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Bronchoscopic Intervention May be Associated with Better Outcomes in Mechanically Ventilated Coronavirus Disease-19 Patients: A Case Series

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Abstract

BACKGROUND: The emergence of a new strain of coronavirus infection, the coronavirus infection disease 2019 (COVID-19), has been a pandemic burden across the globe. Severe COVID-19, particularly in patients with acute respiratory distress syndrome (ARDS), is associated with increased risk of admission to intensive care unit (ICU), mechanical ventilation, and mortality. Bronchoscopy has been widely employed as an adjunctive therapy in mechanically ventilated patients. However, the use of bronchoscopy in patients with COVID-19 has been strictly limited due to aerosol transmission.

CASE REPORT: We reported 3 COVID-19 Cases presented to the hospital with ARDS. All of the patients were immediately intubated to improve oxygenation. During admission, the patients produced immense airway secretions that might have resulted in partial airway obstruction. A conventional tracheal suctioning did not help to promote clinical improvement. We decided to perform bronchoscopy with controlled suctioning by following a very tight protocol to prevent aerosol formation. A significant clinical and respiratory improvement was observed in all patients following bronchoscopy. Three of them were transferred to regular ward, however, one patient died during hospitalization.

CONCLUSION: Bronchoscopic procedures may provide significant therapeutic benefits in severe COVID-19 patients. However, it should be kept in mind that this procedure should only be performed with a rigorous protocol to reduce the risk of aerosol generation and subsequent viral transmission.

Introduction

The emergence of a new strain of coronavirus has been a pandemic burden across the globe. Due to the similarity in the genomic sequence and clinical consequence with the previous strains of coronavirus, it has later been named as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) that causes a disease called coronavirus infection disease 2019 (COVID-19) [1], [2]. Firstly reported in Wuhan, Hubei Province, China, by the end of December 2019, the number of confirmed SARS-CoV-2 infection cases has been dramatically increasing [3]. As per July 1, 2020, there have been more than 10.6 million cases and over 514,000 COVID-19-related deaths reported by the World Health Organization. A substantial number of new cases has been published in the United States recently, making it the only country that reaches a total of more than 1 million confirmed cases.

On the other hand, although it has been reported to be steadily increasing, the incidence rates in Indonesia are not as overwhelmingly high, as stated in the different parts of the world. This may be attributed to the low rates of screening in our population. However, the case fatality rate of SARS-CoV-2 infection in Indonesia is relatively higher, indicated by the mortality rates of 7.2% [4]. Severe COVID-19, particularly in patients with acute respiratory distress syndrome (ARDS), is associated with an increased risk of admission to the intensive care unit (ICU), mechanical ventilation, and mortality [5], [6]. It has been well documented that patients suffering from ARDS most probably produce thick mucus secretion. This is associated with an increased risk of mucous plug formation and subsequent lung collapse [7]. Similar characteristics of airway secretion have also been reported in COVID-19 infection [8]. Proper and timely secretion management plays essential roles in both the prevention and treatment of respiratory failure. Bronchoscopy has been widely employed for various purposes in severe pulmonary infection, particularly among mechanically ventilated patients. This includes therapeutic suctioning as a part of effective secretion management, both as diagnostic and therapeutic measures [7], [9], [10]. However, the use of bronchoscopy in patients with COVID-19 has been strictly limited as it is associated with the aerosol generation and intensifies viral transmission. It can be performed only in certain situations, such as mucous plug removal as well as to ascertain the presence of any coinfection in patients who do not respond to the standard therapy, by following a very tight protocol as proposed by currently available consensus [3], [11], [12], [13], [14]. However, to the best of our knowledge, there is no presently available data regarding the use of the bronchoscopic intervention in COVID-19 patients with severe clinical presentation. Here, we describe the outcomes of bronchoscopic intervention performed in three cases of mechanically ventilated, COVID-19-confirmed patients.

Case I

A 47-year-old woman was admitted to our facility due to shortness of breath accompanied cough since 1 day before admission. The patient also reported a 1-week course of fever, nausea, and vomitus. She had neither a history of lung nor heart disease. The patient was diagnosed with severe pneumonia. On the 3rd day of hospitalization, the patient experienced clinical deterioration with more intense dyspnea. The initial clinical examination showed decreased oxygen saturation (SpO_2) to 84%, and the patient was immediately given oxygen supplementation. Arterial blood gas (ABG) analysis showed pH 7.480, $PaCO_2$ 34.6 mmHg, PaO_2 159.5 mmHg, and SpO_2 98%. Chest X-ray results were suggestive for bilateral pneumonia (Table 1). The patient was decided to undergo early intubation with subsequent mechanical ventilation. The following ventilator setting was used: Volume-controlled synchronized intermittent mandatory ventilation (VC-SIMV) mode, a fraction of inspired oxygen (FiO_2) 70%, positive end-expiratory pressure (PEEP) 12 cmH_2O, pressure support 12 cmH_2O, tidal volume (VT) 300 ml, and respiratory rate (RR) 20 breaths/min that resulted in oxygen saturation (SpO_2) of 98% immediately. One day following intubation, the patient showed clinical improvement. Subsequent blood gas analysis results showed improved PaO_2 that reached 195.5 mmHg. On the next day, from the physical examination, it was found that there was an excessive mucus production that might have partially obstructed the patient's airway. We performed tracheal suctioning as the primary measure to evacuate the obstructing mucus; however, no clinical improvement was observed. Subsequently, we decided to perform controlled suction through bronchoscopy. Pre-bronchoscopy ABG showed pH 7.492, PaO_2 150 mmHg, $PaCO_2$ 34 mmHg, and SpO_2 99%. Even when there was no vivid hypoxemia, we considered that early bronchoscopic suction would be a favorable measure to improve the patient's clinical status. The ventilator parameters before bronchoscopy were set as pressure support ventilation (PSV), PEEP +5 cmH_2O, RR 19 breaths/min, VT 400 ml, FiO_2 40%, and PS 6 cmH_2O. Bronchoscopy was performed on day 24 of hospitalization in a negative-pressured room. We use fentanyl, atracurium, and midazolam as sedation before bronchoscopy. Bronchoscopy was performed with Olympus TF180, and we found a large amount of thick reddish black-colored secretions were evacuated from the lower airway. Ventilator settings were adjusted to SIMV, PEEP +6 cmH2O, RR 15 breaths/mnt, VT 360 ml, FiO_2 70%, and PS 5 cmH_2O. Immediate post-bronchoscopy ABG evaluations showed the following results: pH 7.5230, pO_2 242.9 mmHg, pCO_2 29 mmHg (Figure 1). On the following days, the patient showed significant clinical and respiratory improvement. Weaning of the respiratory support was started on day 3 and was discharged from the ICU on 28 days of hospitalization.

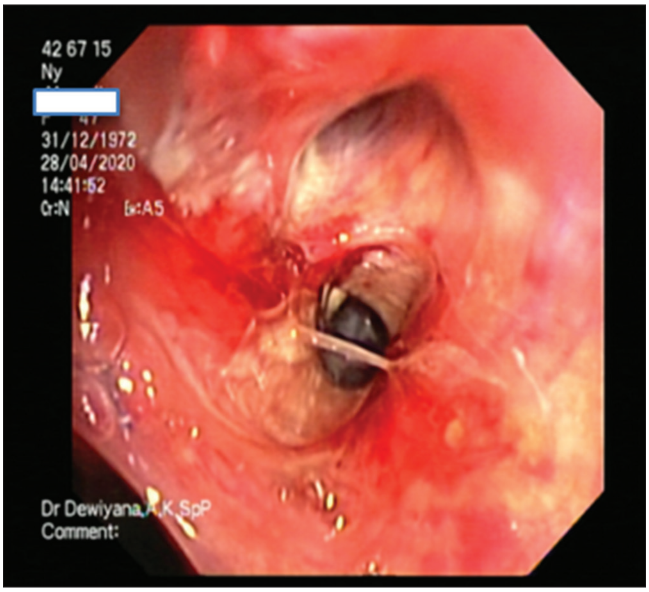

Figure 1: Bronchsocopy showed thick reddish black colored secretions

Case II

A 70-year-old man was admitted to our facility due to cough and fatigue. After a series of examination, the patient was confirmed to have suffered from COVID-19 pneumonia. On day 16 post-hospital admission, the patient experienced worsening shortness of breath. Immediate ABG evaluation showed pH 7.48, PCO_2 31.5 mmHg, PO_2 121.3 mmHg, and SpO_2 84.3%. Accordingly, he was decided to undergo endotracheal intubation with subsequent mechanical ventilation support with the following ventilator settings: VC-SiMV, VT 400 ml, PEEP 10, PSV 10, RR 12 breaths/minute, and FiO_2 80%. A significant hemodynamic improvement was observed following mechanical ventilation. Around 6 days following intubation, it was noted that the patient produced enormous airway secretions, as evidenced by pulmonary auscultation showing significant pulmonary rales. Further, ABG showed pH 7.57, PCO_2 26.6 mmHg, and PO_2 145.3 mmHg. Similarly, tracheal suction was performed initially as an effort to evacuate the obstructing mucus. However, the attempt was not successful. Therefore, a controlled suction was also performed through bronchoscopy. We were able to evacuate the thick obstructing secretion from the lower respiratory tract. The bronchoscopy showed the presence of thick secretion obstructing the distal trachea, which was removed (Figure 2). Subsequently, the ventilatory settings were adjusted to SIMV, PEEP +6 cmH_2O, RR 12 breaths/mnt, VT 360 ml, FiO_2 60%, and PS 6 cmH_2O after the procedure. The patient demonstrated clinical improvement. Subsequent ABG evaluation showed pH 7.52, PCO_2 35.1 mmHg, and PO_2 171.7 mmHg. Ventilator weaning was successfully attempted on day 16, and the patient was discharged from the ICU on 26 days of hospitalization.

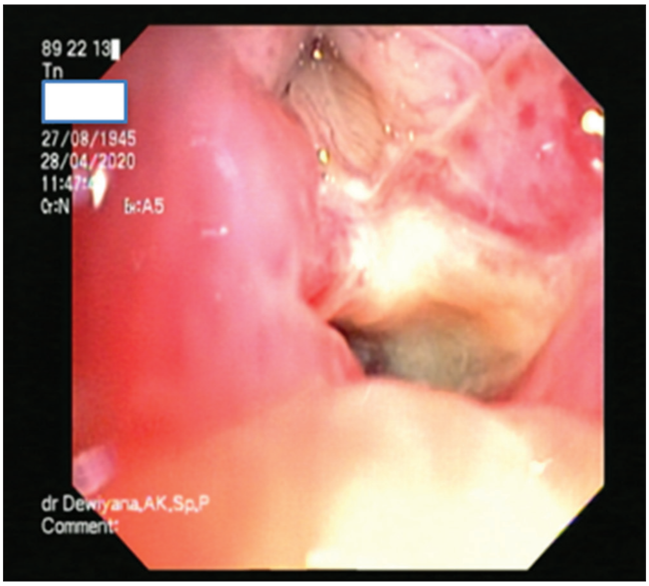

Figure 2: Bronchoscopy showed thick secretion obstrutcting the ditstal trachea

Case III

A 75-year-old man was confirmed to have suffered from COVID-19 pneumonia. The patient had a history of diabetes mellitus, hypertension, and cardiac disease. On day 3 post-hospital admission, the patient experienced worsening shortness of breath and decreasing of saturation. Immediate ABG evaluation showed pH 7.5, PCO_2 22.6 mmHg, PO_2 60.3 mmHg, and SpO_2 86%. Accordingly, he was decided to undergo endotracheal intubation with subsequent mechanical ventilation support with the following ventilator settings: VC-SiMV, VT 600 ml, PEEP 10, PSV 10, RR 12 breaths/min, and FiO_2 60%. A significant hemodynamic improvement was observed following mechanical ventilation. Around 7 days following intubation, tracheal suction was performed initially as an effort to evacuate thick and green mucoid obstructing mucus. However, the attempt was not successful. Therefore, a controlled suction was also performed through bronchoscopy. The bronchoscopy showed thick yellow mucoid secretion, hyperemic in entire bronchus lumen, and prone to bleed (Figure 3). There are no adjusting ventilatory settings. The patient demonstrated clinical improvement. Subsequent ABG evaluation showed pH 7.466, PCO_2 34.8 mmHg, and PO_2 173.2 mmHg. Ventilator weaning was successfully attempted on day three, and the patient was discharged from the ICU on 15 days of hospitalization. Unfortunately, the patient had a cardiac arrest and died in the hospital ward.

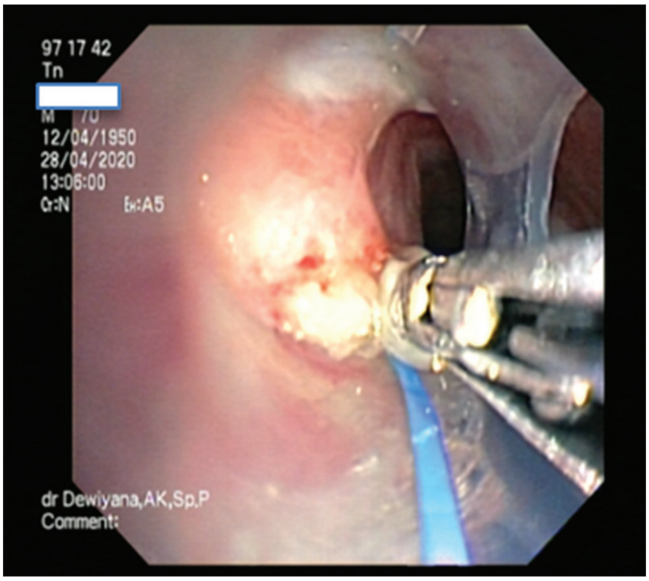

Figure 3: Bronchoscopy showed thick yellow mucoid secretion and hyperemic bronchus lumen

Discussion

COVID-19 is an extremely infectious disease caused by a newly identified SARS-CoV-2 virus. It has affected more than 3.5 million individuals in almost every country within the past 4 months [4]. SARS-CoV-2 is an enveloped, non-segmented, positive-sense, and single-stranded RNA virus that is considered a member of beta-coronavirus [15], [16]. The clinical presentations of COVID-19 vary among individuals. Some people may not have any signs and symptoms of infection and become carriers. Some others may develop symptoms within 14 days following the initial exposure to the viral particles [17], [18]. The majority of patients (81%) demonstrated mild symptoms; only 14% and 5% of patients presented with a severe and critical disease, respectively [19]. The most common symptoms reported include fever (83–98%), cough (50–80%), fatigue (34–69%), and dyspnea (20–40%) [5], [20], [21], [22]. Patients with severe manifestations may present with signs and symptoms of pneumonia, ARDS, sepsis, and septic shock [23]. Patients who initially present with mild

Table 1: Characteristics of the presented patients

Parameters	Patient 1	Patient 2	Patient 3
Age (years)	47	70	74
Sex	Female	Male	Male
Symptoms			
Fever	Yes	No	Yes
Cough	Yes	Yes	Yes
Myalgia or fatigue	Yes	Yes	Yes
Headache	No	No	No
Hemoptysis	No	No	No
Diarrhea	No	No	No
Dyspnea	Yes	No	Yes
Comorbidities			
Diabetes	No	No	Yes
Hypertension	No	No	Yes
Cardiovascular disease	No	No	Yes
Chronic obstructive pulmonary disease	No	No	No
Malignancy	No	No	No
Chronic liver disease	No	No	No
Immunosuppresion	No	No	No
Vital signs at admission			
Blood pressure (mmHg)	136/80	124/73	167/81
Heart rate (bpm)	103	68	98
RR (×/min)	30	20	28
Temperature (°C)	38	36	36.8
Oxygen saturation (%)	84%	88%	98%
Laboratory parameters*			
Hemoglobin (g/dL)	11.3	11.2	16.4
White blood cell count (×10)	5820	7490	14690
Neutrophil count (×10)	80	56	91
Lymphocyte count (×10)	14	37	6
Platelet count (×10)	231	227	296
PT (s)	13.1	11.8	10.9
APTT (s)	37.4	40	25.9
D-dimer (mg/dL)	380	3480	2130
Albumin (g/L)	3.9	3.2	2.9
ALT (U/L)	39	19	40
AST (U/L)	52	21	25
Sodium	145	130	137
Potassium	3.6	4.1	3.9
Creatinine (mg/dl)	0.79	1.01	2.27
Ureum (mg/dl)	19	42	70
Swab results	Yes	Yes	Yes
CRP	7.84	14.14	24.47
Radiographic signs of pneumonia	Yes	Yes	Yes
Treatment			
Antiviral	Yes	Yes	Yes
Antifungal	No	No	No
Antibiotic	Yes	Yes	Yes
Antiparasitic	Yes	Yes	Yes
High-dose Vitamin C	Yes	Yes	Yes
Ventilator-related parameters			
Onset to mechanical ventilation (days)	3	16	2
Modea	VC-SIMV	VC-SiMV	VC-SiMV
Peak pressure (cmH_2O)a	12	10	10
PEEP (cmH_2O)a	12	10	10
FiO_2 (%)	70%	80%	50%
Bronchoscopy-related parameters			
Day of bronchoscopy	24	28	10
Onset to bronchoscopy (days)	31	31	13
Positioning	Prone	Prone	Prone
Bronchoscope diameter (mm)	2.1	2.1	2.1
ETT diameter (mm)	7.5	7.5	7.5
BAL	No	No	No
Monitoring			
MAP (mmHg)			
Baseline	83	86	93
During bronchoscopy	93	86	93
Oxygen saturation (%)			
Baseline	99	99	99
During bronchoscopy	99	99	98
Outcomes			
Discharged from hospital	Yes	Yes	No
Discharged from ICU	Yes	Yes	Yes
Dead	No	No	Yes

ALT: Alanine aminotransferase, APTT: Activated partial thromboplastin time, AST: Aspartate aminotransferase, BAL: Bronchoalveolar lavage, CRP: C-reactive protein; PCO_2: Carbon dioxide, ETT: Endotracheal tube, FiO_2: Fractional concentration of inspired oxygen, ICU: Intensive care unit, LDH: Lactate dehydrogenase, LOS: Length of stay, MAP: Mean arterial pressure, PCT: Procalcitonin, PEEP: Positive end-expiratory pressure, PT: Prothrombin time, VC-SIMV: Volume-controlled synchronized intermittent mandatory ventilation, RR: Respiratory rate.

symptoms could also experience clinical progression toward more severe illness. Rapid progression can also be encountered in an otherwise healthy patient without any significant medical history.

Goh *et al*. reported a case with a similar pattern of progression affecting a 64-year-old Singaporean man. The patient presented to the hospital with mild symptoms since around 1 week before admission and rapidly deteriorated with severe hypoxemic respiratory failure within only 48 h following admission [24]. Other evidence also suggested that the median time of ARDS development was 2 days from the admission day [6]. All of our cases presented with relatively mild disease complaining of having some respiratory and constitutional symptoms, including fever, cough, fatigue, and dyspnea. Following the previous evidence, the first patient demonstrated rapid progression, of which she demonstrated worsening of her clinical status within 3 days of admission. The second case, on the other hand, demonstrated a relatively slower clinical course, where the patient experienced an intense worsening of his complaints after 2 weeks of hospitalization.

One of the biggest concerns in COVID-19 is a further compromise in respiratory function. It has been noted that COVID-19 patients, particularly those who develop ARDS, produce thick mucus secretion. This puts the patients at a substantial risk of developing airway obstruction due to plug formation and subsequent lung collapse [7], [8]. Hence, airway management and optimal oxygenation serve as the constructing pillars in the management of severe COVID-19 infection. The concept of early intubation in COVID-19 patients has been a matter of debate. It is noteworthy that mechanical ventilation itself can exacerbate functional and structural alterations in the lung and is related to the morbidity and mortality in ARDS [25]. Therefore, timely, but not premature, endotracheal intubation is always preferred [26]. In our cases, all of the patients experienced clinical deterioration. Both of the patients experienced respiratory alkalosis, as indicated by their ABG results. Hence, endotracheal intubation was performed, followed by mechanical ventilation which resulted in clinical improvement. During observation in the ICU, both patients showed clinically significant production of airway secretions, as evidenced by abnormal lung sound on physical examination. Conventional tracheal suction has failed to evacuate the airway secretion, and hence, bronchoscopy was scheduled to vacate the secretion and prevent further airway compromise. Conventionally, bronchoscopy has been widely used as a standard procedure in the setting of severe respiratory problems for both diagnostic and therapeutic purposes in patients with a critical illness [10]. Unfortunately, the practice of performing bronchoscopy during the COVID-19 pandemic has been very restricted. Bronchoscopy is considered an aerosol-generating procedure, and hence, it possesses a substantial risk of viral transmission to the surrounding and puts both medical professionals and unconfirmed patients at risk of getting the infection. Therefore, it is always recommended to consider the risks and benefits of performing bronchoscopy, particularly among patients with confirmed COVID-19 disease. The decision should be individualized based on the patient's clinical condition. Once decided to perform a bronchoscopic intervention, it has to be done only in a negative-pressure room and by a highly experienced clinician to minimize the amount of time needed to complete the response. It is recommended to perform bronchoscopy with general anesthesia as well as with muscle relaxant administration while avoiding emergent intubation to reduce the risk of aerosol generation. Standard personal protective equipment and disinfection protocol are highly warranted [14]. Indications for performing bronchoscopy during COVID-19 pandemic have been categorized into emergent, semi-urgent, and elective indications. Patients with symptomatic central airway obstruction related to either neoplasm, foreign body aspiration, or mucous plug; massive hemoptysis, tracheal stenosis, and stent migration should be referred for further bronchoscopic evaluation. As for the evaluation of lung nodules, mediastinal lymph node enlargement, whole pulmonary lavage, suspected lung infection in patients with impaired immune function, assessment of obliterative bronchiolitis in transplant recipients, as well as evaluation of lobar atelectasis, bronchoscopy is advised to be performed in a semi-urgent manner. Among patients in an otherwise stable condition, elective bronchoscopy can be performed for tracheobronchomalacia evaluation, bronchial thermoplastic, cryobiopsy, as well as bronchoscopic lung volume reduction surgery [11], [14].

The role of bronchoscopy in the management of patients with a severe phenotype of COVID-19 infection is minimal. Bronchial or pulmonary toileting is not recommended as a routine therapeutic intervention in these subsets of patients. However, therapeutic aspiration is advisable in patients with airway obstruction due to mucous impaction that impairs gas exchange function. In our cases, the main reasons for performing bronchoscopy were the evidence of enormous airway secretions, as evidenced by clinical examination. We decided to perform bronchoscopy-directed bronchial toilet as an effort to help to evacuate the abundant mucoid secretion in the patients lower respiratory tract and to prevent the formation of mucus plug. We performed this bronchoscopic intervention under a very secure protocol as proposed by various consensus. Following the response, the patients showed favorable clinical and hemodynamic outcomes. Weaning of the mechanical ventilation could be performed earlier with desirable results. One of the primary concerns in performing bronchoscopy is which technique would result in a limitation of infection spread while maintaining the safety of the procedure. Some data suggested that prone positioning is associated with a reduction in mortality in mechanically ventilated patients with severe ARDS and that bronchoscopy performed in a prone position is safe without significantly aggravating the risk of clinical deterioration [9], [27]. In addition, fiberoptic bronchoscopy performed in a prone position helps to avoid undesirable premature interruption of mechanical ventilation and consequent loss of physiological gains, an increase in intrapulmonary shunt, a fall in the oxygen saturation as well as elevated pulmonary artery resistance [9].

At present, there is no standardized recommendation on a ventilator setting during bronchoscopy. Guarracino *et al*. (2012) successfully and safely performed bronchoscopy by increasing FiO_2 to 1, reducing PEEP level and respiratory frequency to avoid an increase in PEEP while increasing inspiratory pressure to maintain minute volume and prevent an increase in carbon dioxide [9]. Some data suggested that bronchoscopic tube internal diameter of 4 mm is optimal and safer in patients with ARDS [7]. In a case series of patients with severe ARDS who were mechanically ventilated, Kalchiem-Dekel *et al*. (2018) showed that no significant hemodynamic compromise was observed during bronchoscopic aspiration and BAL procedures using a maximum internal diameter of 4 mm and without changing the mode of mechanical ventilation except for 100% FiO_2. However, significant oxygen desaturation and rising in COs_2 pressure were observed in one patient. At last, 4 out of 7 patients survived 30 days following discharge from ICU [28].

Conclusion

Bronchoscopic procedures may provide significant therapeutic benefits in severe COVID-19 patients. However, it should be kept in mind that this procedure should only be performed with a rigorous protocol to reduce the risk of aerosol generation and subsequent viral transmission. More well-designed studies are needed to elucidate further the role of bronchoscopic intervention among severely ill COVID-19 patients as well as addressing the most optimal and the safest ventilator setting during the procedure.

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