







# The Safety of Fiberoptic Bronchoscopy in Airway Pressure Release Ventilation Mode in Critically Ill Patients with Severe Acute Respiratory Distress Syndrome: A Preliminary Study

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## Abstract

**OBJECTIVE:** The most appropriate ventilatory mode during fiberoptic bronchoscopy is still not yet known clearly for patients with acute respiratory distress syndrome. Airway pressure release ventilation is used as a recovery treatment for patients with severe acute respiratory distress syndrome. In this study, the aim was to evaluate the safety of the fiberoptic bronchoscopy process in patients with severe acute respiratory distress syndrome ventilated with airway pressure release ventilation mode and its effect on gas exchange and respiratory mechanics.

**MATERIAL AND METHODS:** Single-center retrospective observational study was performed in the intensive care unit of a tertiary referral center from September 2018 to November 2019. Patients with severe ARDS ventilated with APRV mode and undergoing FB were included. Fiberoptic bronchoscopy was performed by an expert intensivist-pulmonologist. All ventilator parameters set by the clinician were kept stable, and no change was made other than O<sub>2</sub> concentration. The mechanical ventilation parameters and arterial blood gas values before and after the procedure and fiberoptic bronchoscopy-related complications were recorded for the first 24 hours.

**RESULTS:** A total of 14 acute respiratory distress syndrome patients who were ventilated with airway pressure release ventilation were enrolled. No significant deteriorations were detected in gas exchange, pulmonary compliance, and airway resistance values in our case series. It was observed that a small reduction in PaO<sub>2</sub> and an increase in PaCO<sub>2</sub> were present after the 1st hour; however, both were returned to baseline values in the 24th hour. Only 1 patient developed fiberoptic bronchoscopy-induced hypoxemia (7.1%). Complications, such as fiberoptic bronchoscopy-induced barotrauma, pneumothorax, hemodynamic deterioration, and bleeding, were not detected.

**CONCLUSION:** According to our preliminary findings, performing fiberoptic bronchoscopy under airway pressure release ventilation mode by an experienced bronchoscopist does not bring additional complication risks in patients with severe acute respiratory distress syndrome.

**KEYWORDS:** Acute respiratory distress syndrome, airway pressure release ventilation, fiberoptic bronchoscopy, pulmonary mechanics

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## INTRODUCTION

Acute respiratory distress syndrome (ARDS) is an important clinical manifestation progressing with refractory hypoxemia and can cause multiple organ failure and mortality.<sup>1</sup> Airway pressure release ventilation (APRV) is used as a novel supportive treatment for acute hypoxemic respiratory failure and in patients with ARDS, especially when conventional mechanical ventilation modes do not provide adequate oxygenation.<sup>2</sup> It was shown that using APRV mode in patients with ARDS could affect ventilation/perfusion balance positively by providing alveolar recruitment, improve oxygenation, and result in reduced ventilator need and length of stay in intensive care.<sup>3</sup>

Fiberoptic bronchoscopy (FB) is a technique that is often used both for diagnostic and therapeutic purposes in the intensive care unit (ICU). The bedside applicability and low complication rates are major advantages. It is well known that severe hypoxemia is an important complication of FB, still, FB may be an indispensable tool for diagnostic purposes in selected ARDS patients with refractory hypoxemia.<sup>4</sup> The most appropriate ventilation method during FB is still unknown in this subgroup of patients.

Airway pressure release ventilation mode is frequently applied to patients with ARDS and deep hypoxemia in our center. In this case series study, our purpose was to evaluate the safety of the FB process in patients with severe ARDS who were ventilated in APRV mode and its effect on gas exchange and respiratory mechanics.

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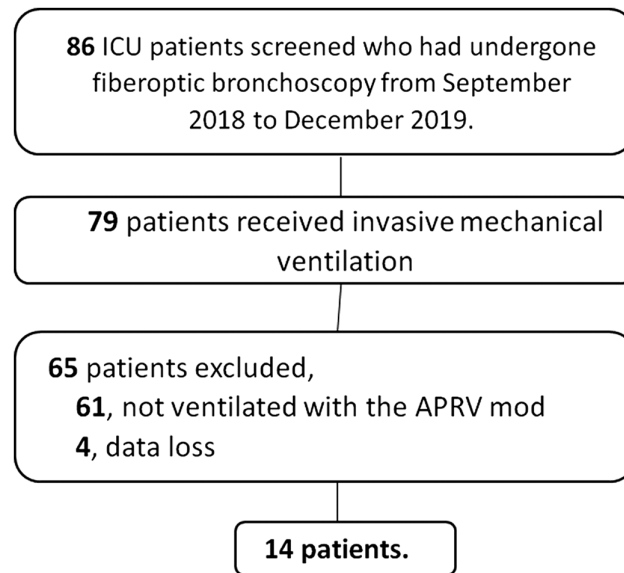


Figure 1. Flowchart of study.

## MATERIAL AND METHODS

### Patients

The study was a case series study. The data were withdrawn from the ICU-FB database, in which the data were collected prospectively since 2017. Patients with severe ARDS who were ventilated in APRV mode between September 2018 and December 2019 and underwent FB were included in the study (Figure 1). This retrospective study was performed in an adult ICU after Dokuz Eylül University ethics committee approval (No:2020/06-29). The informed consent was waived because of the nature of the study.

### Variables

The demographic data of patients, acute physiology and chronic health evaluation (APACHE) II scores, FB indication, previous and ongoing treatments (i.e. vasopressor/sedation) treatment, renal replacement therapy, immunosuppressive treatment) were recorded. All patients were ventilated with Dräger Evita® Infinity® V500.

The mechanical ventilation parameters before sedation application were recorded as tidal volume ( $V_T$ ), fraction of inspired oxygen ( $FiO_2$ ), high airway pressure ( $P_{high}$ ) and the time spent at this pressure ( $T_{high}$ ), low air pressure ( $P_{low}$ ) and the time spent at this pressure ( $T_{low}$ ), mean airway pressure ( $P_{mean}$ ), and peak airway pressure ( $P_{peak}$ ).  $P_{low}$  was used as 0 cm  $H_2O$  and  $T_{low}$  0.5 seconds in all patients. Pre-sedation pulmonary mechanics (i.e., compliance and resistance), arterial blood gas values for pH, partial pressure of oxygen ( $PaO_2$ ), partial pressure of carbon dioxide ( $PaCO_2$ ), oxygen saturation ( $SaO_2$ ), and ratio of  $PaO_2$  to  $FiO_2$  were also recorded.

### Fiberoptic Bronchoscopy Procedure

#### Indication of FB

Indication and the decision for FB were primarily determined by consulting intensivist. All procedures were performed by an intensivist-pulmonologist who had expertise >15 years of performing FB in critically ill patients. According to the local ICU FB protocol, severe hemodynamic instability was considered a contraindication to performing FB.

#### Sedation for FB

The ICU sedation protocol included midazolam and fentanyl infusions for FB procedure. Rocuronium was used as needed for muscle relaxation during the procedure.

#### Fiberoptic bronchoscopy Procedure

After it was confirmed that the endotracheal tubes (ETT) were at least 8.0 mm in diameter, the bronchoscope (5.9-mm outer-diameter Olympus BF 10 bronchoscope) was placed in the ETT with a special adapter valve. At least 5 min before the procedure,  $FiO_2$  was set at 0.9-1.0 and was kept in this setting throughout the procedure. All ventilator parameters set by the consulting intensivist were kept stable, and the inhaled and exhaled tidal volumes and vital findings during the procedure were monitored and recorded closely. The duration of FB and the amount of fluid given and recovered for bronchial lavage and bronchoalveolar lavage (BAL) were noted. Inspired oxygen fraction was decreased gradually to >90% peripheral (pulse) oxygen saturation ( $SpO_2$ ) after FB. After FB procedure,

### MAIN POINTS

- Fiberoptic bronchoscopy (FB) is a technique that is often used both for diagnostic and therapeutic purposes in the intensive care unit.
- Acute respiratory distress syndrome (ARDS) is an important clinical manifestation progressing with refractory hypoxemia and can cause multiple organ failure and mortality.
- Airway pressure release ventilation (APRV) mode is frequently applied to patients with ARDS and deep hypoxemia.
- The most appropriate ventilatory mode during FB is still not yet known clearly for patients with ARDS.
- Performing fiberoptic bronchoscopy in APRV mode by an experienced bronchoscopist does not bring additional complication risks.

and at 1st and 24th hours, patients' vital signs (i.e., peak heart rate, blood pressure, and body temperature), arterial blood gas values, mechanical ventilator parameters, pulmonary mechanics, and PaO<sub>2</sub>/FiO<sub>2</sub> values were recorded. Possible complications in the first 24 h after FB, such as FB-related desaturation (SpO<sub>2</sub> < 90), hemodynamic deterioration, barotrauma-related complications, such as pneumothorax and/or pneumomediastinum, and bleeding, were recorded.

### Statistical Analysis

All categorical variables are expressed as numbers and percentages, and continuous variables were expressed as median and interquartile range (IQR). Categorical variables between groups were compared with chi-square or Fisher's exact test, and continuous variables were compared with Mann-Whitney U-test. A two-tailed *P* value of .05 was considered statistically significant. Statistical analysis was performed with Statistical Package for the Social Sciences (Version 22; IBM Corporation, Armonk, NY, USA) program.

## RESULTS

A total of 14 patients (10 males, 4 females) with severe ARDS were included in the study. Median (IQR) age was 62.5 (43.5-69.7) years, and median (IQR) APACHE II score was 21 (15.7-26.2). Fiberoptic bronchoscopy indication was mainly for sampling of the respiratory tract in order to evaluate/exclude any respiratory infection in 12 patients (85.7%) and suspicion of interstitial lung disease in 2 patients (14.3%). Eight patients (57.1%) had active immunosuppression. Six patients (42.8%) to exclude any opportunistic infection. Five patients (35.7%) were receiving vasopressor agent (nor-adrenaline) due to the presence of refractory septic shock while performing FB (Table 1). The duration of FB was 8 (IQR 6-10) minutes. An average of 100 mL (IQR 50-105 mL) saline fluid was given in BAL process, and 50 mL (IQR 30-60 mL) was recovered.

### Gas Exchange

In the arterial blood gas analysis, it was observed that a small reduction in PaO<sub>2</sub> and an increase in PaCO<sub>2</sub> were present after the 1st hour; however, both were returned to baseline values in the 24th hour (Table 2). Partial pressure of oxygen was below 60 mmHg (57 mmHg and 59 mmHg) in 2 patients at the 1st hour after the procedure and was below 60 mmHg (53 mmHg) in 1 patient at the 24th hour. The changes in SaO<sub>2</sub> were similar to those in PaO<sub>2</sub>. The median value of PaO<sub>2</sub>/FiO<sub>2</sub> rate was below the baseline at the 1st hour after the procedure and was above the basal value at the 24th hour. Clinically nonsignificant changes were observed in pH secondary to PaCO<sub>2</sub> levels.

### Settings and Lung Mechanics

Although P<sub>high</sub> and T<sub>high</sub> changes were made in line with the changes in oxygenation and ventilation parameters in patients, no changes were detected according to the basal values of the median P<sub>high</sub> and T<sub>high</sub> values after the procedure, and no significant changes were detected in P<sub>mean</sub> and P<sub>peak</sub> median values. The median tidal volume remained below the basal value after the procedure, and the values were determined above the basal value at the 1st and 24th hours. There were decreases in the median compliance values just after

the procedure, and they were similar to basal values at the 1st and 24th hours. No significant changes were detected in post-procedure resistance values (Table 3).

### Complications

The procedure was terminated early only in 1 patient (7.1%) because of desaturation. Hypoxemia (SpO<sub>2</sub> < 90%) developed in 1 patient after FB (7.1%), and hypotension developed in 1 patient, which caused an increase in vasopressor requirement within the first 24 h. No new onset arrhythmias were detected. None of the patients developed pneumothorax/pneumomediastinum and bleeding complications in the 24-h follow-ups.

### Results of Bronchoalveolar Lavage Specimen

The culture results of BAL revealed *Stenotrophomonas maltophilia* in 4 patients, *Acinetobacter baumannii* in 3 patients, *Klebsiella pneumoniae* in 2 patients, *Candida parapsilosis*

**Table 1.** Baseline Characteristics of the Study Patients

Variables	Patients (n = 14)
Age	63 (40-71)
Male sex	10 (71.4)
APACHE II score	21 (16-26)
SOFA <sup>1</sup> score	6 (5-7)
GCS score	10 (7-13)
Main reason for ICU admission	
Sepsis/septic shock	5 (35.7)
Pneumonia	9 (64.3)
Comorbidities	
Hypertension	6 (42.9)
Rheumatoid arthritis	1 (7.1)
Coronary artery disease	3 (21.4)
Diabetes mellitus	3 (21.4)
Malignancy	3 (21.4)
Chronic renal disease	1 (7.1)
Common variable immunodeficiency	1 (7.1)
Renal transplantation	1 (7.1)
Dermatomyositis	1 (7.1)
Liver transplantation	1 (7.1)
Indications for FB	
Respiratory infection	12 (85.7)
Suspicion of interstitial lung disease	2 (14.3)
Event on FB day	
Vasopressor need <sup>2</sup>	5 (35.7)
Hemodialysis	5 (35.7)
ICU mortality	10 (71.4)

All values are expressed as numbers (percentages) or median (interquartile range).

APACHE, Acute Physiology and Chronic Health Evaluation;

FB, fiberoptic bronchoscopy; GCS, Glasgow Coma Scale;

ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment.

<sup>1</sup>SOFA score in the first day

<sup>2</sup>Norepinephrine > 0.15 µg/kg/min.

**Table 2.** Arterial Blood Gas Values (n = 14)

	Baseline (Before FB)	Immediate After the FB Procedure	After the FB Procedure (1st Hour)	After the FB Procedure (24th Hour)
pH	7.33 (7.27-7.42)	7.28 (7.21-7.37)	7.34 (7.20-7.38)	7.31 (7.26-7.37)
PaO <sub>2</sub> (mmHg)	83.0 (68.2-100.5)	119.5 (85.0-194.2)	76.5 (68.7-90.5)	84.0 (73.5-107)
PaCO <sub>2</sub> (mmHg)	45.5 (40.7-49.0)	48.5 (46.0-52.0)	44.5 (41.0-53.5)	46.5 (37.7-50.2)
SaO <sub>2</sub> (%)	96.0 (92.5-97.2)	98.0 (95.7-99.0)	94.5 (92.0-96.2)	95.5 (92.0-97.2)

Data are presented as median and interquartile range (IQR). Abbreviations: FB, fiberoptic bronchoscopy; PaO<sub>2</sub>, partial pressure of oxygen; PaCO<sub>2</sub>, partial pressure of carbon dioxide; SaO<sub>2</sub>, oxygen saturation.

in 1 patient, and *Candida albicans* in 1 patient. Revision of antibiotic/antimicrobial therapy was made in 7 patients (50%) after FB results.

**Intensive Care Unit Mortality**

Ten patients died (71.4%). Among 4 who survived, 2 received revised antibiotic/antimicrobial regimen after FB.

**DISCUSSION**

In the present case series, we have analyzed patients with severe ARDS who have undergone FB procedure with APRV mode. The study has 2 important results. First, FB with APRV mode seemed to be safe with no major complications. Second, although these patients were very fragile and considered to be prone to desaturations with FB, it was observed that pulmonary gas exchange and respiratory mechanics did not change.

In the present study, FB-related hypoxemia is 7.1% in patients with severe ARDS. FB in severely hypoxemic patients under high FiO<sub>2</sub> support and/or high PEEP is considered as a relatively high-risk procedure and must be avoided as much as possible.<sup>4</sup> Fiberoptic bronchoscopy-related gas exchange abnormalities may occur in

almost all critical patients at different degrees. Patients with ARDS may have increased complication risks during FB and BAL because of insufficient oxygenation and unstable hemodynamics.<sup>5</sup> Prebil et al<sup>6</sup> evaluated the side effects of FB and BAL procedures in 100 patients who were followed up in intubation mechanical ventilator because of ARDS or severe sepsis. Clinically significant hypoxemia (SaO<sub>2</sub> < 90%) was detected in 6% of the patients, and early termination of the procedure was required in 1 patient. High PEEP requirement was associated with increased complication rates. This is similar to the results of Schnabel et al. hypoxemia (SaO<sub>2</sub> < 88%) with FB was detected in 9% of the patients in patients with mechanical ventilator support, and the mean PaO<sub>2</sub>/FiO<sub>2</sub> values after the 24th hour were similar to the baseline values.<sup>7</sup> Although transient hypoxemia was reported in FB patients with deep hypoxemia and high PEEP requirement, we have found that no significant deteriorations were observed in gas exchange within the 24 h. Median PaO<sub>2</sub> and SaO<sub>2</sub> were detected to be higher than the basal values after the procedure, which may be explained by the increase in FiO<sub>2</sub> during the process and perhaps with the correction of atelectatic segments by aspiration of airway secretions.

**Table 3.** Mechanical Ventilation Parameters (n = 14)

	Baseline (Before FB)	Immediate After the FB Procedure	After the FB Procedure (1st Hour)	After the FB Procedure (24th Hour)
FiO <sub>2</sub>	0.6 (0.5-0.6)	1.0 (0.9-1.0)	0.6 (0.5-0.6)	0.5 (0.5-0.6)
Tidal volume (mL)	530 (477-585)	519 (443-562)	562 (457-600)	541 (450-609)
PaO <sub>2</sub> /FiO <sub>2</sub>	142 (119-221)	130 (88-220)	134 (118-165)	154 (132-220)
P <sub>high</sub> (cm H <sub>2</sub> O)	28 (24.7-28.2)	28 (24.7-28.5)	28 (25-28.5)	28 (24.7-28.2)
P <sub>low</sub> (cm H <sub>2</sub> O)	0	0	0	0
T <sub>high</sub> (seconds)	4.5 (4.5-5.5)	4.5 (4.5-5.5)	4.5 (4.5-5.5)	4.5 (4.5-5.5)
T <sub>low</sub> (seconds)	0.5	0.5	0.5	0.5
P <sub>mean</sub> (cm H <sub>2</sub> O)	25.2 (22.4-25.4)	25.2 (22-25.2)	25.2 (22.9-25.6)	25.2 (22.3-25.7)
P <sub>peak</sub> (cm H <sub>2</sub> O)	28.5 (25-30)	28.5 (25.7-30.2)	28.5 (26.0-30.3)	29.0 (26.0-30.0)
Compliance (mL/cm H <sub>2</sub> O)	29 (23-35)	27 (21.7-31.2)	30.5 (22.2-34.7)	30 (21.5-40.5)
Resistance (cm H <sub>2</sub> O/L/s)	12 (8.7-14.5)	12 (9.7-14)	12 (9.7-13.2)	10.5 (8.7-12.2)

Data are presented as absolute numbers or as median and interquartile range (IQR). FB, fiberoptic bronchoscopy; FiO<sub>2</sub>, fraction of inspired oxygen; P<sub>high</sub>, high airway pressure; T<sub>high</sub>, the time spent at high airway pressure; P<sub>low</sub>, low air pressure; T<sub>low</sub>, the time spent at low airway pressure; P<sub>mean</sub>, mean airway pressure; P<sub>peak</sub>, peak airway pressure.



In our center, we prefer using APRV mode to obtain higher mean air pressures in patients with severe ARDS who require high PEEP support. The purpose of APRV use is to increase oxygenation by providing recruitment with auto-PEEP effect. Theoretically, when the bronchoscope is advanced from ETT, it causes a significant increase in airway pressures in this patient group. Peak inspiratory pressure and intrinsic PEEP increase and might cause significant decreases in ventilation per minute,<sup>8,9</sup> which in turn may cause an increased risk of barotrauma pneumothorax and hemodynamic deterioration. However, in our study group, none of these complications was observed. We think that the key factor for this was the expertise of the bronchoscopist as the median duration of FB was relatively short.

Another important factor in patients with ARDS is performing the BAL procedure. Bronchoalveolar lavage can cause decreased lung compliance and increased airway resistance. The mechanism of changes in compliance and resistance is the direct effect of lavage fluid, the development of inflammatory pulmonary edema, surfactant inactivation, and related atelectasis development.<sup>10</sup> In a previous study, pulmonary compliance decreased from 43.3 to 33 mL/cm H<sub>2</sub>O, and pulmonary resistance increased from 15.16 to 17.54 cm H<sub>2</sub>O/L/s in measurements after BAL. Both parameters returned to similar values as before the procedure 90 minutes after application. Postoperative decrease severity was higher in patients who had higher compliance before the procedure.<sup>11</sup> No significant changes were detected in our study in lung compliance and airway resistance of patients after FB and BAL. This might be due to performing BAL with lower amount of fluid (median fluid amount 100 mL), the return of approximately half of the fluid, and the cleaning of the airways as much as possible while finishing the procedure. Decreased surfactant function and lower compliance may be another reason why our study found no changes in lung compliance as a response to BAL in patients with ARDS.<sup>10</sup>

Hypertension, hypotension, and electrocardiographic changes may occur during FB.<sup>4,8</sup> Since arrhythmia is frequently related to oxygen desaturation, an increase may be expected in cardiovascular complication risks in critical patients. In our study, no hemodynamic deterioration that would require the discontinuation of the procedure occurred during FB; however, 1 patient developed severe hypotension after the procedure, which required an increase in vasopressor support in the first 24 h. We think that this may not be attributable only to the FB procedure itself as about one-third of the patients were receiving vasopressor treatment.

There are several important limitations of this study. First, the study was performed in a single reference ICU; therefore, the results are not generalizable. Second, FB is performed by an experienced bronchoscopist, which may be an important factor for low complication rates. Third, we have included only 14 cases with severe ARDS. Also, we did not compare the APRV mode with other modes, such as the assist control ventilation mode in the present study. Thus, the contribution of APRV mode that improves respiratory

mechanics after the FB procedure has a low quality of evidence. On the other hand, we believe that our study has some important strengths. Airway pressure release ventilation mode is a relatively novel approach in severe ARDS, and this is the first study evaluating the safety of APRV mode during the FB procedure. Another important strength was close monitoring of the occurrence of possible complications after FB.

## CONCLUSION

The most appropriate ventilation strategy for FB has not yet been clarified in critically ill patients with severe ARDS. Airway pressure release ventilation is a novel ventilation mode and is being increasingly used for improving oxygenation in severe ARDS. According to our preliminary findings, performing FB in APRV mode by an experienced bronchoscopist does not bring additional complication risks. The optimal ventilatory strategy during FB merits further research.

**Ethics Committee Approval:** This study was approved by Ethics committee of Dokuz Eylül University, (No:2020/06-29).

**Informed Consent:** Informed consent was waived because of the nature of the study.

**Peer-review:** Externally peer-reviewed.

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