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Management of acute respiratory deterioration in the intensive care unit during the COVID-19 pandemic: Prospective analysis of retrospective data collected from a tertiary intensive care unit

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Abstract

Coronavirus disease-2019 (COVID) is a highly contagious viral disease, spread predominantly by airborne particles. Due to the high dissemination risk of COVID-19, aerosol generating procedures such as orotracheal intubation and bronchoscopy may result in viral spread. Therefore, performing bronchoscopies in infected patients, with insufficient evidence, is controversial. The aim of this study was to assess the requirements for emergency bronchoscopy in COVID-19 patients treated with invasive mechanical ventilation in the ICU, and to evaluate the applicability of the procedure and its effects on clinical progress. Patients with confirmed COVID-19 diagnoses who received invasive mechanical ventilation in the intensive care unit between March 26, 2020 and February 1, 2021, and who underwent emergency bronchoscopy were included into the study. Respiratory parameters before and after the procedure were analyzed with the paired t test. Among 395 patients diagnosed with COVID-19 pneumonia who received mechanical ventilation, 45 (mean age:48, 17F/28M) underwent an emergency bronchoscopy. The major indication for bronchoscopy was forced mechanical ventilation that did not respond to different measures. In 91.6% of the bronchoscopies there were positive findings, the most common were mucus secretions (82.4%), hematoma secretions (17.7%), mucous plugs (17.6%), and extensive mucosal hyperemia (11.4%). Patients who underwent bronchoscopies were noted to have significant improvements in respiratory mechanics and PO_2/FiO_2 ratios ($p<0.05$). Bronchoscopy can be safely applied in COVID-19 patients to solve the complications of mechanical ventilation, provided that the rules of personal protective equipment are complied with. Immediate improvements in respiratory parameters can be attained with bronchoscopy. In the absence of X ray findings, causes of the acute respiratory deterioration in COVID-19 patients can be investigated with bronchoscopy.

Keywords: COVID-19 pandemic, adult respiratory distress syndrome, critical care, bronchoscopy, occupation safety

1. Introduction

COVID-19 was first described as a pneumonia caused by SARS-COV-2 virus. The disease spread rapidly, becoming a pandemic affecting the whole world. Due to the surge of cases both nationally and internationally, the infrastructure of the health system was challenged against such a pandemic. Therefore, optimal use of resources for an effective professional action against the pandemic, in addition to the limited amount of healthcare workers and the need for uninterrupted care challenged the health systems (1, 2). Due to the high risk of viral dissemination, the use of some procedures (respiratory function test, bronchoscopy, etc.) was limited during the pandemic. Bronchoscopy is widely applied for diagnostic and therapeutic purposes. It is considered a relatively safe procedure due to the low risk of severe complications, and is very useful in the diagnosis and management of respiratory problems (3). In critically ill COVID-19 patients admitted to the intensive care unit (ICU), bronchoscopy may be required to manage complications including atelectasis or hemoptysis, solve problems related to mechanical ventilation, or exclude a superinfection. Working during the coronavirus disease 2019 (COVID-19) pandemic changed the habits of healthcare workers performing bronchoscopies. Guidelines prepared immediately after the spread of COVID-19 stated the common opinion that in patients with known or suspected COVID-19 patients, the use of fiberoptic bronchoscopy (FOB) should be limited and regarded as a relative contraindication due to the risk of spread to healthcare workers and the generation of aerosols during the procedure (4, 5).

COVID-19 may be asymptomatic or manifest itself with a wide array of symptoms including cough, fever, fatigue, or pneumonia causing severe acute respiratory distress syndrome (ARDS). Criteria for admission to the intensive care unit differ between countries and institutions, and the rates of admission are between 5-32% (1). Intensive care may become necessary in severe pneumonia, ARDS, myocarditis, arrythmias,

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cardiogenic shock, cerebrovascular disease, or acute renal failure. In those patients having predominantly hypoxemic respiratory failure, hypercapnic respiratory failure due to mucous plugs may be also observed. Similar to the experiences reported by other centers during the first wave of the pandemic, our observations revealed that especially in ARDS patients requiring mechanical ventilation the needs for bronchoscopy may be increased for various causes, particularly bronco aspiration (6).

The aim of this study was to evaluate the results of endoscopic procedures in COVID-19 patients who were mechanically ventilated in the ICU and developed acute deterioration in the oxygenation status without an identifiable cause after exclusion of pneumothorax and other causes.

2. Materials and Methods

A retrospective analysis of the demographic and respiratory parameters of COVID-19 patients, diagnosed using polymerase chain reaction (RT-PCR) of nasopharyngeal swab samples, hospitalized in the ICU between 26 March 2020 and 1 February 2021, received invasive mechanical ventilation, and underwent bronchoscopy, was performed.

The exclusion criteria were age under 18, diagnosis of COVID-19 not verified with a PCR test, no history of mechanical ventilation, presence of hemodynamic instability, elevated intracranial pressure, bleeding diathesis, thrombocytopenia, thrombocyte function disorder, and severe anemia. The main indication was the presence of severe refractory hypoxemia despite maximum mechanical ventilator support, with respiratory or systemic deterioration under minimal invasive mechanical ventilation (plateau pressure (Pplat)<28 cmH_20, Driving pressure <15 cmH_20). The maximum ventilatory settings were peak pressure (Ppeak>40 cm H_2O, the fraction of inspired oxygen (FiO2) 1, oxygen saturation <80%, respiratory rate ≥36/min, and pressure regulating volume control mode.

2.1. Bronchoscopy Procedure

The standard fiberoptic bronchoscope used for diagnosis and treatment in the ICU is Pentax FB-18V (Pentax Co.: Medical Inst. Division, Japan). The procedures are carried out in supine position, under normal intravenous sedation (Propofol %2 by Fresenius, 1mg/kg/dose) with neuromuscular blocking agents (Rocuronium by Polifarma, 0,5 mg/kg/dose), in pressure regulated volume control (PRVC) mode, and using the minimum number of staff required. Before the procedure, saline, mucolytic drugs, the materials for microbiologic sampling, and all the necessary equipment were prepared outside the patient's room. A negative pressure room was not always available due to the increased demands for intensive care. The staff were protected with the best personal protective equipment recommended for use during bronchoscopy, including N95 or FFP3 masks, goggles, and disposable medical protective uniforms with two layers in the head and neck (7). In COVID-19 patients the inner aspect of the bronchoscope was cleaned with enzymatic detergent and 70% alcohol, the outside was cleaned with antiseptic wipes and attached to the screen.

2.2. Statistical Analysis

The data were analyzed with the SPSS 25.0 software (SPSS Inc., Chicago, IL). Demographic characteristics of the patients were analyzed with the descriptive statistics methods. Normality analysis was made with different methods including histogram, kurtosis and skewness test. Parametric paired t test was used in the analysis of pre procedure and post procedure respiratory parameters. $P<0.05$ was accepted statistically significant.

3. Results

During the study period, 45 of the 495 patients admitted to the ICU underwent emergency bronchoscopy for the indications stated in the methods section. Mean age of the patients (23 males and 22 females) who required emergency bronchoscopy was 53. The patients had comorbidities with chronic diseases; 14 (40%) had hypertension, 8 (27%) had diabetes, 5 (33%) had obesity, 4 had chronic renal failure (CRF), 2 had cancer, and 3 had COPD (chronic obstructive pulmonary disease). All procedures were carried out for the removal of mucous plugs in patients receiving mechanical ventilation. Atelectasis was detected in 4% of the patients who developed sudden worsening in hypoxemia. The results are summarized in the Table 1. During the bronchoscopy examination, the position of the orotracheal tube was checked, the tracheal and bronchial mucosas were assessed, the secretions were removed with airway irrigation. There were no complications related to the bronchoscopy. None of the staff who joined the procedure developed a COVID-19 positivity within the first 3 months following the procedure.

Table 1. Changes in respiratory parameters before and after bronchoscopy were statistically meaningful. p-value ≤ 0.05 "statistically significant"

	Before Bronchoscopy	After Bronchoscopy	P value
pH	7.17	7.39	<0.05
PCO_2	80.39	43.15	<0.05
PO_2/FiO_2	53.15	124.71	<0.05
P_{PEAK}	63.97	28.02	<0.05

Among 45 patients who developed sudden deterioration in the respiratory mechanics and worsening of hypoxemia, 43 were noted to have mucous plugs in the carina. The plugs were removed successfully.

Due to the difficulty in attaining peak pressure ventilation, pressure alarm thresholds were exceeded. The values prior to bronchoscopy were: PO2 112-125 mmHg, Ppeak 30 +/- 5 cmH_2O, and pCO2 36 +/- 6. When an indication for bronchoscopy emerged, the mean values were as follows: $P0_2$ 40-55 mmHg, Ppeak 65+/-15 cmH_2O, PCO_2 90+/-12 mmHg.

In our study, the reasons for performing an emergency bronchoscopy were near total occlusion of the airway by a

mucous plug, difficulties in ventilating the patient, and failure to extract the plug. Assessment of arterial blood gases before and after FOB showed significant improvements in PO_2, PCO_2, SpO_2 levels. Mean values are given in Table 1.

The bronchial mucosa was hyperemic in bronchoscopies. Most of the patients had very thick, dry plugs that were hard to aspirate, resembling limestones. In 45 cases, muco-hematic plugs that occluded the main or lobar bronchi were seen and they were extracted after instilling saline and mucolytic substance. The mucous plugs appeared to be trapped in the tube, the endotracheal tubes were clogging rapidly and required renewal more frequently than normal.

4. Discussion

In this study we report on our experience with emergency bronchoscopy on 45 among 395 patients who had laboratory confirmed COVID-19 infections and acute respiratory failure, and who were admitted to the ICU and received invasive mechanical ventilation. Patients who experienced acute respiratory deterioration during ICU stay for Covid 19 pneumonia significantly recovered from acute respiratory distress, and none of the health care workers were infected with virus.

Can age, presence of comorbid diseases, or a delay in hospital referral be factors in patients who are admitted to the hospital with acute respiratory failure which is present at admission or which develops later, and who have deterioration in the overall status? The answer to this question remains unclear because the natural course of COVID-19 is still not fully understood (8).

It has been shown that COVID-19 related ARDS is different from the typical ARDS (9, 10). The most important aspect of the former is preservation of respiratory parameters despite severe hypoxemia (11). While the disease itself causes severe hypoxemia, we showed that in patients who have improvements in inflammatory parameters and oxygenation a response to FOB could be attained after extraction of mucous plugs by emergency bronchoscopy, performed due to acute deterioration in oxygen status. Because it is regarded necessary and urgent due to the severity of the clinical condition, the difficulty of performing bronchoscopy during COVID-19 period is emphasized (Fig. 1).

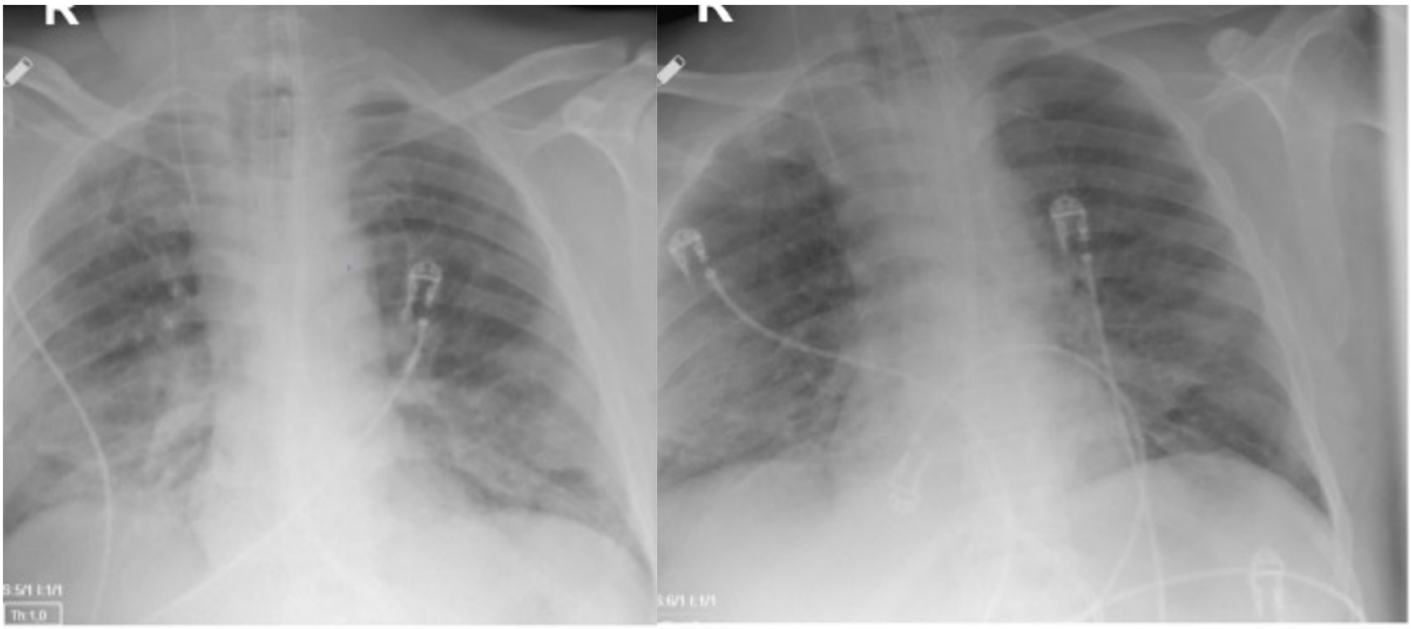

Fig. 1. On the left side is the patient's X-Ray before bronchoscopy, and on the right side is the X-Ray after bronchoscopy. Although fibrinous plug made clinical changes on respiration, the X-ray did not show these changes

The high contagiousity of the SARS-CoV-2 virus, the long incubation period, and possibility of asymptomatic infection has led to numerous deaths. There has been a great concern for the safety of healthcare workers who are especially under risk of contracting the SARS-CoV-2.

The first transmission to healthcare workers was reported in January 2020, and the first COVID-19 related death was of an ear nose throat specialist in Wuhan city, China (12). The airways of people infected with COVID-19 were seen to contain a high viral load (13). Any intervention on the airways will aerosolize the virus, which significantly increases the risk of infection in healthcare workers. Regarding the safety of healthcare workers, those who attended the bronchoscopies did not show any COVID-19 symptoms during a 3-month observation period, which suggested that protective equipments were adequately safe. Performing these procedures with protective equipment is cumbersome, with sweating, mucosal dryness, and extra fatigue. Putting the protective equipment on and off is time consuming and adds to workload (14). Despite all these difficulties, the infection risk is reduced by safety precautions.

Although the Association of Bronchology recommends

single use of bronchoscopes, due to the difficulties in the supply of materials and high costs we used the available bronchoscope on only COVID-19 patients, complying with the disinfection recommendations (4).

The most striking finding in the bronchoscopies of COVID-19 patients was the presence of thick secretions in many cases (23%), which were hard to aspirate and which formed real endobronchial molds (4, 5). As the authors stated, the high rates of mucous plugs in critically ill COVID-19 patients may be explained by the limitation of aerosolization and humidification treatments in compliance with current recommendations (6). The management of these thick mucous plugs required maneuvers that significantly prolonged the procedure times, which were around 45-60 minutes even in the hands of experienced bronchopists.

Although scientific societies recommend limiting the aerosolization and humidification treatments due to air spread risk of the coronavirus, a decision was made to initiate active humidification in all patients receiving mechanical ventilation in order to minimize the presence of these mucous plugs. Although the management of bronchial secretions in these patients continue to be the main indication for bronchoscopy, the secretions became thinner and easier to aspirate. Thus, the bronchoscopy time decreased significantly to approximately 10-20 minutes.

Most of international pulmonology societies do not recommend therapeutic bronchoscopy except in selected patients such as those with hemorrhage or lung atelectasis. On the other hand, our study showed that radiologic changes may lack the sensitivity for the detection of prominent mucous plugs and atelectasis may be missed. It is likely that at least a fraction of the ground glass appearances observed in COVID-19 patients represent, whether a segmental atelectasis is present or not, congestion of the alveolar spaces with mucus and a possibly worse outcome.

A study by Torrego et al. confirmed the presence of mucus during bronchoscopy in the airways of 95% of 101 COVID-19 patients with mean ventilation period of 6.6 days (6). Importantly, Earhart et al. showed that mucolytic dornase alfa improved the results and shortened the ventilation times in COVID-19 patients (15). A randomized clinical study in COVID-19 patients receiving oral mucolytic bromhexine showed that the benefits of bromhexine were maximized when the drug was initiated early. It also decreased the respiratory symptoms, requirements for intubation and intensive care unit hospitalizations, times for mechanical ventilation, and mortality (16).

Although our paper has the advantage of reporting on the experience from a large number of cases, it has also limitations. The first is the nature of our study. Due to long work hours our data were collected retrospectively and evaluated prospectively. The indication for bronchoscopy procedure was based primarily on the first author's experience which depended on the previous ICU and bronchoscopy practices. Bronchoscopy procedures were performed for additional support to the patients, with the author's decision contrary to the recommendations in the guidelines. The number of patients who underwent bronchoscopy in ICU seems to be low but when compared with the previous studies, however it is important to underline the ICU set up and single center single physician experience.

In conclusion, Removal of mucous plugs may be lifesaving, and may decrease ventilator days or even mortality. In the absence of X ray findings, causes of acute respiratory deterioration in COVID-19 patients can be investigated and managed with bronchoscopy.

In this study we showed that during the treatment of COVID-19 patients who have persistent hypoxemia, when an acute worsening in respiratory parameters occurs, mucous plugs should come into mind before a clinical deterioration is considered. The treatment of airway obstruction by removal of mucous plugs using the FFB may be lifesaving and improve acute respiratory deterioration. It has been shown that when personal protective equipment is used, FFB is a reliable and safe method that assists the treatment of COVID-19 patients.

Ethical Statement

All procedures performed in studies including human participants were according to the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study protocol was approved by the Clinical Research Ethics Committee of Istanbul Kanuni Training and Research Hospital (Date: 03.2022, No: KAEK 2022/03/65).

Conflict of interest

The authors declare that they have no competing interests.

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None to declare.

Authors' contributions

Concept: E.K., Ö.K., A.S.Ş., Design: E.K., Ö.K., A.S.Ş., Data Collection or Processing: E.K., S.D., Analysis or Interpretation E.K., Ö.K., Literature Search: A.S.Ş., Writing: A.S.Ş.

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