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ABOUT COVER

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Two mechanically ventilated cases of COVID-19 successfully managed with a sequential ventilation weaning protocol: Two case reports

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Abstract

BACKGROUND

Patients with critical coronavirus disease 2019 (COVID-19), characterized by respiratory failure requiring mechanical ventilation (MV), are at high risk of mortality. An effective and practical MV weaning protocol is needed for these fragile cases.

CASE SUMMARY

Here, we present two critical COVID-19 patients who presented with fever, cough and fatigue. COVID-19 diagnosis was confirmed based on blood cell counts, chest computed tomography (CT) imaging, and nuclei acid test results. To address the patients' respiratory failure, they first received noninvasive ventilation (NIV). When their condition did not improve after 2 h of NIV, each patient was advanced to MV [tidal volume (Vt), 6 mL/kg ideal body weight (IBW); 8-10 cmH₂O of positive end-expiratory pressure; respiratory rate, 20 breaths/min; and 40%-80% FiO₂] with prone positioning for 12 h/day for the first 5 d of MV. Extensive

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infection control measures were conducted to minimize morbidity, and pharmacotherapy consisting of an antiviral, immune-enhancer, and thrombosis prophylactic was administered in both cases. Upon resolution of lung changes evidenced by CT, the patients were sequentially weaned using a weaning screening test, spontaneous breathing test, and airbag leak test. After withdrawal of MV, the patients were transitioned through NIV and high-flow nasal cannula oxygen support. Both patients recovered well.

CONCLUSION

A MV protocol attentive to intubation/extubation timing, prone positioning early in MV, infection control, and sequential withdrawal of respiratory support, may be an effective regimen for patients with critical COVID-19.

Key words: Mechanically ventilated cases; COVID-19; Sequential weaning protocol; Case report

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Core tip: An effective and practical weaning protocol is of the utmost importance to coronavirus disease 2019 (COVID-19) patients with respiratory failure requiring mechanical ventilation. Here, we present two patients with critical COVID-19. Such patients can achieve good outcomes following a sequential weaning protocol that is attentive to the timing of intubation and extubation, early prone positioning, infection control, and sequential advancement and withdrawal of invasive ventilation.

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INTRODUCTION

The viral pathogen severe acute respiratory syndrome-related novel coronavirus (SARS-CoV-2, also known as 2019 novel coronavirus or 2019-nCoV), which has been determined to have originated in Wuhan, China, has infected patients around the globe and produced the ongoing grave pandemic^[1,2]. Human-to-human SARS-CoV-2 transmission between people in close contact has been known to occur since the middle of December 2019^[3,4]. By late February 2020, there were tens of thousands of cases of coronavirus disease 2019 (COVID-19), the disease caused by infection with SARS-CoV-2, and several thousand deaths due to COVID-19 had been reported in China alone, in addition to thousands of COVID-19 cases in other countries^[5]. Giving the immense spread of COVID-19, there is an urgent need for treatment options to support these patients.

Mortality due to COVID-19 is associated predominantly with respiratory failure requiring invasive mechanical ventilation (MV). In a small study of 36 patients diagnosed with COVID-19 and admitted to the intensive care unit (ICU) in a Wuhan hospital between January 1 to January 28, 2020, 17 (47.2%) received MV, of which 4 were switched to extracorporeal membrane oxygenation (ECMO), and the overall mortality rate for the sample was 4.3%^[6]. An effective and practical weaning protocol is of the utmost importance for mitigating mortality, minimizing MV duration, and reducing the need for conversion to ECMO. Here, we present two cases of COVID-19 who received MV and were managed successfully with a sequential weaning protocol.

CASE PRESENTATION

Chief complaints

Two critically ill patients with a median age of 60.5 years are described in this report.

Patient 1 was a 65 year-old woman who was admitted on January 20, 2020 after 16 d of persistent cough, 4 d of fever, and 1 d of chest tightness. Patient 2 was a 56-year-old man who was admitted on February 3, 2020 after 4 d of persistent cough, 4 d of fever and 11 h of dyspnea.

History of present illness

Patient 1 experienced progressive aggravation of her cough without productive sputum, since its initial onset 16 d prior to her admission. 4 d before being admitted, she had sought care in a community health center, at which time she had a fever of 38.5°C without chills, sweating, abdominal pain, dyspnea, or any unusual changes in urination frequency or urgency. At the health center, she was presumed to have a common cold and was prescribed medications for cold symptoms. Three days later, 1 d before being admitted, she developed chest tightness, fatigue, and loss of appetite.

Patient 2 had a fever and cough 4 d before admission, accompanied by fatigue and poor appetite. He experienced dyspnea 11 h before being admitted. He was transferred to our hospital from Nanshan District People's Hospital, where a nucleic acid test following nasopharyngeal swabs was performed and confirmed that he was infected with SARS-CoV-2.

History of past illness

Both patients had a preexisting medical condition. At the time of admission, Patient 1 had a 15-year history of type 2 diabetes mellitus and Patient 2 had a 30-year history of hypertension. Neither patient was taking any medications.

Personal and family history

Only Patient 1 had a Wuhan contact history. Neither patient had a family history of a disease cluster.

Physical examination

At the time of admission, Patient 1 had normal body temperature (36.3°C) with a borderline normal/high respiratory rate (RR) (22 breaths/min), and a normal heart rate (69 beats/min) with normal blood pressure (138/79 mmHg). At the time of admission, Patient 2 had a body temperature consistent with a low-grade fever (38°C), an elevated RR (30 breaths/min), and a normal heart rate (84 beats/min) with normal blood pressure (124/76 mmHg). Pulmonary crepitations were heard in both patients. Physical examination did not reveal any other abnormal findings.

Laboratory examinations

Laboratory test results for both patients are reported in [Table 1](#). Notably, both patients were found to have normal or lower than normal white blood cell (WBC) and lymphocyte counts, and the renal and liver function index tests were unremarkable in both cases. Real-time reverse-transcriptase polymerase chain reaction nucleic acid testing performed with respiratory specimens (nasopharyngeal swabs, sputum, or bronchoalveolar lavage) confirmed that both patients were infected with SARS-CoV-2. These patients experienced respiratory failure with a low partial pressure of oxygen (PaO₂)/inspired fraction of oxygen (FiO₂) ratio (P/F ratio) (136, 68 mmHg, respectively) prompting transfer to the ICU on January 24 for Patient 1 and on February 3 for Patient 2.

Imaging examinations

Pretreatment computed tomography (CT) imaging examinations of these two patients revealed bilateral patchy shadows or ground-glass opacity in the lungs ([Figure 1](#)).

FINAL DIAGNOSIS

Suspected diagnoses of COVID-19 were made based on clinical symptoms. WBC count, lymphocyte count, and chest CT findings were consistent with COVID-19. Finally, nuclei acid test results confirmed the COVID-19 diagnoses. Following confirmation of COVID-19, both patients suffered respiratory failure requiring MV and their disease was re-classified from serious to critical. Both patients were further diagnosed with acute respiratory distress syndrome (ARDS) secondary to COVID-19.

Table 1 Laboratory findings upon admission.

Blood analysis variable	Patient 1	Patient 2
WBC count, $\times 10^9/L$	5.89	6.51
Neutrophil count, $\times 10^9/L$	5.35	5.36
Lymphocyte count, $\times 10^9/L$	0.42	0.93
Lactate, mmol/L	2.7	2.6
Creatinine, $\mu\text{mol/L}$	54.1	94.6
Urea, mmol/L	4.48	8.48
Albumin, g/L	34.6	35.5
Alanine aminotransferase, U/L	15.7	34.8
Total bilirubin, $\mu\text{mol/L}$	8.4	12.2
Nucleic acid result	+	+

WBC: White blood cells.

TREATMENT

Both patients received noninvasive ventilation (NIV) with a 60% FiO_2 and inspired/expiratory positive airway pressure (IPAP/EPAP) levels of 8-12 cmH_2O and 6 cmH_2O , respectively. Both patients remained in respiratory distress with persistently low P/F ratios for 2 h (Table 2). Consequently, each patient was advanced to invasive MV with a tidal volume (V_t) of 6 mL/kg ideal body weight (IBW) and 8-10 cmH_2O of positive end-expiratory pressure (PEEP), RR of 20 breaths/min and 40%-80% FiO_2 . For the first 5 d of MV, each patient lay in the prone position 12 h/d (9 pm to 9 am).

In addition, both patients were treated with a pharmacotherapy regimen consisting of an antiviral treatment [oral lopinavir/ritonavir tablets (500 mg every 12 h) together with atomized inhaled α -interferon (5.0 MU every 12 h)] and an immune-enhancer (1.6 mg thymosin $\alpha 1$ daily *via* subcutaneous injection). Low-molecular-weight heparin (4000 IU) was injected subcutaneously to prevent thrombosis.

Enteral nutrition was administered according to weight (25 kcal/kg). Hence, at 60 kg, Patient 1 received 1500 kcal/d in 1500 mL. At 70 kg, Patient 2 received 1750 kcal/d in 1750 mL. To reduce reflux aspiration risk, feeding was supplied *via* a nasal jejunal tube at a rate of 90-100 mL/h while each patient lay in the supine position and at a rate of 40-50 mL/h while each patient lay in the prone position. To enable closely monitored airway management, each patient received 1:1 nursing care. The patients were kept sedated at Richmond Agitation-Sedation Scale levels of -4 and -2 while in the prone and supine position, respectively. Strict hand hygiene was maintained to prevent secondary nosocomial infection.

As shown in Table 2, each patient's P/F ratio improved gradually during the course of MV with prone positioning, which was particularly notable after approximately 4-5 d. When the patients' P/F ratios remained above 250 consistently, we stopped placing the patients in the prone position, and reduced their sedation level to improve their alertness. Each patient received a follow-up CT scan, which showed absorption of most of the imaging signs of lung pathology (Figure 2), as well as nucleic acid SARS-CoV-2 testing, which was negative in both cases. Supported by the improvements observed on CT and no detectable viral load, we felt comfortable proceeding with an extubation plan.

In preparation for extubation, the patients were subjected to a sequential MV weaning protocol that commenced with weaning screening, during which each patient was first transitioned to pressure support ventilation (PSV) (pressure support 8-10 cmH_2O , PEEP 5-8 cmH_2O , FiO_2 40%). Each patient was alert and breathing smoothly with a P/F ratio over 250 and stable hemodynamics while on PSV and thus was advanced to a 3 min 5 cmH_2O PSV, spontaneous breathing test, wherein both patients breathed smoothly, without remarkable changes in RR, V_t , oxygen saturation, heart rate or blood pressure. Then, following 30 min of spontaneous breathing with a smooth airbag leak test, each patient was extubated and placed on NIV (IPAP 8-12 cmH_2O , EPAP 6 cmH_2O , and FiO_2 40%). After 24 h on NIV with a stable RR, oxygen saturation and cardiovascular condition, each patient was transferred to high-flow

Table 2 PaO₂/FiO₂ ratios during mechanical ventilation

Time point	PaO ₂ /FiO ₂ ratio (mmHg)	
	Patient 1	Patient 2
Admission to ICU	136	68
After 2 h of NIV	141	116
Day 1 of MV	153	190
Day 2 of MV	227	176
Day 3 of MV	308	258
Day 4 of MV	318	269
Day 5 of MV	334	258
Day 6 of MV	340	316
Day 7 of MV	318	362
Day 8 of MV	+	+

Patient 1 and Patient 2 received MV for 8 d and 7 d, respectively. ICU: Intensive care unit; NIV: Noninvasive ventilation; MV: Mechanical ventilation.

nasal cannula oxygen (HFNC) (flow rate, 40-50 L/min; FiO₂ 40%-50%) and remained stable. As shown in Table 2, Patient 1 received 8 d of MV and Patient 2 received 7 d of MV (median 7.5 d). Neither patient received ECMO.

OUTCOME AND FOLLOW-UP

While on HFNC, our patients continued to exhibit clinically smooth breathing without a fever or any other COVID-19 symptoms. These observations together with the aforementioned resolution of lung changes in both cases (Figure 2) led us to transfer these patients from the ICU to the common ward. The hospital discharge criteria for recovered COVID-19 patients in our hospital, followed in both of these cases, are as follows: a normal body temperature for > 3 d, clinically significant alleviation of respiratory symptoms, majority resolution of radiological lung changes, and two consecutive negative respiratory sample nucleic acid tests performed at least 24 h apart. At the writing of this report, both patients have been discharged with a good prognosis.

DISCUSSION

The SARS-CoV-2 virus has sustained human-to-human community transmission within regions and can be transferred rapidly between regions and countries^[7]. As of May 12, 2020, the WHO Dashboard reports a total of 4098018 confirmed COVID-19 cases globally (including 84451 in China and 1298287 in the USA), which have caused 283271 deaths. Following the SARS-CoV outbreak in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012, the emergence of SARS-CoV-2 and the associated worldwide COVID-19 pandemic^[8] marked the third introduction of a highly pathogenic coronavirus into the human population this century. Like SARS-CoV, the novel coronavirus SARS-CoV-2 relies on binding to angiotensin-converting enzyme 2 and spreads mainly through the respiratory tract.

As critical COVID-19 is characterized by respiratory failure requiring MV, there is a need for a practical weaning protocol for this patient population. A comprehensive MV weaning protocol with checklists across four dimensions (spontaneous breathing, extubation, prophylactic non-invasive positive pressure ventilation, and post-extubation monitoring), may prevent respiratory failure following extubation which would require reintubation, and reduce mortality^[9]. In accordance with this recommendation, we summarize our weaning procedure and associated experience with two critical COVID-19 patients, including intubation timing, use of the prone position, infection control, and sedation titration. Together with our weaning

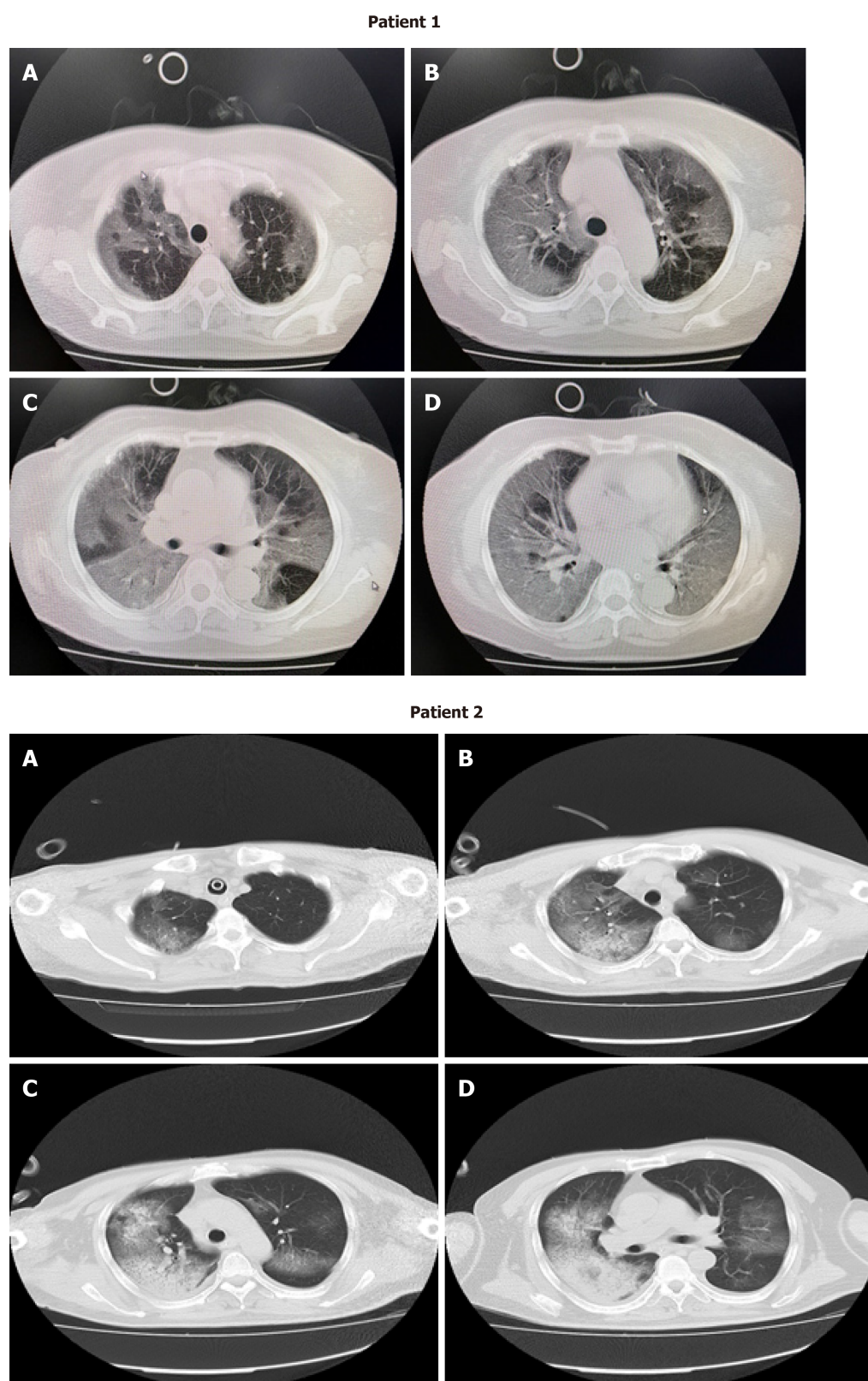
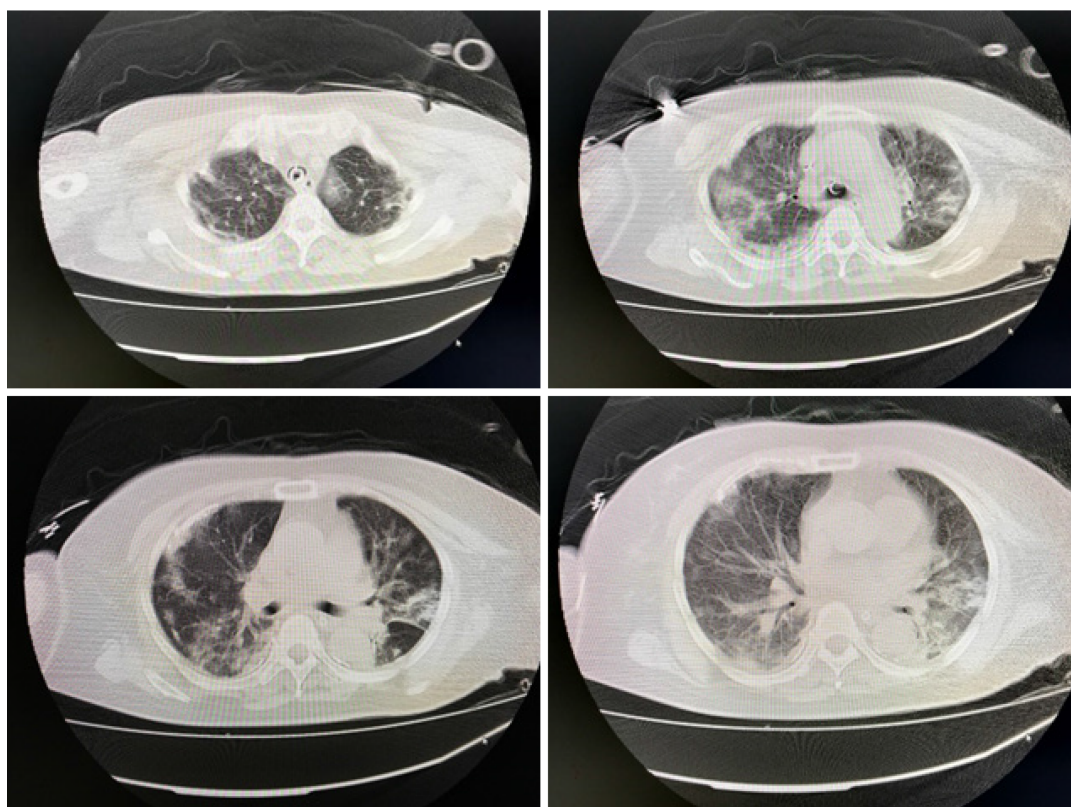


Figure 1 Chest computed tomography scans pretreatment. B (below) showing bilateral patchy shadows or ground-glass opacity in the lungs.

procedures, we share the pharmacotherapy that has become standard practice for critical COVID-19 patients in our hospital.

Intubation timing is of vital importance. Within China, some 3.2% of patients with COVID-19 have required MV. Timely intubation prevents potentially lethal oxygen debt worsening^[10]. Pre-MV NIV duration should be limited to allow respiratory muscle rest, particularly when patients exhibit a persistent oxygen debt despite NIV. Thus, when the respiratory condition of these 2 patients did not improve after 2 h of NIV

Patient 1



Patient 2

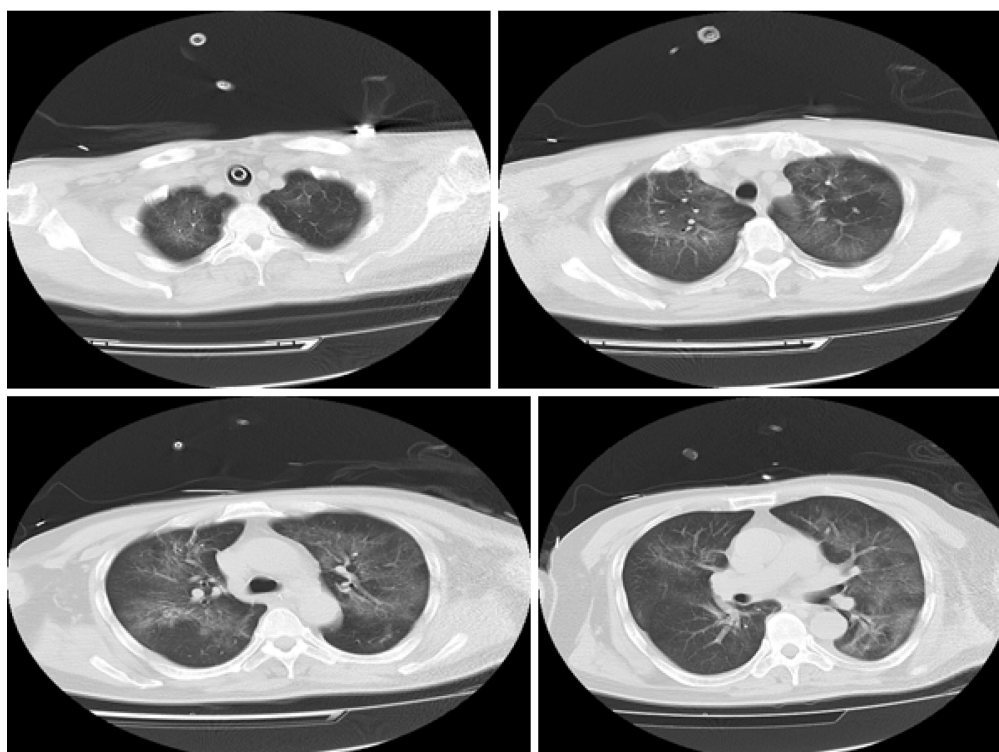


Figure 2 Chest computed tomography scans before extubation. Chest computed tomography scans on the final day of mechanical ventilation, before extubation, for Patient 1 (above) and Patient 2 (below) showing absorption and dissipation of most of the pathological changes observed before treatment

(IPAP 8–12 cmH₂O, EPAP 6 cmH₂O, FiO₂ 60%), they were transferred to MV (Vt 6 mL/kg IBW, PEEP 8–10 cmH₂O, RR 20 breaths/min, FiO₂ 40%–80%).

We place patients in the prone position 12 h a day during the first 5 d of MV. Prone positioning is thought to be a beneficial strategy for patients with ARDS as it allows for greater chest wall expansion than the supine position, thereby improving alveolar

recruitment and the ventilation/perfusion ratio. These benefits are thought to improve survival outcomes owing to improved oxygenation and reduced lung injury^[11,12].

Infection control must be maintained during the weaning process. Mortality due to ventilator-associated pneumonia (VAP) can extend ICU and hospital stays. Thus, non-pharmacological and pharmacological infection-prevention measures should be employed to reduce the risk of VAP^[13]. Accordingly, we are attentive to factors such as jejunal tube placement, enteral feeding rate, sedation control, strict hand hygiene, and close monitoring for signs of potential VAP.

Pharmacotherapy during the provision of respiratory support should include an antiviral, an immune enhancer, and thrombosis prophylaxis, with the goal of minimizing the duration of MV. Notwithstanding, MV weaning is a delicate process that should be undertaken with a careful phased plan, including a weaning screening test, a spontaneous breathing test, and an extubation screening test. Moreover, after extubation, we returned our patients to NIV and then HFNC sequentially and smoothly.

CONCLUSION

Our patients responded well to the sequential MV withdrawal protocol presented which includes careful attention to timing, use of the prone position early in the course of MV, infection control and monitoring, and sequential transition from IMV to NIV to HFNC. Based on our observations and the good outcomes of our patients, we recommend that this sequential respiratory support protocol be considered for patients with critical COVID-19.

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