment, TBIL = total bilirubin.

[a] Normal range, 3.5–9.5 $\times 10^9$ cells/L.

[b] Normal range, 0.56–1.11 $\times 10^9$ cells/L.

[c] Normal range, 125–350 $\times 10^9$ cells/L.

[d] Normal range, 9–50 U/L.

[e] Normal range, 0–23.0 μmol/L.

[f] Normal range, 120–250 U/L.

[g] Normal range, 41–73 mmol/L.

[h] Normal range,0–0.04 ng/mL.

[i] Normal range, 0–900 pg/ml.

[j] Normal range, 0–5.0 mg/L.

[k] Normal range, 0–0.05 ng/ml.

intubation was 11.5 days (range, 3–19 days), and the median duration of IMV was 15.7 days (range, 6–29 days). Figure 2 summarizes the time course of the disease. The comorbidities of each patient are shown in Supplementary Table 1; http://links.lww.com/MD/G45.

3.1. Respiratory manifestation and support

Acute severe hypoxemic respiratory failure was a prominent feature of the presentation, and all patients required IMV (Table 2). Of these, 1 patient switched to ECMO assistance for 14 days. Before intubation, 7 patients had received a failed trial of non-invasive positive-pressure ventilation (NIPPV) and 4 patients received high-flow nasal cannula (HFNC) therapy (Table 3). Chest radiography beside the bed at the time of intubation showed ground-glass opacity in the bilateral lungs, consistent with acute respiratory distress syndrome (ARDS) (Fig. 3).

All patients received intravenous heavy sedation and neuromuscular blockade to reduce autonomous respiration and ventilator-patient dyssynchrony, which deteriorated hypoxemia in the early stage of IMV. Owing to refractory hypoxemia, prone positioning was practiced in 7 patients (63.6%) as rescue therapy, and 1 patient was treated using ECMO. The median duration of IMV was 15.7 days (range, 6–29 days). Tracheotomy was performed in 5 patients (45.5%) and bronchoscopy in 3 patients (27.3%).

A lung-protective strategy with lower tidal volume ventilation and proper driving pressure is the main strategy of IMV. In our study, on days of IMV, the median tidal volume was no more than 7 ml/kg, and the median respiratory rate and median positive end-expiratory pressure were as shown in Table 2.

3.2. Circulatory

Vasopressors were required in 8 patients (72.7%) during the hospital stay. Elevated hscTNI was observed in 7 patients (63.6%); of these, elevated NT-proBNP was found in 5 patients.

Table 3

Main interventions and complications.

Variable	Value
Noninvasive positive-pressure ventilation before invasive ventilation, n *(%)*	7 (63.6)
High-flow nasal cannula before invasive ventilation, n (%)	9 (81.8)
Invasive ventilation, n (%)	11 (100)
Neuromuscular blockade, n (%)	11 (100)
Extracorporeal membrane oxygenation, n (%)	1 (9.1)
Prone positioning, n (%)	7 (63.6)
Tracheostomy, n (%)	5 (45.5)
Renal replacement therapy, n (%)	6 (54.5)
ALSS, n (%)	5 (45.5)
Tracheostomy, n (%)	5 (45.5)
Bronchoscope, n (%)	3 (27.3)
Median duration of mechanical ventilation (range), d	15.7 (6–29)
Cardiac Arrest, n (%)	2 (18.2)
Barotrauma, n (%)	3 (27.3)
Pulmonary infections, n (%)	6 (54.5)
Bloodstream infections, n (%)	4 (36.4)
Vasopressors, n (%)	8 (72.7)

ALSS = artificial liver support system.

Two patients briefly experienced cardiac arrest around the time of intubation and returned to life through cardiopulmonary-cerebral resuscitation.

3.3. Renal

AKI was identified and classified based on the highest serum creatinine level or urine output criteria according to kidney disease, improving global outcome classification.[11] AKI occurred in 6 patients (54.5%), and the same quantity; however, not the same patients received renal replacement therapy owing to AKI or fluid negative balance.

3.4. Hepatic

The ALT was elevated in 10 patients, and the TBIL level was elevated in 4 patients during hospitalization. To reduce the inflammatory reaction, an artificial liver support system (ALSS) therapy was used for 5 patients at the Renmin Hospital of Wuhan University.

3.5. Hematologic

All patients had marked lymphopenia during hospitalization, and all patients had elevated leukocyte counts during IMV.

3.6. Microbiological investigations

Hospital-acquired infections were noted in 7 (63.6%) patients, including 2 patients who had pulmonary and bloodstream infections of carbapenem-resistant *Acinetobacter baumannii*. Patient G, who was assisted with ECMO, had a bloodstream infection with arbapenem-resistant *Klebsiella pneumoniae* and pulmonary infection with carbapenem-resistant *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*. *Candida albicans* were identified in the blood culture of 1 patient. Other microorganisms identified from respiratory tract secretions in 3 patients included carbapenem-resistant *A. baumannii*, carbapenem-resistant *K. pneumoniae*, and *Pseudomonas aeruginosa*, with each microorganism found in 1 patient each.

Figure 4 shows the results of the sequential real-time polymerase chain reaction test. Two patients experienced a recurrence of SARS-CoV-2 RNA after 2 negative throat swab samples. Positivity for SARS-CoV-2 was tested only once in the 3 patients, while the longest duration from the first to the last positive result was 38 days among other patients.

3.7. Antimicrobial therapy, corticosteroids, and intravenous immunoglobulin

All patients received broad-spectrum antimicrobials and 1 type of antiviral drug, and 9 patients (81.8%) received methylprednisolone (20–80 mg) for more than 10 days. Six patients received intravenous immunoglobulin.

4. Discussion

We report that 11 critically ill patients with confirmed COVID-19 were successfully weaned from a ventilator and extubation after receiving IMV for 6 to 29 days from 3 ICUs and a sub-ICU in 2 hospitals in Wuhan city. All enrolled patients had underlying intrapulmonary manifestations and developed acute respiratory failure characterized by severe hypoxemia and illness, a high mortality rate, and a long hospitalization time.

Severe ARDS is the fundamental pathophysiology of severe and critical COVID-19.[12,13] Male patients and those older than 65 years are more likely to develop ARDS.[5,14,15] The survivors in our study were mostly male and the mean age was older than non-ICU patients; however, younger than non-survivors in previous studies.[5,6] A previous study concluding that the overall age distribution is older in Italy relative to that in China may explain, in part, the higher average case-fatality rate in Italy.[3] A meta-analysis also revealed that comorbidities, including hypertension, diabetes, cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, and malignancy, contributed significantly to the disease severity and prognostic endpoints of COVID-19.[16] In our study, 6 patients had hypertension and 1 had diabetes.

Quantitative RT-PCR, which has high sensitivity and rapid detection characteristics, is a commonly used technique for virus detection.[17] A negative result may be associated with different disease course, sampling skill, sample quality, delayed transportation to the laboratory, and variable viral shedding. Simultaneously, the quality of SARS-CoV-2 testing kits may also affect the results.[18] Three patients in Jin Yingtan Hospital tested positive only once in their whole course. However, 5 patients in Renmin Hospital of Wuhan University tested positive even 3 weeks after confirmation. The longest duration was 38 days. It appeared that the differences due to subjective factors in different hospitals or the persistent positive result may not necessarily be associated with worse conditions or infectiousness. Therefore, further research is needed.

Respiratory support is the main strategy for COVID-19 and can improve oxygenation and reduce mortality.[19] NIPPV and HFNC play an essential role in the treatment of critically ill COVID-19 patients; however, they increase the risk of aerosol transmission.[20,21] Some experts do not recommend NIPPV for patients with viral pneumonia infections as even though NIPPV improves oxygenation and reduces breathing work, it cannot change the natural disease course of these patients and may cause delayed intubation.[22] All patients in our study presented with acute hypoxemic respiratory failure requiring IMV after failure

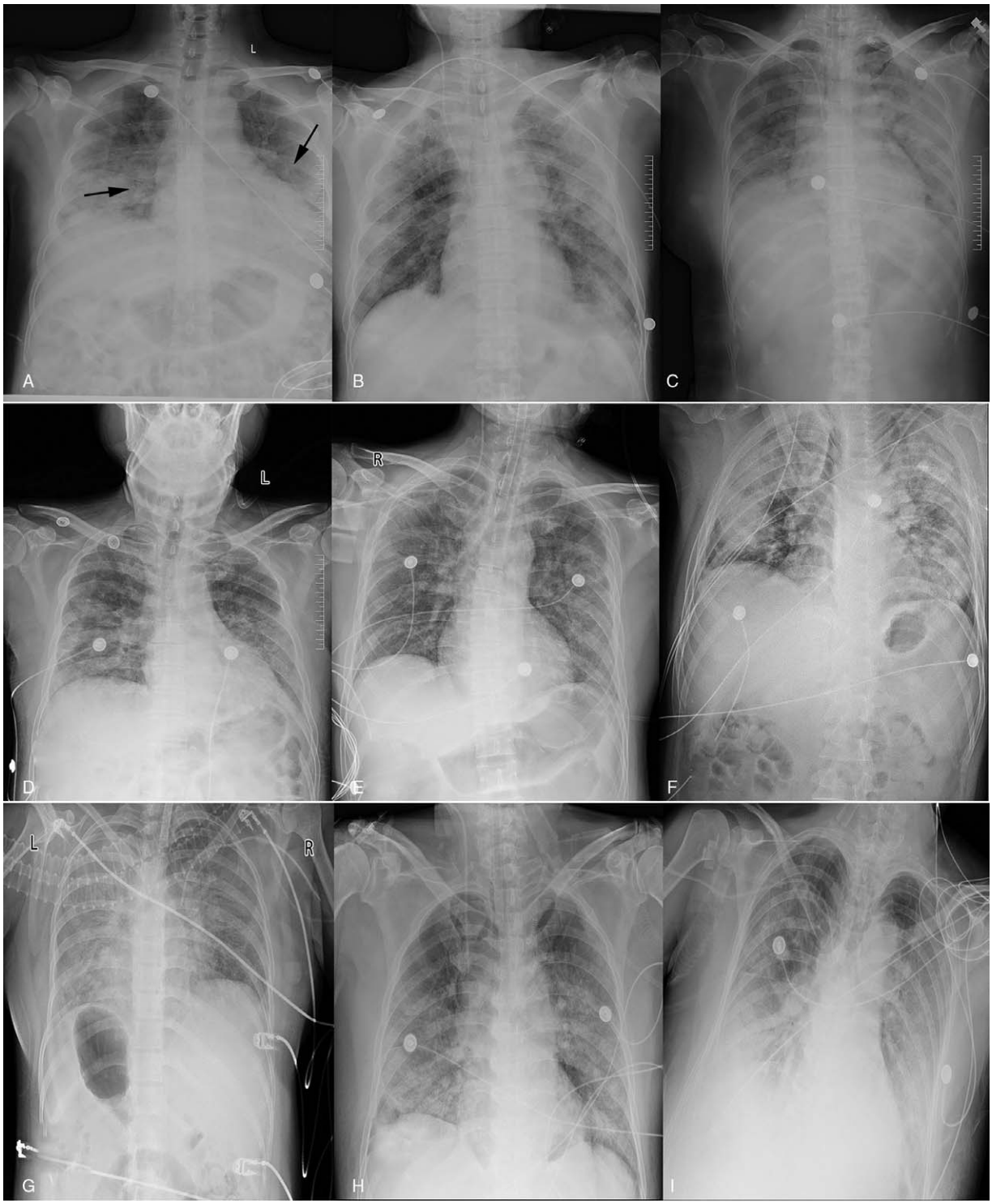

Figure 3. Chest radiographs of enrolled patients (2 patients are not acquired) on the day of intubation showing ground-glass opacity in the bilateral lung. Annotation: The arrow points show ground-glass opacity in the bilateral lungs of patient A.

with NIPPV and/or HFNC. A lung-protective strategy with lower tidal volume ventilation and proper driving pressure is the main strategy of IMV,[23] which may aggravate the fractional pressure of CO_2 in arterial blood. Therefore, a high respiratory rate was set to increase the minute volume. In our study, on day 2 of IMV, the median tidal volume was 6.3 ml/kg and the median respiratory rate was 23.8 breaths per minute, which complied with the lung-protective strategy.

Studies have shown significant survival benefits with prone positioning and neuromuscular blockade in patients with ARDS,[24] and it has also been proposed for the treatment of COVID-19 in China.[25] Seven patients in our study benefited

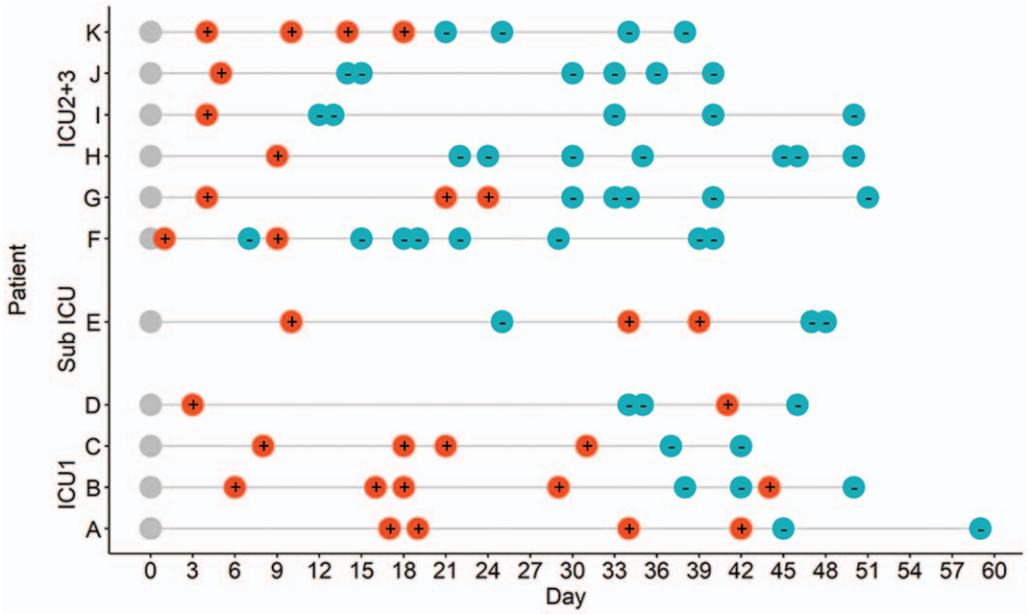

Figure 4. Results of sequential real-time polymerase chain reaction. Annotation: The gray circles indicate the onset day of symptoms; red circles indicate a positive result for SARS-CoV-2; green circles indicate negative results. ICU = intensive care unit.

from prone positioning. Recent evidence suggests that the use of ECMO in severe cases of ARDS is associated with reduced mortality.[26] However, in practice, several challenges facing ECMO may influence its role in the treatment of emerging infectious diseases. These include professional skilled staff, available equipment, careful observation, and strict rules to avoid nosocomial infections.[27] In our study, patient G received IMV and subsequently received ECMO for 14 days; however, he eventually suffered serious secondary infections, including bloodstream infection with carbapenem-resistant *K. pneumonia*, ventilator-associated pneumonia of carbapenem-resistant *A. baumannii*, and *S. maltophilia*.

However, no special drug has been proven to be effective for COVID-19, although several options, such as antiviral drugs, monoclonal antibodies, oligonucleotide-based therapies, interferon therapies, convalescent plasma, and small-molecule drugs, have been used in an attempt to treat the disease.[28,29] Even without evidence, all patients were administered a single type of antiviral drug in our study. However, the use of corticosteroids in patients with viral pneumonia and ARDS remains controversial.[4,30] In this study, all patients were administered intravenous glucocorticoids, considering that the overwhelming inflammation and cytokine-related lung injury might cause rapidly progressive pneumonia in critically ill patients with COVID-19. Of these, 9 patients (81.8%) received intravenous glucocorticoids at low to moderate doses for more than 10 days. Well-designed randomized controlled trials are required to promote a more solid foundation for treatment.

All enrolled patients in our study suffered from AKI, hepatic insufficiency, and/or myocardial injury, which can slowly recover to normal levels as the disease progresses. The mechanisms underlying organ dysfunction in COVID-19 remain unknown. It remains to be elucidated whether organ dysfunction is mainly related to direct virus damage, hypoxemia, cytokine storm, or severe inflammatory reaction owing to the high prevalence of lymphopenia. High levels of hs-CRP, LDH, and PCT were found in all patients. Academician Li considered that organ dysfunction and hypoxemia are usually caused by a cytokine storm.[31] With the assistance of her team, 5 patients in our study received ALSS, which could rapidly remove inflammatory mediators and block cytokine storm. Moreover, it also favored the balance of fluid, electrolyte, and acid-base, and thus improved treatment efficacy in critical illness.

5. Conclusions

In conclusion, critical cases of COVID-19 are characterized by acute hypoxemic respiratory failure and subsequent dysfunction of other organs, and have a high mortality rate. The evidence for specific therapies is lacking and long-term hospitalization is required. Correct ventilation strategies to improve oxygenation and avoid ventilator-associated lung injury, switching to ECMO based on the skilled trained group, and availability of equipment are the key methods to rescue lives. Regardless of the strategy, strict infection control rules must be established to avoid nosocomial infections and to increase the survival rate.

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