Flexible Bronchoscopy Is Safe and Effective in Adult Subjects Supported With Extracorporeal Membrane Oxygenation

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BACKGROUND: Previous studies have demonstrated the safety of flexible bronchoscopy (FB) in mechanically ventilated subjects. However, the safety of FB in adult subjects receiving extracorporeal membrane oxygenation (ECMO) has not been described previously. **METHODS:** A retrospective review was conducted of all adult subjects who underwent FB while receiving ECMO support at the University of Alabama at Birmingham Hospital from January 1, 2013, to December 31, 2014. Physiologic variables, pre- and post-FB ECMO, and ventilator settings were recorded. **RESULTS:** 79 adult subjects underwent FB receiving ECMO with a total of 223 bronchoscopies. The most common indications for bronchoscopy included diagnostic evaluation of infection in subjects with pneumonia (29%) and clearance of excessive secretions (22%). In 70% of subjects, moderate or greater amounts of secretions were noted. FB yielded positive culture data in 37 subjects (47%), which resulted in a change to the antibiotic regimen in 14 subjects (38%) with positive culture data. No significant differences in mean P_{aO_2}/F_{IO_2} , mean ECMO flow, mean sweep gas, ventilator settings, or hemodynamic parameters (heart rate, oxygen saturation, and mean blood pressure) were noted before and after FB. Complications were mild and transient: blood-tinged secretions after FB in 21% cases, which resolved spontaneously, intraprocedural hypoxemia in 2.2% of cases, and dysrhythmia in <1% of cases. There were no episodes of ECMO cannula dislodgement or inadvertent extubation. **CONCLUSIONS:** FB can be used safely in adult subjects supported with ECMO and is not associated with significant hemodynamics changes, bleeding, or mechanical complications during ECMO support. *Key words:* ECMO; bronchoscopy; ARDS; cardio-respiratory failure; veno-venous ECMO; veno-arterial ECMO. [Respir Care 2016;61(5):646–651. © 2016 Daedalus Enterprises]

Introduction

In the past decade, there has been an increase in the utilization of extracorporeal membrane oxygenation (ECMO) to support critically ill patients with cardiopul-

monary failure.^{1,2} ECMO-supported patients often have respiratory infections and increased airway secretions complicating the course of their illness.³ To aid in the diagnosis of respiratory infections and facilitate secretion clearance, flexible bronchoscopy (FB) has become a necessary tool in modern critical care practice.^{4,5} Although FB is a relatively safe procedure in most patients, it can be associated with complications, such as worsening hypoxemia, endotracheal tube (ETT) dislodgement, and airway trauma, in critically ill subjects receiving mechanical ventilation.^{6–12} Additionally, FB may entail a greater risk of complications in ECMO patients due to the use of systemic anticoagulation and greater degree of illness in these patients.^{13,14} Previous studies have demonstrated the safety of FB in subjects receiving mechanical ventilation.^{15,16} However, its safety profile in adult patients supported with ECMO is not well established.

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In this retrospective study, we present our experience with FB in adult subjects supported with ECMO and analyze its safety and utility in this cohort. We hypothesize that FB is a safe and well-tolerated procedure for patients receiving ECMO support.

Methods

Subject Population and Data Collection

We performed a retrospective review of all ECMO subjects who underwent FB for any indication at the University of Alabama Hospital at Birmingham from January 1, 2013, to December 31, 2014. This project was reviewed and approved by the University of Alabama Hospital at Birmingham institutional review board for human research (Protocol X140909006).

Subject Selection

A total of 141 subjects were supported with ECMO for any indication during the period of interest. Of these, 79 subjects underwent a total of 223 FBs.

Outcome Measures

Variables collected before and after bronchoscopy included demographics, FB indication, vital signs, ventilator settings, ECMO settings, chest radiograph changes, and complications. Vital signs and ventilator and ECMO settings recorded immediately before and 2 h after the procedure were utilized for this study. Chest radiograph reports as interpreted by attending radiologists before ECMO and the first after FB were used for analysis.

ECMO Management

At our institution, an internal jugular double-lumen cannula is used for venovenous (VV) support, and a jugulo-femoral route is preferred for venoarterial (VA) ECMO in a majority of patients. Less commonly, a mixed configuration (combination of the above) is utilized, according to the patient's condition and oxygen requirement. Anticoagulation is managed per protocol¹⁷ and monitored using anti-factor Xa and thromboelastography. An anti-factor Xa of 0.2–0.4 IU/ml and R time on thromboelastography of 2.5–3 times the control value are usually maintained. No changes were made to anticoagulation before or after FB. Either a supervised critical care trainee or the attending physician performed FB. In addition, a critical care nurse, respiratory therapist, and perfusionist were also present during the procedure.

QUICK LOOK

Current knowledge

In the past decade, there has been an increased utilization of ECMO to support patients with severe cardio-respiratory failure. Flexible bronchoscopy has become an important tool to diagnose respiratory infections and manage airway secretions in these critically ill patients receiving ECMO. Although the safety of flexible bronchoscopy in mechanically ventilated patients has been well described, its safety and utility have not been established in adult patients supported with ECMO.

What this paper contributes to our knowledge

Flexible bronchoscopy is safe in adult subjects supported with ECMO. Flexible bronchoscopy is not associated with significant hemodynamics changes, bleeding, and/or mechanical complications during ECMO support. Flexible bronchoscopy during ECMO support facilitates pulmonary secretion clearance and improves antibiotic selection in subjects with respiratory infections.

Flexible Bronchoscopy

At our institution, FB is performed via the ETT, tracheostomy, or the oral route (in extubated patients) while the patient is receiving ECMO support. The ventilator F_{IO_2} is transiently increased to 100% for the duration of the procedure and lowered back to baseline as tolerated after the procedure. Bronchoalveolar lavage (BAL) is performed if indicated. Both therapeutic (distal tip 5.9 mm, insertion tube diameter of 6.0 mm, working channel of 3.0 mm) and diagnostic bronchoscopes (distal tip 4.8 mm, insertion tube diameter of 4.9 mm, working channel of 2.0 mm) are used for FB in ECMO patients based on the clinical indications. In patients receiving mechanical ventilation, usually an ETT and tracheostomy tube size ≥ 8 mm in diameter is preferred for performing FB. Before FB, patients are premedicated with sedative agents, such as fentanyl, midazolam, or propofol, as clinically determined by the physician. Occasionally, in patients with recent lung transplants who are receiving ECMO, sedation-free awake bronchoscopy is performed. Lidocaine is atomized or nebulized via the ETT/tracheostomy before scope insertion. Most FBs are performed in the recumbent or semirecumbent position. Mean duration of FB is usually 5–15 min, depending on the indication of FB, need for BAL, and amount of secretions present. Although the average time period for each bronchoscope insertion is 60–90 s, this may be increased to 2–5 min if BAL is being performed. Culture specimens

are obtained from bronchial washes, BAL (100 mL of sterile saline is used in 4 sequential aliquots of 25 mL each) or sometimes using a protected specimen brush. Although most of our patients are supported with the pressure control continuous mandatory ventilation mode during ECMO support, we have not found it to be superior (in terms of reduced complication rates) compared with other modes of ventilation during FB.

Statistical Analysis

We performed descriptive analyses of measured variables using proportions, means $\pm$ SD, or medians with interquartile ranges as appropriate. Changes in parameters before and after FB were compared using an unpaired 2-way *t* test or Mann-Whitney test. A *P* value of $<.05$ was considered significant. Statistical analyses were performed with JMP 10.0 (SAS Institute, Cary, North Carolina).

Results

Baseline Characteristics

Of 141 patients supported with ECMO during the study period, 79 underwent FB and were included in the analysis. A total of 223 FB procedures were performed: 76 (34.1%) of subjects underwent one FB, 48 (21.4%) had 2 FBs, 34 (15.1%) had 3 FBs, and 65 (29.4%) had ≥ 4 procedures. Indications for ECMO support and use of FB are detailed in Table 1. Clearance of excessive secretions and identification of pathogens involved in pneumonia were the most common indications for FB. Median age was 46 y (range 19–83 y). A majority of subjects (59%) were male. Most subjects (71%) were supported using VV ECMO, whereas 23% were supported by VA ECMO and 6% by a mixed ECMO configuration. A low tidal volume ventilation strategy was preferred for all subjects. Pressure control continuous mandatory ventilation was the ventilatory mode used in 70% of subjects (Table 2). Whereas a majority of bronchoscopies (56%) were performed via the ETT, 42% were performed via a tracheostomy, and 2% were performed via the oral route. BAL was performed in 34% of the procedures. Mean P_{aO_2}/F_{IO_2} ratio before ECMO initiation was 63 ± 22.1 . Qualitative bronchoscopy findings included no secretions in 4%, mild secretions in 25%, and moderate or greater secretions in 71%.

Bronchoscopy Outcomes

Mean pre-FB P_{aO_2}/F_{IO_2} for all subjects was 164 ± 133 . The pre-FB P_{aO_2}/F_{IO_2} was significantly lower in subjects supported with VV ECMO (149 ± 109) as compared with those supported with VA ECMO (200 ± 156) and mixed ECMO configurations (229 ± 224), *P* = .009. Overall,

Table 1. Indications for Initiation of Extracorporeal Membrane Oxygenation Support and Use of Flexible Bronchoscopy

Indications	Percentage
For ECMO	
Bacterial pneumonia	29
Influenza pneumonia	18
Cardiogenic shock	13
Combined bacterial and viral pneumonia	8
Respiratory failure not otherwise specified	6
Trauma	6
Bridge to transplantation	6
Postoperative complication	6
Other	3
Pulmonary embolus	5
For FB	
Pneumonia	29
Abnormal chest radiograph	20
Excessive secretions	22
Atelectasis	7
Tracheostomy placement	6
Hemoptysis	5
Refractory hypoxemia	4
Diffuse parenchymal disease	4
Airway inspection	2
Dislodged endotracheal tube	1

ECMO = extracorporeal membrane oxygenation
FB = flexible bronchoscopy

Table 2. Mode of Ventilation Used During Extracorporeal Membrane Oxygenation Support

Mode of Ventilation	Percentage of Subjects
PC-CMV	70
VC-CMV	22
PSV	3
PC-IMV	3
VC-IMV	1

1% of subjects were extubated and off mechanical ventilation while on extracorporeal membrane oxygenation support.

PC-CMV = pressure control continuous mandatory ventilation
VC-CMV = volume control continuous mandatory ventilation
PC-IMV = pressure control intermittent mandatory ventilation
VC-IMV = volume control intermittent mandatory ventilation
PSV = pressure support ventilation

mean P_{aO_2}/F_{IO_2} did not change significantly after FB (178 ± 163 , *P* = .35) (Table 3).

Mean pre-FB ECMO flow was similar for all ECMO configurations. Overall, no significant change in ECMO flow was noted before versus after FB. However, post-FB ECMO flow was significantly higher in subjects with the mixed configuration (4.3 ± 0.83 L/min) group as compared with the VA (3.74 ± 0.96 L/min) and VV (3.8 ± 0.6 L/min) ECMO groups (*P* = .009). Likewise, baseline

Table 3. Bronchoscopy Outcomes on Extracorporeal Membrane Oxygenation Support

	Pre-FB	2 h Post-FB	P
Mean P_{aO_2}/F_{IO_2}			
Overall	164 ± 133	178 ± 163	.35
VV subjects	149 ± 109	156 ± 118	.54
VA subjects	200 ± 156	203 ± 168	.93
Mixed configuration subjects	229 ± 224	317 ± 343	.36
Mean ECMO flow, L/min			
Overall	3.85 ± 0.69	3.86 ± 0.70	.97
VV subjects	3.84 ± 0.60	3.83 ± 0.60	.93
VA subjects	3.86 ± 0.90	3.74 ± 0.96	.58
Mixed configuration subjects	3.99 ± 0.89	4.3 ± 0.83	.24
Mean ECMO sweep gas flow, L/min			
Overall	4.01 ± 2	4.0 ± 2.05	.97
VV subjects	4.13 ± 1.97	4.11 ± 2.01	.92
VA subjects	2.84 ± 1.62	2.87 ± 1.59	.94
Mixed configuration subjects	5.4 ± 1.99	5.4 ± 2.2	.94
Mean ventilator F_{IO_2}	0.68 ± 0.23	0.64 ± 0.22	.09
Mean PEEP, cm H_2O	9.5 ± 3.1	9.4 ± 4.16	.53
Mean peak pressure, cm H_2O	33.2 ± 7.65	32.3 ± 7.65	.25
Mean arterial pressure, mm Hg	84 ± 13	82 ± 11	.14
Mean heart rate, beats/min	97 ± 19	96 ± 20	.81
Mean oxygen saturation, %	95 ± 5	99 ± 6	.29

Data are reported as means ± SD.

FB = flexible bronchoscopy

VV = venovenous extracorporeal membrane oxygenation

VA = venoarterial extracorporeal membrane oxygenation

ECMO = extracorporeal membrane oxygenation

pre-FB sweep gas flow was higher in the mixed configuration group (5.4 ± 1.9 L/min) as compared with the VA (2.8 ± 1.6 L/min) and VV (4.1 ± 1.9 L/min) ($P < .001$) ECMO groups. Again, no significant differences were observed between the pre- and post-FB sweep gas rates (see Table 3). Ventilator changes before and after FB were also evaluated. Overall, no significant differences in mean F_{IO_2} (0.68 ± 0.23 vs 0.64 ± 0.22 , $P = .09$), PEEP (9.5 ± 3.1 cm H_2O vs 9.4 ± 4.16 cm H_2O , $P = .53$), and peak airway pressures (33.2 ± 7.65 cm H_2O vs 32.3 ± 7.65 cm H_2O , $P = .25$) were noted before and after the FB. Additionally, no significant variations were observed in the pre- and post-FB vital signs, including mean blood pressure, heart rate, and oxygen saturation (see Table 3). These results did not differ when compared by the type of ECMO configuration. FB (BAL and bronchial washings) yielded positive culture data (yeast was excluded) in 37 subjects (47%), which resulted in a change to the antibiotic regimen in 14 subjects (38%) with positive culture data (Table 4).

Complications

Chest radiographs before and after the procedures were compared: 63.2% remained unchanged, 22.2% showed im-

Table 4. Flexible Bronchoscopy Culture Data

Pathogen	Percentage
<i>Pseudomonas</i>	24
<i>Enterobacter</i>	12
<i>Klebsiella</i>	12
<i>Serratia</i>	10
Methicillin-resistant <i>Staphylococcus aureus</i>	10
<i>Acinetobacter</i>	7
<i>Aspergillus</i>	7
Influenza A	5
<i>Streptococcus pneumoniae</i>	2
β hemolytic streptococci	2
Vancomycin-resistant enterococcus	2
<i>Achromobacter</i>	2
Methicillin-sensitive <i>S. aureus</i>	2

provement in opacities, and 14.6% showed worsening of opacities. In addition, 4 cases of new pneumothorax and 5 cases of worsening of existing pneumothorax were noticed on the radiograph following the procedure. Of the 4 new cases of pneumothorax, one occurred after internal jugular double-lumen cannula placement that preceded the FB, 2 were after FB-guided percutaneous tracheostomy, and one was after thoracentesis before FB. In these cases, the chest radiographs were performed after FB; it is unclear whether pneumothorax was precipitated by FB or due to the preceding procedures. Given that the risk of pneumothorax associated with percutaneous tracheostomy (0.5–12.5%),¹⁸ thoracentesis (4.6–7.8%),¹⁹ and internal jugular double-lumen cannula placement (5–19%)²⁰ is higher than the risk with FB without a trans-bronchial biopsy (<1%),²¹ it is possible that the pneumothorax was not a consequence of FB. The presence of preexisting pneumothorax before FB was known in 7 cases. Of these, 5 cases had worsening of existing pneumothorax, and 3 occurred in subjects who underwent BAL. All subjects with known pneumothorax before FB had preexisting small (8.5 French) or medium bore (14 French) chest tube catheters in place before FB. The intraprocedural adverse event rate was low; 96% of the FBs had no immediate procedural complication. Five subjects had hypoxia during the procedure. Of these, persistent hypoxia (oxygen desaturation to 60% on pulse oximetry) occurred in one case, requiring abortion of the procedure. Two subjects had moderate hypoxia (70 and 74%, respectively, on pulse oximetry), and another 2 had mild hypoxia (82 and 86%, respectively, on pulse oximetry). All of these 4 episodes of hypoxia improved with transient withdrawal of the bronchoscope. Whereas 2 subjects had transient arrhythmias (one bradycardia and one atrial fibrillation), another 2 had reduction in ECMO blood flow due to excessive coughing during the procedure. All of the above events resolved immediately after withdrawal of the bronchoscope. Blood-tinged secretions were noted

Table 5. Extracorporeal Membrane Oxygenation Outcomes

	ICU Survival in Subjects Receiving ECMO Who Underwent FB (%)	ICU Survival in Subjects on ECMO Who Did Not Undergo FB (%)
Overall	75	65
VV subjects	73	76
VA subjects	72	60
Mixed configuration	100	67

ECMO = extracorporeal membrane oxygenation
 FB = flexible bronchoscopy
 VV = venovenous extracorporeal membrane oxygenation
 VA = venoarterial extracorporeal membrane oxygenation

in 21% of the FBs. Moderate bleeding requiring cold saline instillation occurred in one FB, and minor bleeding requiring no intervention occurred in 4 procedures.

ECMO Outcomes

The overall ICU survival in our cohort of ECMO subjects who underwent FB was 75%. Subjects supported with mixed ECMO configuration (100%) had a higher ICU survival than those with VV (73%) and VA (72%) (Table 5). Overall ICU survival for all ECMO subjects at our institution for the study period was 70%.

Discussion

Fiberoptic bronchoscopy has become an indispensable tool for both diagnostic evaluation and therapeutic intervention in modern day critical care practice.²² In most patients, it is a relatively low-risk procedure, and previous studies have demonstrated its safety.^{15,23} However, there are no studies validating the safety of FB in adult patients receiving ECMO. Data from the Extracorporeal Life Support Organization¹ suggest that the risk of spontaneous pulmonary hemorrhage in subjects receiving ECMO is 8.1% and may increase to 19% in subjects undergoing a procedure. Additionally, dislodgement of the ECMO cannula and/or loss of ECMO flow during coughing spells with FB may also occur.²⁴

Our study confirms that FB can be safely used in adults supported with ECMO for cardiorespiratory failure. We found that FB in subjects supported with ECMO was not associated with significant worsening of hemodynamic parameters or escalation of ventilator or ECMO support. None of the subjects had a major complication involving the ECMO circuit (ie, cannula dislodgement). Although 21% of the subjects had bloody secretions after FB, this was self-limited and resolved without any intervention. The majority of chest radiographs remained unchanged after the procedure, although improvement in imaging was observed among subjects who had mucous plugging or

copious secretions. As expected, worsening of imaging was observed in subjects who underwent BAL. Previous studies have shown that the prognosis of subjects with respiratory failure due to infections depends on the prompt identification of the causative organisms.^{25,26} In our cohort, FB resulted in positive culture data in 47% of subjects, and a subsequent change in antibiotic therapy occurred in 38% of subjects with positive culture data. This is in line with the FB culture yield of 35–71% reported in studies conducted in critically ill subjects not receiving ECMO.^{8,27–30}

Our literature search did not yield any studies evaluating the safety of bronchoscopy in adult ECMO patients. However, our results were comparable with those of 3 studies describing the safety of FB in pediatric ECMO subjects. In 1993, Karlson et al³¹ reported no bleeding complications after FB in 14 pediatric subjects receiving ECMO undergoing FB. In their cohort, 14% of subjects had worsening of static lung compliance assessed on mechanical ventilation, and 20% had radiographic worsening after FB. Although we did not notice significant worsening of static lung compliance, 14.6% of the post-FB chest radiographs worsened. Similarly, in a retrospective study of 79 pediatric subjects receiving ECMO, Kamat et al³² showed that FB was associated with low incidence of complications. As in our study, 30% of the ECMO subjects in their cohort also had blood-tinged secretions, although none had any mild to moderate bleeding episodes. Also, no new pneumothorax was reported in their study. The differences in bleeding between the studies may be related to the populations (adult vs pediatric) studied or the level of anticoagulation used. More recently, Prentice and Mastropietro³³ demonstrated the safety of FB in pediatric subjects receiving ECMO for cardiac failure. Although their sample size was relatively small, no major bleeding was reported after FB in their cohort. Likewise, FB outcomes and/or complication rates were similar between subjects supported with VA or VV ECMO in our cohort.

Our study is not without limitations. Although our results are based on objective parameters, it is unclear whether any improvement or worsening of radiographic findings after FB is a result of the procedure or rather the underlying disease process. Additionally, given the retrospective nature of the study, results may be biased by documentation or collection errors.

Conclusions

We conclude that FB can be safely performed in adult patients supported with ECMO. FB is not associated with significant hemodynamics changes, bleeding, and/or mechanical complications during ECMO support. Additionally, FB may improve clinical care by facilitating pulmonary secretion clearance and by possibly increasing

diagnostic yield and improving antibiotic selection in patients with respiratory infections.

REFERENCES

1. Paden ML, Conrad SA, Rycus PT, Thiagarajan RR, ELSO Registry. Extracorporeal Life Support Organization Registry Report 2012. *ASAIO J* 2013;59(3):202-210.
2. Sauer CM, Yuh DD, Bonde P. Extracorporeal membrane oxygenation use has increased by 433% in adults in the United States from 2006 to 2011. *ASAIO journal* 2015;61(1):31-36.
3. Cork G, Barrett N, Ntoumenopoulos G. Justification for chest physiotherapy during ultra-protective lung ventilation and extra-corporeal membrane oxygenation: a case study. *Physiother Res Int* 2014;19(2):126-128.
4. Guerreiro da Cunha Fragoso E, Goncalves JM. Role of fiberoptic bronchoscopy in intensive care unit: current practice. *J Bronchology Interv Pulmonol* 2011;18(1):69-83.
5. Vaidya PJ, Leuppi JD, Chhajed PN. The evolution of flexible bronchoscopy: from historical luxury to utter necessity!! *Lung India* 2015;32(3):208-210.
6. Montravers P, Gauzit R, Dombret MC, Blanchet F, Desmonts JM. Cardiopulmonary effects of bronchoalveolar lavage in critically ill patients. *Chest* 1993;104(5):1541-1547.
7. Prebil SE, Andrews J, Cribbs SK, Martin GS, Esper A. Safety of research bronchoscopy in critically ill patients. *J Crit Care* 2014;29(6):961-964.
8. Reynolds HY. Bronchoalveolar lavage. *Am Rev Respir Dis* 1987;135(1):250-263.
9. Trouillet JL, Guiguet M, Gibert C, Fagon JY, Dreyfuss D, Blanchet F, Chastre J. Fiberoptic bronchoscopy in ventilated patients: evaluation of cardiopulmonary risk under midazolam sedation. *Chest* 1990;97(4):927-933.
10. Lukomsky GI, Ovchinnikov AA, Bilal A. Complications of bronchoscopy: comparison of rigid bronchoscopy under general anesthesia and flexible fiberoptic bronchoscopy under topical anesthesia. *Chest* 1981;79(3):316-321.
11. Prakash UB, Offord KP, Stubbs SE. Bronchoscopy in North America: the ACCP survey. *Chest* 1991;100(6):1668-1675.
12. Pereira W Jr, Kovnat DM, Snider GL. A prospective cooperative study of complications following flexible fiberoptic bronchoscopy. *Chest* 1978;73(6):813-816.
13. Pallone TL, Silldorff EP, Turner MR. Intrarenal blood flow: microvascular anatomy and the regulation of medullary perfusion. *Clin Exp Pharmacol Physiol* 1998;25(6):383-392.
14. Muntean W. Coagulation and anticoagulation in extracorporeal membrane oxygenation. *Artif Organs* 1999;23(11):979-983.
15. Steinberg KP, Mitchell DR, Maunder RJ, Milberg JA, Whitcomb ME, Hudson LD. Safety of bronchoalveolar lavage in patients with adult respiratory distress syndrome. *Am Rev Respir Dis* 1993;148(3):556-561.
16. Jolliet P, Chevrolet JC. Bronchoscopy in the intensive care unit. *Intensive Care Med* 1992;18(3):160-169.
17. Sharma NS, Wille KM, Bellot SC, Diaz-Guzman E. Modern use of extracorporeal life support in pregnancy and postpartum. *ASAIO J* 2015;61(1):110-114.
18. Fikkers BG, van Veen JA, Kooloos JG, Pickkers P, van den Hoogen FJ, Hillen B, van der Hoeven JG. Emphysema and pneumothorax after percutaneous tracheostomy: case reports and an anatomic study. *Chest* 2004;125(5):1805-1814.
19. Gordon CE, Feller-Kopman D, Balk EM, Smetana GW. Pneumothorax following thoracentesis: a systematic review and meta-analysis. *Arch Intern Med* 2010;170(4):332-339.
20. Tsotsolis N, Tsirgogianni K, Kioumis I, Pitsiou G, Baka S, Papaiwannou A, et al. Pneumothorax as a complication of central venous catheter insertion. *Ann Transl Med* 2015;3(3):40-41.
21. Pue CA, Pacht ER. Complications of fiberoptic bronchoscopy at a university hospital. *Chest* 1995;107(2):430-432.
22. Raoof S, Mehrishi S, Prakash UB. Role of bronchoscopy in modern medical intensive care unit. *Clin Chest Med* 2001;22(2):241-261, vii.
23. Hertz MI, Woodward ME, Gross CR, Swart M, Marcy TW, Bitterman PB. Safety of bronchoalveolar lavage in the critically ill, mechanically ventilated patient. *Crit Care Med* 1991;19(12):1526-1532.
24. Borrelli U, Costa C. ECMO-Extracorporeal Life Support in Adults. Chapter 6, Materials: cannulas, pumps, oxygenators. Sangalli F, Patroniti N, Pesenti A, editors. 2014;72-73.
25. Fagon JY, Chastre J, Domart Y, Trouillet JL, Pierre J, Darne C, Gibert C. Nosocomial pneumonia in patients receiving continuous mechanical ventilation. Prospective analysis of 52 episodes with use of a protected specimen brush and quantitative culture techniques. *Am Rev Respir Dis* 1989;139(4):877-884.
26. Meduri GU. Ventilator-associated pneumonia in patients with respiratory failure: a diagnostic approach. *Chest* 1990;97(5):1208-1219.
27. Estella A. [Analysis of 208 flexible bronchoscopies performed in an intensive care unit]. *Med Intensiva* 2012;36(6):396-401.
28. Jain P, Sandur S, Meli Y, Arroliga AC, Stoller JK, Mehta AC. Role of flexible bronchoscopy in immunocompromised patients with lung infiltrates. *Chest* 2004;125(2):712-722.
29. Turner JS, Willcox PA, Hayhurst MD, Potgieter PD. Fiberoptic bronchoscopy in the intensive care unit: a prospective study of 147 procedures in 107 patients. *Crit Care Med* 1994;22(2):259-264.
30. Vélez L, Correa LT, Maya MA, Mejía P, Ortega J, Bedoya V, Ortega H. Diagnostic accuracy of bronchoalveolar lavage samples in immunosuppressed patients with suspected pneumonia: analysis of a protocol. *Respir Med* 2007;101(10):2160-2167.
31. Karlson KH, Jr., Pickert CB, Schexnayder SM, Heulitt MJ. Flexible fiberoptic bronchoscopy in children on extracorporeal membrane oxygenation. *Pediatr Pulmonol* 1993;16(4):215-218.
32. Kamat PP, Popler J, Davis J, Leong T, Piland SC, Simon D, et al. Use of flexible bronchoscopy in pediatric patients receiving extracorporeal membrane oxygenation (ECMO) support. *Pediatr Pulmonol* 2011;46(11):1108-1113.
33. Prentice E, Mastropietro CW. Flexible bronchoscopy for children on extracorporeal membrane oxygenation for cardiac failure. *Pediatr Crit Care Med* 2011;12(4):422-425.