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Bronchoscopy in Patients with COVID-19 with Invasive Mechanical Ventilation: A Single-Center Experience

To the Editor:

Severe coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection leads to acute respiratory distress syndrome and hypoxemic respiratory failure (1).

The University Hospital de la Santa Creu i Sant Pau serves an area of downtown Barcelona, Spain, of about 420,000 citizens. The first case of COVID-19 at our hospital was detected on March 17, 2020. The first two cases in the ICU were detected on March 13, and the number of beds dedicated to intensive care multiplied by four,

with 163 new ICU admissions and 139 patients requiring mechanical ventilation between March 13 and April 4. During this period, 59 patients were discharged, 23 died, and 81 were still in the ICU.

BAL, bronchial wash, and protected specimen brush are bronchoscopic procedures used to provide microbiological samples from lower respiratory airways. However, because of the risk of viral transmission, bronchoscopy is not routinely indicated for the diagnosis of COVID-19 (2).

Bronchoscopy in critically ill patients with COVID-19 has been required to manage complications (atelectasis, hemoptysis, etc.) as well as to obtain samples for microbiological cultures and to assist in the management of artificial airways (guide intubation and percutaneous tracheostomy) (3).

Because no series of intubated patients with COVID-19 submitted to bronchoscopy has been published so far, we describe our experience in performing flexible bronchoscopies in patients with COVID-19 with severe acute hypoxemic respiratory failure requiring invasive mechanical ventilation during the first 3 weeks of the epidemic outbreak.

Between March 16 and April 4, 2020, a total of 101 bronchoscopies were performed in 93 patients with COVID-19. Eight patients required two bronchoscopies.

Indications for bronchoscopy were as follows: radiological and/or clinical deterioration suggesting possible superinfection (63/101) as well as airway secretion management with/without atelectasis (38/101). Intensivists indicated procedures 6.6 days (range, 1–17) after intubation. At the time of indication, the median F_{IO_2} was 0.8 (interquartile range [IQR], 0.67–0.82), the median positive end-expiratory pressure was 10 cm H_2O (IQR, 9–11), and the median Pa_{O_2}/F_{IO_2} ratio was 111 (IQR, 103–125).

Procedures were performed in either supine (74/101) or prone (27/101) position, under usual intravenous sedation and with pressure-controlled ventilation mode. Disposable scopes were used in all cases (Ambu aScope 4 Broncho, Large 5.8/2.8. Ambu A/S), and minimal staff attended the procedure bedside (one expert bronchoscopist occasionally accompanied by a staff intensivist). One out of two bronchoscopists got infected with SARS-CoV-2 and developed COVID-19. As a consequence, our colleague had to be replaced by another bronchoscopist during the third week.

Before the procedure, all the necessary equipment and materials were prepared outside the patient room, including saline, syringes, mucoactive drugs, microbiological recipients, connections, and bronchoscopy system (scope and screen). A negative-pressure room was not always available for the procedures owing to the variety of locations adapted for intensive care support. As recommended (2), level III of personal protective equipment was used, including N95 or FPP3 mask, goggles, double gloves, and a plastic protective gown including head and neck cover.

Bronchoscopic examination included orotracheal tube positioning check, direct inspection of tracheal and bronchial mucosa, suctioning of secretions, and mucoactive agent instillation if necessary (hypertonic saline combined with hyaluronic acid), and in 63 cases, a mini-BAL with 60-ml saline aliquots at room temperature was performed just before the end of procedure for microbiological sampling. The bronchial segment to
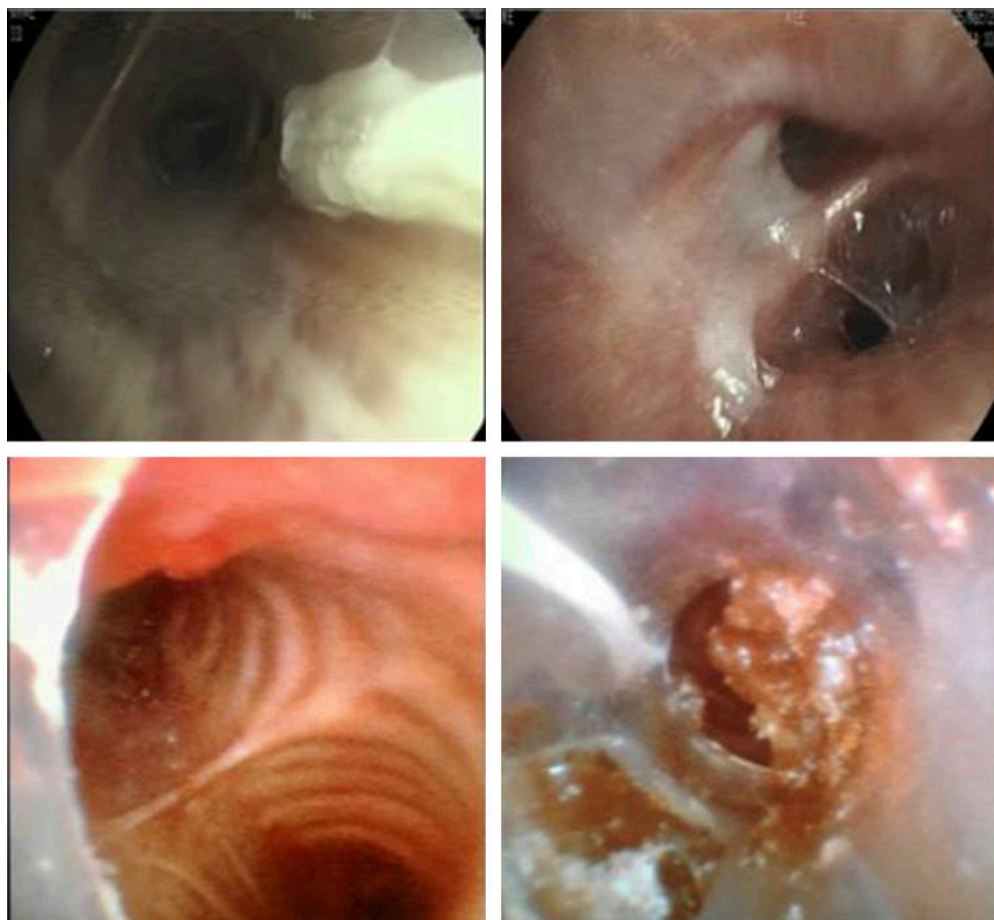
Figure 1. Bronchial findings in coronavirus disease (COVID-19) cases. White, gelatinous secretions and normal-colored mucosa (top panels), hyperemic bronchial mucosa (lower left panel), and thick mucohematic plug distal to endotracheal tube (lower right panel) are shown.

perform the BAL was chosen according to the radiological information.

The duration of the procedures was never more than 10 minutes. Before the procedure, $F_{I_{O_2}}$ was increased so as to reach a peripheral oxygen saturation of 95%–98%. Bronchoscopy was well tolerated in most cases. A transient drop in oxygen saturation as measured by pulse oximetry (Sp_{O_2}) below 90% was occasionally observed during the procedure. In those patients, the bronchoscope was removed for a few seconds until Sp_{O_2} recovery (i.e., >90%). Major desaturation did not force the abortion of any procedure. The mini-BAL was not associated with a greater number of complications as compared with patients in whom BAL was not performed. Apart from transient drops in Sp_{O_2}, no other complications were detected during the procedures.

Bronchoscopy results showed normal or mildly hyperemic bronchial mucosa. The presence of white and gelatinous secretions, difficult to suction, was observed in 95% (88/93) of patients. In 12 cases, mucohematic plugs occupying the main or lobar bronchi were observed and removed after instillation of saline and a mucolytic agent. Figure 1 shows examples of the described findings, which to the best of our knowledge have not been reported in peer-reviewed journals. The fact that we used closed-circuit suctioning systems together with heat and moisture exchangers (EdithFlex HME;

Vyaire) may also help explain why this complication was encountered so often. Because our usual way to provide proper inspired gas conditioning is the use of heated humidifiers, we cannot ascertain if thick secretions are due to the viral infection *per se* or the change in our humidification strategy. Nevertheless, in past scenarios in which our patients used the same kind of passive humidification, this observation was uncommon. The main results are summarized in Table 1.

Table 1. Bronchoscopy in Intubated Patients with Severe COVID-19

Main Results Summary (*n* = 101)
27% performed in prone position
29% positive BAL cultures
95% presence of thick secretions in the airway*
BAL (60 ml) was not associated with more desaturation as compared with bronchoscopy without BAL
One bronchoscopist (out of three) got infected[†]

Definition of abbreviation: COVID-19 = coronavirus disease.
*Possibly related to humidification and closed suctioning system.
[†]We do not have definitive evidence relating the infection to the procedure.

Table 2. Microbiological Isolations from ICU Bronchoscopic Studies in Immunocompetent Patients during Year 2017 and Patients with COVID-19

Microbiological Isolations (Year 2017)* (n = 137)		Microbiological Isolations (COVID-19, March 2020) (n = 63)	
Microbe or Virus	**n (%)**	**Microbe or Virus**	**n (%)**
Total positive results	57/137 (41.6%)	Total positive results	18/63 (28.6%)
Polymicrobial	8 (14%)		
P. aeruginosa	9 (15.8%)	P. aeruginosa	7 (38.8%)
S. aureus	6 (10.5%)	S. aureus	2 (11.1%)
E. cloacae	4 (7%)	E. cloacae	2 (11.1%)
S. marcescens	4 (7%)	E. faecalis	2 (11.1%)
S. maltophilia	3 (5.3%)	K. aerogenes	2 (11.1%)
Influenza virus	3 (5.3%)	P. melaninogenica	1 (5.3%)
S. pneumoniae	2 (3.5%)	E. coli	1 (5.5%)
K. pneumoniae	2 (3.5%)	S. anginosus	1 (5.5%)
Candida sp.	2 (3.5%)		
P. melaninogenica	2 (3.5%)		
S. pyogenes	1 (1.7%)		
A. israelii	1 (1.7%)		
A. baumannii	1 (1.7%)		
C. freundii	1 (1.7%)		
A. pittii	1 (1.7%)		
H. influenzae	1 (1.7%)		
Streptococcus viridans	1 (1.7%)		
Herpes virus	1 (1.7%)		
P. mirabilis	1 (1.7%)		
E. faecalis	1 (1.7%)		
E. coli	1 (1.7%)		
K. oxytoca	1 (1.7%)		
S. epidermidis	1 (1.7%)		
A. ursingii	1 (1.7%)		
Capnocytophaga sp.	1 (1.7%)		
Mycobacterium tuberculosis	1 (1.7%)		

Definition of abbreviations: A. baumannii = Acinetobacter baumannii; A. israelii = Actinomyces israelii; A. pittii = Acinetobacter pittii; A. ursingii = Acinetobacter ursingii; C. freundii = Citrobacter freundii; COVID-19 = coronavirus disease; E. cloacae = Enterobacter cloacae; E. coli = Escherichia coli; E. faecalis = Enterococcus faecalis; H. influenzae = Haemophilus influenzae; K. aerogenes = Klebsiella aerogenes; K. oxytoca = Klebsiella oxytoca; K. pneumoniae = Klebsiella pneumoniae; M. tuberculosis = Mycobacterium tuberculosis; P. aeruginosa = Pseudomonas aeruginosa; P. melaninogenica = Prevotella melaninogenica; P. mirabilis = Proteus mirabilis; S. anginosus = Streptococcus anginosus; S. aureus = Staphylococcus aureus; S. epidermidis = Staphylococcus epidermidis; S. maltophilia = Stenotrophomonas maltophilia; S. marcescens = Serratia marcescens; S. pneumoniae = Streptococcus pneumoniae; S. pyogenes = Streptococcus pyogenes.
*Data from 2017 are from Reference 5.

Regarding BAL results, 18/63 (28.6%) had positive cultures for *Pseudomonas aeruginosa* (n = 7), *Staphylococcus aureus* (n = 2), *Klebsiella aerogenes* (n = 2), *Enterobacter cloacae* (n = 2), *Enterococcus faecalis* (n = 2), *Escherichia coli* (n = 1), *Streptococcus anginosus* (n = 1), or *Prevotella melaninogenica* (n = 1). These results are similar to microbiological flora usually observed in ventilator-associated pneumonia (4). As a result of BAL, a new antibiotic was prescribed in 15/18 (83%) patients. The present isolates do not differ from those obtained during nonepidemic periods (Tables 1 and 2). BAL processing did not yield mycobacteria, fungi (including *Aspergillus* sp., verified by microbiological culture), or other viruses. BAL galactomannan was determined in only one patient.

In summary, in critically ill, mechanically ventilated patients with COVID-19, thick hypersecretion in the airway is the most common complication observed, and these patients can benefit from specific bronchoscopy management. Guided mini-BAL can be of help to confirm a clinical suspicion of superinfection. However, with this observational study, it is impossible to weigh the benefits of bronchoscopy against the potential harms to the patient and the bronchoscopist. A different study design would have been required to address the influence on patient-centered outcomes. ■

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Respiratory Mechanics of COVID-19– versus Non–COVID-19–associated Acute Respiratory Distress Syndrome

To the Editor:

Most patients admitted to the ICU with a severe presentation of coronavirus disease (COVID-19) fulfill the acute respiratory distress syndrome (ARDS) criteria (1) and require invasive mechanical ventilation (2). In such patients, knowledge of respiratory mechanics and potential for lung recruitability may provide valuable information to guide adjustments in ventilator settings. Some authors have regularly reported from their clinical experience that the key feature of COVID-19 respiratory mechanics would be an uncommon association of severe hypoxemia and preserved respiratory system compliance, altogether with poor recruitability (3–5). However, a dramatic decrease in respiratory system

compliance has also been reported in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–related ARDS (6). Gattinoni and colleagues recently proposed to reconcile these different observations, hypothesizing that the different phenotypes may result from interactions between the time course and severity of the disease and the patient's ventilatory response, with an early L phenotype (low lung elastance, low recruitability) and a late H phenotype (high lung elastance, high recruitability) (5). However, physiological descriptions of COVID-19–associated ARDS and its comparison with non–COVID-19 classical ARDS remain scarce in the literature.

The aim of the present study is to describe the respiratory mechanics and lung recruitability of patients with COVID-19–associated ARDS, to compare it with that of non–COVID-19–associated ARDS, and to explore their possible relation with COVID-19 phenotypes.

Methods

This is an ancillary report of an ongoing prospective monocentric observational study on respiratory mechanics in patients with ARDS, conducted in the Henri Mondor University Hospital medical ICU, Créteil, France (Institutional Review Board 2018-A00867–48). Inclusion criteria were age >18 years and presence of ARDS according to the Berlin definition (7). Exclusion criteria were intubation for more than 24 hours prior to ICU admission. All consecutive patients with COVID-19 included in this study are reported here and compared with consecutive patients without COVID-19 who were previously enrolled. Written informed consent was waived owing to the observational nature of the study. The ventilator was set by the attending physician. During the first 48 hours of invasive mechanical ventilation, the ventilator's settings were collected and the respiratory mechanics and lung recruitability were assessed once in supine position. Thus, airway and esophageal (when available) pressures were recorded during a 0.3-second end-inspiratory and a 1- to 2-second end-expiratory occlusion maneuver, at the positive end-expiratory pressure (PEEP) level previously set by the physician. The potential airway closure phenomenon was detected by measuring the airway opening pressure during a low flow ($\leq$6 L/min) insufflation, as previously described (8). The potential for lung recruitment was assessed by the mean of the recruitment-to-inflation ratio (R/I ratio) computation, as previously detailed (8). By default, R/I ratio was assessed between 15 and 5 cm H_2O of PEEP. However, in case of airway closure, the low PEEP was set above the airway opening pressure. Comparisons were made using nonparametric tests. A $P < 0.05$ was considered significant.

Results

Thirty consecutive patients with non–COVID-19–associated ARDS and 30 consecutive patients with COVID-19–associated ARDS were included in the report. Patients without COVID-19 were enrolled between January 17, 2019, and March 3, 2020, and those with COVID-19 were enrolled between March 11, 2020, and April 3, 2020. Five patients with COVID-19 and five without COVID-19 experienced prone position before inclusion in the study. Etiologies for non–COVID-19–associated ARDS were as follows: pneumonia ($n = 27$, of which 10 were related to respiratory viruses), pulmonary vasculitis ($n = 2$), and noncardiogenic shock ($n = 1$). A bacterial coinfection was documented in four patients with COVID-19 at the time of inclusion. Patients with and without COVID-19 did not