



# Factors influencing management modifications following fiberoptic bronchoscopy in critically ill ICU patients

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**Background:** Fiberoptic bronchoscopy (FOB) has evolved into a crucial diagnostic and therapeutic procedure for respiratory tract conditions over the years. Despite its benefits, this approach poses increased risks to critically ill patients. This study aimed to identify clinical parameters that influence management modifications after FOB in the general intensive care unit (ICU) population, an area not extensively explored.

**Methods:** In this retrospective study, critically ill adults admitted to a medical ICU in Bangkok, Thailand, who underwent FOB between January 2013 and December 2022 were enrolled. Clinical parameters, imaging findings, and indications were analyzed to identify factors associated with modifications in post-bronchoscopic management.

**Results:** A total of 118 patients were reviewed and management modifications occurred in 69 patients (58.5%), in which antibiotic modification (78.3%) was the leading reason. Chronic steroid use and suspected interstitial lung disease were associated with management modifications after FOB, while alveolar infiltration on chest radiography was not. Although management modifications showed a trend toward lower mortality, statistical significance was not reached. Multivariate analysis identified chronic steroid use as the only independent factor [adjusted odds ratio (aOR): 2.26; 95% confidence interval (CI): 1.01–5.06; P=0.048].

**Conclusions:** Among critically ill patients, chronic steroid use was a predictor of management modifications after FOB and is likely to be beneficial.

**Keywords:** Corticosteroids; bronchoalveolar lavage (BAL); fiberoptic bronchoscopy (FOB); immunocompromised; intensive care unit (ICU)

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## Introduction

### Background

Since bronchoscopy was first introduced in 1897, it has continuously evolved into one of the crucial diagnostic and therapeutic procedures for various respiratory

tract conditions. It is generally considered safe when performed by an experienced bronchoscopist, with proper preprocedural assessments and monitoring during the procedure.

Critically ill patients constitute a special group who not only suffer from respiratory problems but also experience

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multi-organ dysfunction, increasing the risk associated with this procedure. The international guideline has proposed recommendations for fiberoptic bronchoscopy (FOB) in the intensive care unit (ICU), including its use to diagnose or treat lobar collapse and hemoptysis, and to aid in the diagnosis of lung infections, especially in immunocompromised cases (1,2).

There is evidence indicating that FOB can effectively reverse lobar collapse with a high success rate ranging from 79% to 89% (3-5). For active pulmonary hemorrhage, FOB provides diagnostic information about the hemorrhage site that is on par with that obtained from a computed tomography (CT) scan (6). However, the strength of FOB lies in its ability to perform therapeutic interventions (7,8). Although there have been several studies that focus on the utility of FOB in ICU infections, most of them have focused on immunocompromised patients. The results have consistently shown that FOB can provide a more definitive diagnosis and lead to modification in management, but has not been associated with a mortality benefit (9-11).

### *Rationale and knowledge gap*

Despite the established benefits of FOB, there is a significant knowledge gap regarding its broader application in the general ICU population. The elevated risks associated with this procedure in critically ill patients necessitate a deeper understanding of the specific factors that influence its impact on patient management (12).

#### **Highlight box**

##### **Key findings**

- Chronic steroid use was a predictor of management modification after fiberoptic bronchoscopy (FOB) in the intensive care unit (ICU).

##### **What is known and what is new?**

- Immunocompromised patients are likely to benefit from FOB in the ICU.
- This study specifies that within the immunocompromised subgroup, chronic steroid use is a significant predictor of management modification resulting from FOB.

##### **What is the implication, and what should change now?**

- When clinically indicated, FOB should be encouraged in critically ill patients who are chronic steroid users to facilitate management modifications and may improve patient outcomes.

### *Objective*

This research aims to investigate the variables that affect the management and outcomes of FOB in a more diverse ICU cohort. These, in turn, can optimize the decision-making process for clinicians, enhance patient safety, and improve overall outcomes. We present this article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-1040/rc>).

### **Methods**

#### *Study setting and population*

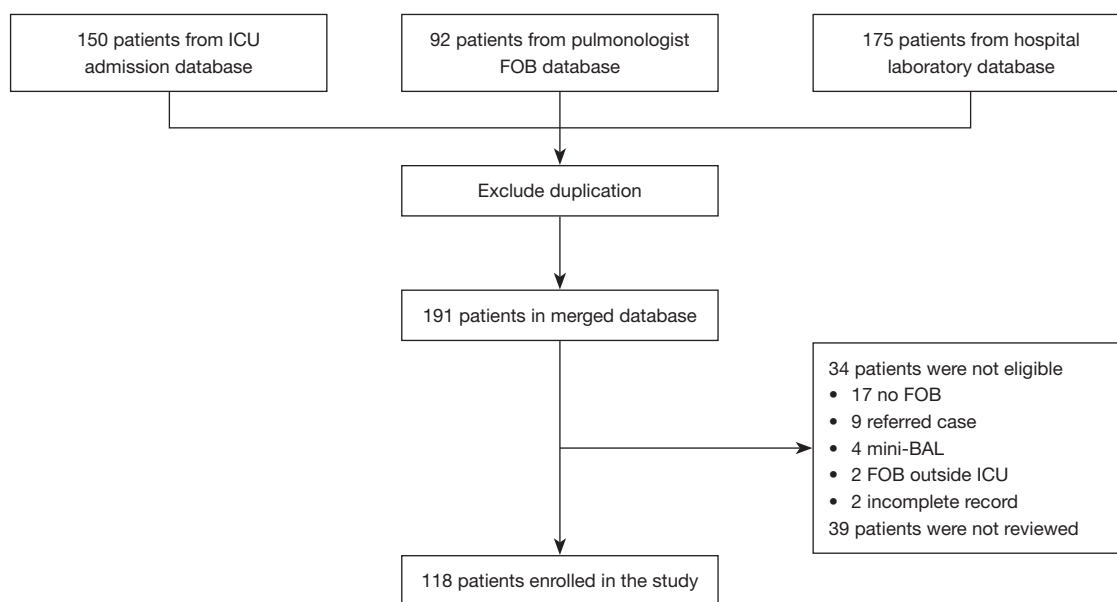
This retrospective study included adult patients (age  $\geq 18$  years) who were admitted to the medical ICU of Siriraj Hospital in Bangkok, Thailand and underwent FOB in the ICU between January 2013 and December 2022. We excluded patients with incomplete bronchoscopic records.

#### *Data collection*

We collected the list of patients who underwent FOB from three separate databases: the ICU admission database, the pulmonologist bronchoscopic database, and the hospital laboratory database. After merging all three databases, the authors checked eligibility using electronic medical records and chronologically extracted demographic and bronchoscopic data from eligible patients, starting with the most recent bronchoscopic date (*Figure 1*).

#### *FOB and bronchoalveolar lavage (BAL)*

The FOB was performed by an intensivist or consultant pulmonologist according to standard practice under appropriate sedation and monitoring in the ICU. The decision to perform FOB was guided by established indications, including suspected infections, hemoptysis, lobar collapse, airway conditions, and interstitial lung disease. These indications were based on the bronchoscopic record or the pre-bronchoscopic differential diagnosis made by the bronchoscopist, which took into account the patient's clinical history, respiratory symptoms, imaging studies, and laboratory findings. BAL was obtained from the pulmonary segment most affected, which corresponded to the imaging and sent for cell count and differential, bacterial staining, and culture. Further analysis was conducted as clinically indicated.



**Figure 1** Study flow diagram. ICU, intensive care unit; FOB, fiberoptic bronchoscopy; BAL, bronchoalveolar lavage.

### Diagnostic definitions

The clinical and radiographic characteristics of pneumonia, along with the identification of bacterial organisms from BAL samples, were used to define bacterial pneumonia, while serology positivity, polymerase chain reaction (PCR) assays, or pathological identification of viral cytopathic changes from BAL were used to define viral pneumonia. The diagnosis of invasive fungal disease was based on the consensus of the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group (13). For pneumocystis pneumonia, apart from a clinical background, imaging and serodiagnosis, *Pneumocystis jirovecii* needed to be identified from respiratory specimens by special staining, immunofluorescence assay or PCR assay.

The diagnosis of alveolar hemorrhage was made when sequential BAL was positive or when the BAL hemosiderin score was >100 (14). The bronchoscopist diagnosed lobar collapse and airway conditions based on the findings of the bronchoscope. Pathological diagnosis or exclusion of other plausible conditions was necessary before diagnosing interstitial lung disease.

Immunocompromised status was defined as human immunodeficiency virus (HIV) infected individuals, those with active malignancy, neutropenia, transplant recipients or patients receiving daily steroids of at least 20 mg of prednisolone or equivalent for more than 14 days, ongoing

chemotherapy, or other immunosuppressive agents (15).

### Measurement of outcomes

The primary outcome was the pre-bronchoscopic clinical parameters associated with management modifications. Management modifications included the introduction of new therapeutic measures or the cessation of current therapeutic measures, such as antibiotic treatment, immunosuppressive agents, or plasmapheresis, based on bronchoscopic results.

### Statistical analysis

We based our sample size calculation on a previous study that evaluated the benefits of bedside FOB in mechanically ventilated patients (16). A review of the literature revealed that after the bronchoscopic results arrived, in the group of management modifications, 29.2% of the patients were immunocompromised, while in the group of nonmanagement modifications, this percentage was 64.3%. With a 95% confidence interval (CI) ( $Z=1.96$ ) and a power of 90% ( $\beta=0.1$ ), we calculated the sample size using two proportions with an independent sample and adjusted it with a square multiple correlation coefficient of 0.3. A total of 118 subjects were needed to be included in the study. We collected and managed study data using REDCap (Research

Electronic Data Capture) tools hosted at the Faculty of Medicine Siriraj Hospital, Mahidol University (17).

Continuous variables were compared using the independent samples *t* test for normally distributed data and the Mann-Whitney *U* test for nonnormally distributed data. As appropriate, categorical variables were compared using Pearson's  $\chi^2$  test or Fisher's exact test. Probability values (*P*) <0.05 were considered statistically significant. All potential clinical parameters were analyzed in univariate to determine the predictive factors of the primary outcome. Clinical parameters that showed an association with the primary outcome, indicated by a *P* value of <0.1 in the univariate analysis, were entered into a multivariate logistic regression model. All analyzes were performed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA).

### **Ethical statement**

Before starting this research, the Institutional Review Board of the Faculty of Medicine of Siriraj Hospital, Mahidol University, approved its protocol (Si833/2022). Informed consent was exempted due to the retrospective design of the study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was registered with the Thai Clinical Trials Registry (TCTR20230202002).

## **Results**

### **General demographic data**

In total, 118 patients were enrolled, with 69 patients (58.5%) experiencing a modification in management after FOB, while 49 patients (41.5%) did not. Sex, age, body mass index, and comorbidities were comparable in both groups. Among the patients, 72 (61.0%) were immunocompromised. In this group, a definitive diagnosis was established in 55 patients (76.4%), resulting in management modifications in 46 patients (63.9%). Chronic steroid use (39.0%), other immunosuppressive drugs (23.7%), and active hematologic malignancy (17.8%) were the leading causes of immunocompromised status, but only chronic steroid use was significantly higher in the changed management group (47.8% *vs.* 26.5%; *P*=0.02). Almost half of the patients were admitted due to pulmonary-related diagnoses (47.5%), while around one third were admitted directly to the ICU (30.5%). For those who did not, the median time before admission to the ICU was 3 days [interquartile range (IQR), 0–7.5 days].

The severity, measured by the Acute Physiology and Chronic Health Evaluation II (APACHE II) score (19.91±6.79 *vs.* 19.80±6.52; *P*=0.93), Sequential Organ Failure Assessment (SOFA) score (7.65±3.66 *vs.* 7.57±3.27; *P*=0.90), and the Murray lung injury score (8.58±3.60 *vs.* 8.78±3.32; *P*=0.76), did not differ between the groups (*Table 1*).

### **Clinical characteristics**

The presenting symptoms were not different between the groups; almost every patient had dyspnea (98.3%). The most common infiltration on chest radiographs was an alveolar pattern (88.1%), but this finding was associated with unmodified management (82.6% *vs.* 95.9%; *P*=0.03). Other types of infiltration or distribution on chest radiographs were comparable. The main indication for FOB was to work up the infection (99.2%), followed by hemoptysis (35.6%), but working up interstitial lung disease was significantly more common in the modified management group (11.6% *vs.* 0.0%; *P*=0.02). The median durations to FOB did not differ in both groups (*Table 2*).

### **Bronchoscopic result**

The microbiological diagnosis was made by bacteria (26.3%), fungi (16.1%), and viruses (11.0%). Bacterial infection was significantly higher in the unmodified management group (15.9% *vs.* 40.8%; *P*=0.002), contradictory, the positivity of BAL galactomannan was higher in the modified management group (31.9% *vs.* 12.2%; *P*=0.01). If the final result was non-infectious, it was also associated with management modifications (33.3% *vs.* 6.1%; *P*<0.001). In the chronic steroid group, most of the organisms identified were fungi (30.4%), with invasive pulmonary aspergillosis (23.9%) being the most frequent, followed by viruses (15.2%) and bacteria (13.0%). The complications in this study were low, with an overall rate of complication of less than 10%, mainly transient desaturation during the procedure (3.4%). None of the complications led to mortality (*Table 3*).

### **Bronchoscopic outcomes**

Overall, FOB led to a definitive diagnosis in 75.4% of cases, a change in diagnosis in 58.5%, and a change in antibiotics in 45.8%. Management modifications after FOB led to lower mortality across the admission, but were not statistically significant: ICU mortality (37.7% *vs.* 51.0%;

**Table 1** Baseline demographics

Demographics	Overall, n=118	Modified management, n=69	Unmodified management, n=49	P value
Female	64 (54.2)	39 (56.5)	25 (51.0)	0.55
Age, years	54.54±18.64	53.64±18.01	55.82±19.61	0.53
Body mass index, kg/m <sup>2</sup>	22.51±4.58	22.67±4.67	22.30±4.49	0.67
Pre-existing comorbidities				
Diabetes mellitus	26 (22.0)	15 (21.7)	11 (22.4)	0.93
Renal disease	41 (34.7)	27 (39.1)	14 (28.6)	0.24
Liver disease	6 (5.1)	2 (2.9)	4 (8.2)	0.23
Pulmonary disease	15 (12.7)	10 (14.5)	5 (10.2)	0.49
Autoimmune disease	34 (28.8)	23 (33.3)	11 (22.4)	0.20
Immunocompromised status				
Any immunocompromised	72 (61.0)	46 (66.7)	26 (53.1)	0.14
HIV infection	4 (3.4)	2 (2.9)	2 (4.1)	>0.99
Active solid malignancy	2 (1.7)	0 (0.0)	2 (2.9)	0.51
Active hematologic malignancy	21 (17.8)	14 (20.3)	7 (14.3)	0.40
Solid organ transplant	5 (4.2)	2 (2.9)	3 (6.1)	0.65
Hematologic stem cell transplant	6 (5.1)	4 (5.8)	2 (4.1)	>0.99
Chronic steroid use	46 (39.0)	33 (47.8)	13 (26.5)	0.02*
Other immunosuppressive drugs	28 (23.7)	18 (26.1)	10 (20.4)	0.48
Recent chemotherapy	16 (13.6)	11 (15.9)	5 (10.2)	0.37
Neutropenia	9 (7.6)	5 (7.2)	4 (8.2)	>0.99
Neutropenic duration, days	–	18.00 [4.00, 19.00]	16.00 [10.50, 33.50]	0.81
Admission data				
Pulmonary-related admission diagnosis	56 (47.5)	35 (47.5)	21 (42.9)	0.40
Initial ICU admission	36 (30.5)	20 (29.0)	16 (32.7)	0.67
Days before ICU, days	3 [0.0, 7.5]	3 [0, 7]	3 [0, 10]	0.83
APACHE II score	19.86±6.65	19.91±6.79	19.80±6.52	0.93
SOFA score	7.62±3.49	7.65±3.66	7.57±3.27	0.90
Murray score	8.66±3.47	8.58±3.60	8.78±3.32	0.76
Mechanical ventilator	113 (95.8)	66 (95.4)	47 (95.9)	>0.99
Vasopressor	77 (65.3)	45 (65.2)	32 (65.3)	>0.99
Extracorporeal life support	28 (23.7)	16 (23.2)	12 (24.5)	0.87

Data are presented as n (%), median [IQR] or mean ± standard deviation. \*, statistically significant. HIV, human immunodeficiency virus; ICU, intensive care unit; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; IQR, interquartile range.

Table 2 Pre-bronchoscopy characteristic

Characteristic	Overall, n=118	Modified management, n=69	Unmodified management, n=49	P value
Symptoms, n (%)				
Dyspnea	116 (98.3)	68 (98.6)	48 (98.0)	>0.99
Cough	83 (70.3)	48 (69.6)	35 (71.4)	0.83
Sputum production	91 (77.1)	50 (72.5)	41 (83.7)	0.15
Hemoptysis	36 (30.5)	23 (33.3)	13 (26.5)	0.43
Fever	89 (75.4)	48 (69.6)	41 (83.7)	0.08
Imaging, n (%)				
CXR, alveolar infiltration	104 (88.1)	57 (82.6)	47 (95.9)	0.03*
CXR, interstitial infiltration	9 (7.6)	7 (10.1)	2 (4.1)	0.30
CXR, alveolar and interstitial infiltration	4 (3.4)	4 (5.8)	0 (0.0)	0.14
CXR, focal infiltration	23 (19.5)	12 (17.4)	11 (22.4)	0.49
CXR, multifocal infiltration	30 (25.4)	18 (26.1)	12 (24.5)	0.84
CXR, diffused infiltration	64 (54.2)	38 (55.1)	26 (53.1)	0.83
CT scan performed	32 (27.1)	16 (23.2)	16 (32.7)	0.25
Indication, n (%)				
Infection	117 (99.2)	68 (98.6)	49 (41.9)	>0.99
Hemoptysis	42 (35.6)	29 (42.0)	13 (26.5)	0.08
Lobar collapse	8 (6.8)	6 (8.7)	2 (4.1)	0.47
Airway condition	4 (3.4)	4 (5.8)	0 (0.0)	0.14
Interstitial lung disease	8 (6.8)	8 (11.6)	0 (0.0)	0.02*
Duration, median (IQR), days				
Symptom onset to bronchoscopy	7 (4.0, 10.25)	6 (5.0, 10.0)	7 (4.0, 11.0)	0.57
Hospital admission to bronchoscopy	9 (5.0, 21.0)	9 (6.0, 19.0)	9 (4.0, 21.0)	0.81
ICU admission to bronchoscopy	5 (3.0, 13.25)	5 (3.0, 11.0)	4 (3.0, 16.0)	0.86

\*, statistically significant. CXR, chest radiography; CT scan, computed tomography scan; IQR, interquartile range; ICU, intensive care unit.

P=0.15), 28-day mortality (30.4% *vs.* 36.7%; P=0.47), and hospital mortality (46.4% *vs.* 57.1%; P=0.25) (*Table 3*). Antibiotic modification (78.3%) was the leading reason for management modification, followed by immunosuppressive drug modification (21.7%) and diffuse alveolar hemorrhage management (15.9%) (*Table 4*).

### Factors related to management modification

Regarding the primary outcome, chronic steroid use was a predictive factor for treatment modifications after FOB [odds ratio (OR): 2.54; 95% CI: 1.15–5.60; P=0.02].

However, alveolar infiltration acted differently (OR: 0.20; 95% CI: 0.04–0.95; P=0.03) (*Table 5*). A multivariate analysis model was conducted to determine the pre-bronchoscopic factors significantly associated with a modification in management, and only chronic steroid use remained significant [adjusted odds ratio (aOR): 2.26; 95% CI: 1.01–5.06; P=0.048] (*Table 5*).

### Discussion

To our knowledge, this study represents the first attempt to identify factors associated with changes in management



Table 3 Bronchoscopy result

Result	Overall, n=118	Modified management, n=69	Unmodified management, n=49	P value
Procedures				
BAL performed	118 (100.0)	69 (100.0)	49 (100.0)	–
Instilled BAL volume, mL	113.52±35.66	111.45±21.64	116.43±49.2	0.46
Retrieved BAL volume, mL	39.96±16.51	40.05±14.99	39.84±18.59	0.95
%retrieved BAL volume, mL	37.38±16.55	37.08±15.36	37.81±18.24	0.82
Biopsy performed	1 (0.8)	0 (0.0)	1 (2.0)	0.42
Mechanically ventilated during bronchoscopy	115 (97.5)	66 (95.7)	49 (100.0)	0.27
BAL cell count and differential				
BAL nucleated cell	246.5 [114.75, 698.75]	237.5 [103.5, 586.5]	335.0 [133.0, 1,070.0]	0.20
%polymorphonuclear neutrophils	65 [42.75, 86.00]	66 [40, 86]	64 [44, 88]	0.75
%lymphocyte	8 [4, 16]	8 [4, 16]	8 [3, 16]	0.98
%eosinophil	2 [1, 3]	1 [1, 3]	2 [1, 3]	0.14
%macrophage	16.5 [7, 34.25]	17 [8, 39]	14.5 [7, 32.5]	0.76
BAL investigation				
BAL staining positive	36 (30.5), 36/118	21 (30.4)	15 (30.6)	0.98
BAL culture positive	61 (51.7), 61/118	39 (56.5)	22 (44.9)	0.21
BAL serology positive	2 (1.7), 2/31 (6.5)	2 (2.9)	0 (0.0)	0.51
BAL galactomannan positive	28 (23.7), 28/61 (41.8)	22 (31.9)	6 (12.2)	0.01*
BAL PCR positive	22 (18.6), 22/109 (20.2)	11 (15.9)	11 (22.4)	0.37
BAL cytology positive	14 (11.9), 14/103 (13.6)	11 (15.9)	3 (6.1)	0.10
Sequential BAL positive	11 (9.3), 11/39 (28.2)	9 (13.0)	2 (4.1)	0.12
BAL hemosiderin score positive	14 (11.9), 14/45 (31.1)	9 (13.0)	5 (10.2)	0.64
BAL hemosiderin score	33 [0.5, 137.5]	40 [6, 140]	19 [0, 122]	0.48
Diagnosis				
Infection	73 (61.9)	41 (59.4)	32 (65.3)	0.52
Bacterial	31 (26.3)	11 (15.9)	20 (40.8)	0.002*
Fungus	19 (16.1)	13 (18.8)	6 (12.2)	0.34
Virus	13 (11.0)	10 (14.5)	3 (6.1)	0.15
Parasite	2 (1.7)	1 (1.4)	1 (2.0)	>0.99
Mixed infection	8 (6.8)	6 (8.7)	2 (4.1)	0.47
Non-infectious	26 (22.0)	23 (33.3)	3 (6.1)	<0.001*
Non-diagnostic	19 (16.1)	5 (7.2)	14 (28.6)	0.002*
Alveolar hemorrhage	16 (13.6)	12 (17.4)	4 (8.2)	0.15
Positive lobar collapse	8 (6.8)	6 (8.7)	2 (4.1)	0.47
Positive airway condition	4 (3.4)	4 (5.8)	0 (0.0)	0.14
Interstitial lung disease	8 (6.8)	8 (11.6)	0 (0.0)	0.02*

Table 3 (continued)

Table 3 (continued)

Result	Overall, n=118	Modified management, n=69	Unmodified management, n=49	P value
Complications				
Desaturation	4 (3.4)	3 (4.3)	1 (2.0)	0.64
Pneumothorax	1 (0.8)	0 (0.0)	1 (2.0)	0.42
Hypertension	1 (0.8)	1 (1.4)	0 (0.0)	>0.99
Arrhythmia	1 (0.8)	0 (0.0)	1 (2.0)	0.42
Hypotension	2 (1.7)	1 (1.4)	1 (2.0)	>0.99
Cardiac arrest/death	0 (0.0)	0 (0.0)	0 (0.0)	–
Outcomes				
Definitive diagnosis	89 (75.4)	65 (94.2)	24 (49)	<0.001*
Change diagnosis	69 (58.5)	60 (87.0)	9 (18.4)	<0.001*
Antibiotic modification	54 (45.8)	54 (78.3)	0 (0.0)	<0.001*
ICU mortality	51 (43.2)	26 (37.7)	25 (51.0)	0.15
28-day mortality	39 (33.1)	21 (30.4)	18 (36.7)	0.47
Hospital mortality	60 (50.8)	32 (46.4)	28 (57.1)	0.25

Data are presented as n (%), median [IQR] or mean  $\pm$  standard deviation. \*, statistically significant. BAL, bronchoalveolar lavage; PCR, polymerase chain reaction; ICU, intensive care unit; IQR, interquartile range.

Table 4 Management modification

Reason for management modification	Modified management, n=69
Antibiotics modification, n (%)	54 (78.3)
De-escalation	5 (7.2)
Escalation or added	34 (49.3)
Discharge	15 (21.7)
Immunosuppressive drug modification, n (%)	15 (21.7)
Diffuse alveolar hemorrhage management, n (%)	11 (15.9)
Initiation of treatment	6 (8.7)
Cessation of treatment	5 (7.2)
Airway condition management, n (%)	3 (4.3)
Lobar collapse management, n (%)	2 (3.9)

after FOB in patients in general ICU. In our overall ICU population, FOB yielded a definitive diagnosis in 75.4% of cases, with both changes in diagnosis and modifications in management accounting for an equal percentage of 58.5%.

Following international recommendations, FOB should

be conducted to diagnose infections in immunocompromised patients with uncertain etiology and causative organisms (1,18). The diagnostic yield of FOB in immunocompromised individuals varies between 33.0% and 60.8%, depending on specific immune deficiencies (9,15-18). In our cohort, 61.0% of the patients were immunocompromised and in this group a definitive diagnosis was established in 76.4% of the cases, resulting in management modifications in 63.9%. Few previous studies have focused on the utility of FOB for management modifications in immunocompromised patients. A study by Mayo Clinic in patients with immunocompromised ICU without HIV found that the impact on treatment was 38.3% (11). Another study from Singapore in an ambulatory setting reported a treatment modification rate of 63.3% (19).

In our cohort, the main causes of immunocompromised status were chronic steroid use (39.0%), and FOB in this group led to modifications in treatment in 71.7% of cases. The association with steroid use was also previously demonstrated, with 56.7% of chronic steroid users experiencing management modifications after FOB (11).

Chronic steroid use impairs both phagocytic and cell-mediated immunity, thereby increasing the risk of various infections (20). Many organisms in this setting cannot



**Table 5** Independent variables related to the primary outcome (logistic regression)

Clinical parameters	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	P value	Adjusted odds ratio	95% CI	P value
Chronic steroid use <sup>†</sup>	2.54	1.15–5.60	0.02*	2.26	1.01–5.06	0.048*
Fever <sup>†</sup>	0.45	0.18–1.11	0.08			
CXR, alveolar infiltration <sup>†</sup>	0.20	0.04–0.95	0.03*	0.24	0.05–1.17	0.08
Indication, hemoptysis <sup>†</sup>	2.00	0.91–4.44	0.08			

\*, statistically significant; <sup>†</sup>, clinical parameters which entered into a multivariable logistic regression model. CI, confidence interval; CXR, chest radiography.

be identified by blind catheter aspiration. For example, *Pneumocystis jirovecii* resides in very distal airways (8,21), and BAL galactomannan, highly specific and more sensitive, is crucial for diagnosing invasive pulmonary aspergillosis (22). For a definitive diagnosis of cytomegalovirus (CMV) pneumonitis, documented CMV in lung tissue is mandatory (23). In our chronic steroid group, most of the organisms identified were fungi, with invasive pulmonary aspergillosis being the most frequent, followed by viruses and bacteria. The prevalence of causative organisms may vary across continents (11,19,24).

Other groups, including those taking different immunosuppressive drugs and those with active hematologic malignancies, did not show significant differences. This could be due to smaller sample sizes, diversity in immunosuppressive drugs, and variations in disease stages and treatments, which makes it challenging to demonstrate unified outcomes.

In our cohort, bacteria were the leading cause of infection and were more prevalent in the unmodified management group. This can be attributed to the current practice of early broad-spectrum empirical antibiotics, which generally cover the causative bacterial pathogens (9).

Another important consideration is that non-infectious causes accounted for a significant portion, 22.0% in our cohort, which is comparable to rates reported in previous studies ranging from 17.7% to 28.0% (10,25). When a non-infectious diagnosis was established, the percentage of management modifications increased to 88.5%. This is not surprising because before diagnosing a non-infectious cause, an extensive investigation for infection and CT scan are necessary, and FOB remains the investigation of choice as it can both rule out infection and provide specific investigations, such as sequential BAL for alveolar hemorrhage or pathological diagnosis for interstitial lung disease.

In our series, the median time to FOB did not differ significantly between the groups, with FOB generally performed approximately 5 days after admission to the ICU. Previous research has shown that very early FOB (within 24 hours of ICU admission) is associated with a better diagnostic yield (11). The presence of a focal pattern in chest imaging has also been mentioned as positively affecting diagnostic performance (11,24,26), but in our study, the effect on management modifications could not be demonstrated.

Although FOB increased diagnostic yield and influenced management modifications, benefits in terms of mortality have long been debated. Our study showed a trend towards a mortality benefit associated with management modifications, which aligns with previous research (9-11). This finding can be attributed to the severity of the patients and the nature of the disease. More severely ill patients were more likely to be admitted to the ICU and undergo FOB. However, even with modified management, they may still be too sick to experience improved outcomes.

A major strength of this study is the extensive collection of clinical and laboratory information to identify factors associated with management modifications after FOB in the ICU. The study highlights the association between chronic steroid use and management modifications after FOB in the ICU.

However, there are several notable limitations to our study. First, being a single-center study in a developing country limits the generalizability of the results. Second, the retrospective design, with a low rate of CT scan and no predefined criteria for FOB, left to the bronchoscopist's discretion, might introduce selection bias and limit reproducibility. However, for patients in the ICU at elevated risk of FOB, individualized assessment is mandatory and rigid criteria may not be appropriate. Moreover, the study was conducted over a span of 10 years,

during which diagnostic and laboratory techniques likely evolved. This temporal variability can affect the consistency and comparability of the results, as newer technologies and methodologies may have altered diagnostic yields and treatment outcomes over time. Lastly, most of the FOBs performed in our ICU were intended to diagnose pulmonary infections, so this study may not have had sufficient power to investigate other bronchoscopic indications. Further prospective multinational cohort studies are warranted to overcome these limitations.

## Conclusions

This study highlights the critical role of FOB in managing critically ill patients in the ICU, particularly those who are chronic steroid users, a group identified as a significant predictor of management modifications following FOB. The findings emphasize the necessity of considering FOB in this group of patients, as it can lead to therapeutic changes and may improve patient outcomes.

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## Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Before starting this

research, the Institutional Review Board of the Faculty of Medicine of Siriraj Hospital, Mahidol University, approved its protocol (Si833/2022). Informed consent was exempted due to the retrospective design of the study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was registered with the Thai Clinical Trials Registry (TCTR20230202002).

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