LITERATURE REVIEW

Preparation and Findings in Diagnostic and Therapeutic Flexible Fiberoptic Bronchoscopy Procedures in Patients with COVID-19

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ABSTRACT

The coronavirus disease 2019 (COVID-19), which has raised concerns about infection control for every clinical procedure, including flexible fiberoptic bronchoscopy (FFB), has drawn the attention of clinicians across the globe. A pulmonologist frequently conducts this procedure to diagnose and treat pulmonary diseases like COVID-19. This procedure involves direct airway observation and generates aerosol from the patient. However, it is considered a double-edged sword, as the risk of infection and instrument contamination always haunts its clinical benefit to the patients and the operators. Therefore, a guideline for preparing and indicating FFB in COVID-19 must be addressed appropriately by emphasizing the importance of infection prevention and control. Fortunately, several recommendations and findings have emerged over the past three years, which should support safe FFB procedures for its operators with controlled infection. This study summarizes the indication, objective, contraindication, risk, preparation, and findings in diagnostic and therapeutic FFB patients with COVID-19.

INTRODUCTION

Flexible fiberoptic bronchoscopy (FFB) is a direct visual imaging procedure for the airway (endobronchial) in real-time to identify tracheal and bronchioles conditions and treat pulmonary diseases. With the aid of tools including suction, biopsy needle, forceps, and brushes, the diagnostic FFB procedure is performed by inserting the device via the airway to collect endobronchial specimens, including bronchial wash and tumor samples. A therapeutic FFB procedure is performed to treat an endobronchial disorder, such as foreign body aspiration, tumor, sputum retention, and bleeding.[1]

FFB in a patient with COVID-19 is a double-edged sword. It may be used as a diagnostic and therapeutic measure in a patient with COVID-19 to reduce the risk of complications and death. Still, it also generates aerosol and droplets, which requires preparation and relevant infection prevention and control measures to prevent COVID-19 transmissions between patients and operators and contaminating the device.[2] This literature review discussed indication and objective, contraindication, risk, preparation, and findings in diagnostic and therapeutic FFB patients with COVID-19.

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Indication and Objective of FFB in Patients with COVID-19

FFB in patients with COVID-19 serves as a diagnostic and therapeutic procedure (Table 1). Diagnostic FFB in patients with COVID-19 is to establish COVID-19 diagnosis once oropharyngeal or nasopharyngeal quantitative polymerase chain reaction (qPCR) of SARS-CoV-2 test result comes out negative or inconclusive with clinical manifestations suggesting COVID-19.[2,3] The positivity rate of qPCR SARS-CoV-2 specimens obtained from the bronchial wash or bronchoalveolar lavage (BAL) is higher (93%) than oropharyngeal or nasopharyngeal swab specimen (32%–63%).[4] Diagnostic FFB is indicated for those with clinical deterioration which is expected to benefit from therapeutic FFB, such as atelectasis associated with sputum retention that requires bronchial wash or BAL, and complicated cases of endotracheal intubation that demands FFB visualization.[2,5]

Diagnostic FFB aims to identify conditions leading to airway obstruction which impair ventilation and alveolar diffusion. Torrego, *et al*. (2020) performed 101 diagnostic FFB procedures on intubated patients with confirmed COVID-19 after a median of six days (ranging from 1–17 days) in a hospital in Barcelona.[6] They reported indications including persistent pneumonia (63/101 patients) and atelectasis (38/101 patients) based on radiology findings. Bruyneel, *et al*. (2020) performed 90 FFB procedures in a hospital in Brussels, Belgium, on suspected and confirmed patients with COVID-19 with pneumonia and reported that the primary indication of the procedure was sputum retention (60/90 patients).[7] Observed findings of diagnostic FFB in patients with COVID-19, as suggested by Torrego, *et al*. and Bruyneel, *et al*., include hyperemic endobronchial surface, clear secretion, purulent discharge, mucus plug, and blood clot.[6,7] These findings are identical to the patients with confirmed COVID-19 who underwent FFB procedures in our hospital (Figure 1).

Table 1. Diagnostic and therapeutic FFB indications for COVID-19[2–7]

Diagnostic representations directly associated with COVID-19
qPCR SARS-CoV-2 test result is irrelevant with clinical manifestation
Persistent pneumonia
Atelectasis
Sputum retention
Diagnostic indications associated with COVID-19 treatment
Endotracheal intubation requiring visualization assistance
Evaluation of injury related to airway intubation
Hemoptysis
Bronchopleural fistula
Persistent pneumothorax
Other diagnostic indications affecting complications and COVID-19 prognosis
Intrathoracic malignancy
Foreign body aspiration
Thoracic trauma
Tracheobronchial stricture and stenosis
Vocal cord paralysis
Therapeutic indications for COVID-19
Bronchial wash and BAL in sputum retention
Tamponade for endobronchial hemorrhage
Extraction of foreign body aspiration
Extraction of obstructive tissue in the central airway
Maintaining airway patency through stenting in central airway obstruction
Other interventions, as indicated

BAL = bronchoalveolar lavage; qPCR = quantitative polymerase chain reaction

Thoracic malignancy patient with COVID-19 is at higher risk of death by up to 35% than those without COVID-19.[8] Such condition requires thorough consideration before implementing diagnostic FFB in thoracic malignancy by observing clinical signs and prognosis of patients who also suffer from COVID-19. Elective diagnostic FFB is recommended after COVID-19-associated conditions have been treated.[2–4] Another consideration for diagnostic FFB procedure is preventable complication and death related to COVID-19 treatments, including diagnosis of injury associated with airway intubation, hemoptysis, bronchopleural fistula, and persistent pneumothorax, as well as other indications affecting COVID-19 complication and prognosis, such as identification of foreign body aspiration, thoracic trauma, tracheobronchial stricture and stenosis, and vocal cord paralysis.[4,5]

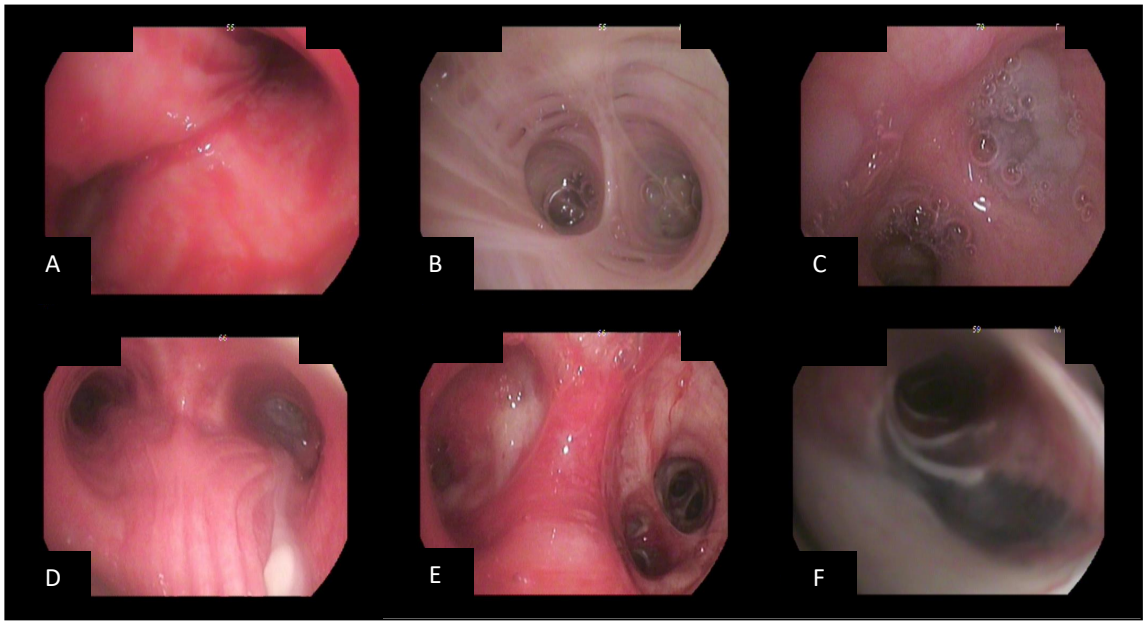

Figure 1. Visual findings of FFB procedure in confirmed patients with COVID-19 in our hospital: hyperemic endobronchial surface (A), clear secretion (B), purulent discharge (C), mucus plug (D), and blood clot (E). We also found a patient with endobronchial anthracosis (F).
Source: Internal document

The therapeutic FFB procedure aims to recover impaired pulmonary ventilation and alveolar diffusion. In COVID-19 pneumonia, sputum retention with hypersecretion causes endobronchial discharge and mucus plug, which are relieved by bronchial washing.[9] It is performed by instilling 10 to 40 mL of normal saline through FFB to dilute the discharge and then extract it by vacuuming and collecting it in a mucus extractor.[10] BAL procedure is a different technique yet bears a similar purpose as a bronchial wash. The distinction between BAL and bronchial wash lies in the volume of normal saline used, ranging from 100–300 mL by streaming 20–50 mL several times in multiple bronchial branches, which later collected in a mucus extractor and its aliquot is subtracted to be analyzed.[11,12]

Both procedures are diagnostic methods for identifying the coinfection of microorganisms in COVID-19 pneumonia to establish definitive antibiotic therapy and improve the patient's prognosis.[4] Bruyneel, *et al*. (2020) observed microbial growth of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Klebsiella aerogenes*, *Prevotella melaninogenica*, *Escherichia coli*, and *Streptococcus anginosus* from BAL test.[7] Report of BAL procedure in patients with COVID-19 by Ora, *et al*. (2020) in a hospital in Rome, Italy, suggested the growth of *Candida albicans*, *Pneumocystis jirovecii*, and *Candida glabrata*.[13] Diagnosis of COVID-19-associated pulmonary aspergillosis is obtained through culture and measurement of galactomannan level of BAL with a positivity rate of 55–61%.[14]

Another therapeutic FFB relates to preventable and treatable COVID-19 complications and prognosis by thoroughly considering the patient's emergency level. Foreign body aspiration and central airway obstruction are major indicators of therapeutic FFB for patients with COVID-19 to restore ventilation function and alveolar diffusion.[2,3,15] Foreign body aspiration is addressed by extraction with forceps or another instrument. Simultaneously, central airway obstruction is treated by relieving the airway through stenting, or other interventions, such as laser, argon plasma coagulation, and cryotherapy.[5] Intervention procedures in patients

with COVID-19 should consider the operator's skill, facility, infection control, and tolerance.[2,15]

FFB Contraindications and Risks in Patients with COVID-19

Direct and indirect COVID-19 conditions and those related to the procedure are the basis for FFB contraindication (Table 2). It is imperative to note this to avoid and mitigate risk during or after the FFB procedure. FFB may instead facilitate the production of droplets and aerosol from patients with COVID-19. Hence, the procedure is a relative contraindication for COVID-19 suspects or confirmed cases from an infection control perspective. Therefore, it is necessary to meticulously consider its clinical benefits and risks for the operator and patient.[2,4,15]

The absolute contraindication of the FFB procedure is hypoxia (i.e., peripheral oxygen saturation <92%) throughout the procedure. That kind of patient is at risk for apnea, cardiac arrest, and death. The condition commonly manifests in a patient with acute or chronic respiratory failure who also suffers from moderate-severe hypoxemia (arterial oxygen partial pressure <60 mmHg) and hypercapnia (arterial carbon dioxide partial pressure ≥100 mmHg). It can be managed by oxygen supplementation, intubation, and mechanical ventilation during the procedure.[5,16,17] Another absolute contraindication includes cervical instability and temporomandibular joint impairment, particularly in rigid bronchoscopy procedures, which is not recommendable for patients with COVID-19.[5,18]

A relative contraindication is mainly attributed to an airway at risk for spasms, such as uncontrolled asthma. It may be treated by administering bronchodilator premedication or intravenously during the procedure.[5,16] Another relative contraindication is an unstable cardiovascular condition that may lead to cardiac arrest since this procedure may stimulate vagal response and catecholamine release in the airway, which induces arrhythmia, hypertension, and hypoxemia.[5,19] The condition may be addressed by providing premedication of cardiac medication, sedation, analgesia, and anesthesia as indicated and closely monitored.[20]

Common FFB procedures for patients with COVID-19 are bronchial wash and BAL. Both procedures have similar contraindications as FFB in other diseases, such as desaturation during the procedure. A pulmonary abscess is also a contraindication of these procedures. Draining bronchial wash and BAL in the bronchial branch afflicted with spots increases the risk for direct infection transmission in the bronchial addition without abscess formation. Thus, this procedure should consider diagnostic and therapeutic benefits and aspiration risks.[5,16]

Table 2. Contraindications of FFB in patients with COVID-19[2–5]

Contraindications directly associated with COVID-19	
Absolute contraindication None	**Relative contraindication** Elective/non-emergency procedure
Contraindications indirectly associated with COVID-19	
Absolute contraindication Hypoxia/desaturated throughout the procedure (SpO_2 <92%)	**Relative contraindication** • Moderate–severe hypoxemia (PaO_2 <60 mmHg) • Hypercapnia ($PaCO_2$ ≥100 mmHg) • Uncontrolled asthma • Risk for a cardiac event • Arrhythmia
Contraindications attributed to the type of procedure	
Bronchial wash and BAL: Invasive procedure:	• Hypoxia/desaturated throughout the procedure (SpO_2 <92%) • Pulmonary abscess • Thrombocytopenia (thrombocyte count <50,000/dL) • Use of anticoagulant • Uremia • Pulmonary hypertension (mPAP ≥25 mmHg)

BAL = bronchoalveolar lavage; mPAP = mean of pulmonary arterial pressure; $PaCO_2$ = carbon dioxide partial pressure; PaO_2 = arterial oxygen partial pressure; SpO_2 = peripheral oxygen saturation

Another FFB procedure for patients with COVID-19 is an interventional procedure, although experts advise against using it for non-emergency cases and should only be used when the COVID-19 condition is alleviated.[18] Should there be no choice, risk for bleeding ought to be considered, especially in thrombocytopenia cases (thrombocyte count <50,000/dL), use of anticoagulant, uremia, and pulmonary hypertension (mean of pulmonary arterial pressure ≥25 mmHg).[5,16] The risk can be mitigated by discontinuing anticoagulant medication and tending to the associated condition before the procedure.[16]

FFB Preparation for Patients with COVID-19

FFB procedure includes preparing the patient, equipment, facility, and operator (Table 3). Infection

control should always be a priority when preparing for an FFB procedure for COVID-19 patients. The Indonesian Society of Respirology published an FFB preparation guide for patients with COVID-19 in emergency settings. If the procedure is performed, clinical conditions might be improved. It is comparable with the recommendation of multiple health professional organizations, particularly in respiratory medicine, including American Association for Bronchology and Interventional Pulmonology, American College of Chest Physicians (CHEST), Infectious Diseases Society of America, Indonesian Medical Association, and World Health Organization (WHO).[2–4,18,21–23]

Medicolegal, clinical judgment, complication risk assessment, and infection control are all components of patient preparation. Informed consent for FFB procedure should comply with hospital policy by obtaining it directly from the patient (if possible) or relative and witnessed by healthcare personnel only after being educated on the indication, goal, and risk of the procedure as prevention and mitigation of complication. The patient's clinical condition should be precisely considered, implying that the FFB procedure is indicated for emergency treatment or after appraising clinical signs, prognosis, risk, and infection for patients with COVID-19. It is also imperative to inform the patient that fever may occur as a major side effect following the FFB procedure (5–10% cases), particularly after BAL (13% cases).[2,3,16,18]

Medical history taking and history of an allergic reaction should be explored as it correlates with the endobronchial condition and hemodynamic and cardiovascular stability during and after the procedure. Patients with asthma and chronic obstructive pulmonary disease (COPD) should have their condition under control/with no exacerbation. Patients with a history of myocardial infarction in less than four weeks are at higher risk for procedure complications. Hence, delaying the procedure should be considered unless necessary. Anticoagulant medication (such as clopidogrel) should be discontinued seven days before the procedure. Warfarin medication is also discontinued five days prior. Heparin is discontinued on the day of the process. Patients should have 5 hours of abstinence from solid food and 2 hours from fluid before the procedure, if possible, except in emergency set-up, although the topic is still up for debate. The non-intubated patient should wear a mask before, during, and after the procedure. The FFB should be inserted through the nose.[2,3,16,18]

A diagnostic test to identify indication and complication risk should be performed. A recent radiological finding is examined, at least posteroanterior and anteroposterior of the thorax image. Another examination, such as a lateral image or chest CT scan with or without contrast, may be conducted if indicated. A recent electrocardiogram (ECG) should be performed and consulted with a cardiologist. Blood tests should be screened, with at least a peripheral blood smear test and a blood gas analysis. Another test, such as hemostasis, may be indicated if there is a high risk for bleeding or if one is about to undergo an interventional procedure.[2,3,16,18]

Equipment preparation involves an FFB set, suction units, sterile sets, sterile intervention accessories, hemodynamic monitors, oxygen supplements, and medication. Bronchoscope unit utility should be disinfected using special detergent and enzymatic liquid. Disposable bronchoscopes or specifically dedicated bronchoscopes for patients with COVID-19 are highly recommended. Cleansing and storing FFBs for patients with COVID-19 should be performed separately from non-COVID-19 FFBs. Other FFB accessories, including an image processor or light source, monitors, and keyboards, should be disinfected accordingly and comply with the manufacturer's recommendation. The utility of the suction unit and catheters should be confirmed with good suction capacity and connected to sterile mucus-collecting pots.[2,16]

Additional requisite sterile equipment includes pure linens, specimen pots, containers/bowls for lidocaine and normal saline, and 20 mL syringes for drainage. Should an interventional procedure be required, disposable and specimen fixation kits must be prepared, including object glasses, formalin 40%, and fixation pots with alcohol 96%. Hemodynamic monitoring devices such as ECG, sphygmomanometers, and finger pulse oximeters should function properly, disinfect accordingly, and comply with the manufacturer's recommendation. Supplementary oxygen should be prepared with the preoxygenation recommendation of 100% inspired oxygen fraction.[2,3,16]

Drugs and intravenous fluids are provided for sedation, anesthesia, FFB procedural purposes, or other emergency drugs requiring intravenous access regularly. Lidocaine gel is used for local anesthesia and lubricant before introducing the bronchoscope. Medicines and intravenous fluids used for FFB include room temperature and normal cold saline for bleeding control that may be diluted with epinephrine 1:100. Emergency medication in FFB procedure includes, but is not limited to, aminophylline, tranexamic acid, atropine sulfate, dexamethasone, epinephrine, sodium bicarbonate, and 40% $MgSO_4$. Invasive FFB procedures should be conducted separately from the bronchial wash or BAL if not indicated. FFB procedure in patients with COVID-19 should be performed swiftly and appropriately, both during bronchoscope introduction and pulling it out (quick in, quick out).[2,16,18]

The preparation of facility and personnel for FFB patients with COVID-19 primarily emphasizes infection control standards for the treatment room, personal protective equipment (PPE), and protocols for each staff member. The aerosol-generating procedure, such as FFB, should be conducted inside an isolation room with negative pressure (negative pressure airborne infection isolation room/AIIR), which allows air exchange of up to 12 air changes per hour (ACH) or more based on air velocity meter or anemometer, the difference in air pressure with exhaust up to 15 pa, room temperature between 20°C and 26°C, and humidity of 30%–60% to increase air dilution. The number of personnel involved in the procedure should be kept minimum, with a maximum of seven staff, comprising of two operators and assistants, two bronchoscopies and circulating nurses, an anesthesiologist, and an anesthesiologist assistant. Students or trainees should not be allowed to participate in the procedure unless properly trained in infection control and PPE. All FFB personnel should comply with standardized protocol during donning and doffing PPE. FFB requires level 3 PPE, incorporating a coverall, a full gown, an apron, surgical latex gloves, respiratory protection equipment, such as an air-purifying respirator or N95 masks with minimum FFP2, and face and head covers, such as goggles and face shields, boots, and boot covers.[2,3,18,23,24]

Table 3. FFB preparation in patients with COVID-19[2,3,16,18,23,24]

Patient preparation
1. Informed consent of FFB
2. Clinical indication is appropriate (prioritizing emergency cases)
3. Assessment and mitigation preparation of complication risk based on medical history
4. Abstinence from foods and liquids for 2–5 hours, except in emergencies
5. Non-intubated patients should wear a surgical mask, and nasal introduction is recommended
6. Diagnostic test (radiology, ECG, blood test, hemostasis function) is screened as indicated
Equipment and medication preparation
1. Equipment and medication preparation generally focus on the disinfection and sterilization process and disposable kits or items specifically used for patients with COVID-19
2. Cleansing and storing bronchoscopes for patients with COVID-19 should be performed separately from non-COVID-19 bronchoscopes
3. Bronchoscope unit functions properly
4. FFB accessories unit has been disinfected and confirmed for its readiness
5. Suction unit functions properly and is connected to a sterile mucus-collecting pot
6. Equipment is sterile (linen, specimen pot, lidocaine and normal saline container/bowl, 20 mL syringe)
7. Interventional procedures and specimen fixation tools are available
8. Hemodynamic monitoring device is disinfected and properly functioning
9. Oxygen supplementation is applied, with FiO_2 100% preoxygenation
10. Drugs, lidocaine gel, IV fluid and access, and an emergency cart are available
11. Invasive procedures should be performed separately from the bronchial wash or BAL
12. The procedure is completed swiftly and appropriately (quick in, quick out)
Facility and personnel preparation
1. The procedure is conducted inside an isolation room with negative pressure AIIR and room temperature between 20°C and 26°C and a humidity range between 30% and 60%
2. Limiting the number of personnel involved in the procedure
3. All healthcare personnel should properly be trained for infection control and PPE and perform PPE donning and doffing according to standard protocol with level 3 PPE

AIIR = airborne infection isolation room; BAL = bronchoalveolar lavage; ECG = electrocardiogram; FiO_2 = inspired oxygen fraction; PPE = personal protective equipment

SUMMARY

Diagnostic and therapeutic FFB procedure for patients with COVID-19 is a double-edged sword. It is critical if indicated and may provide clinical advantages, yet it requires thorough consideration and adherence to infection control standards. The procedure suggests conditions associated with airway obstruction, impairing respiratory ventilation and alveolar diffusion, particularly in central airway emergencies. Endobronchial visual finding for patients with COVID-19 includes hyperemic endobronchial surface, clear secretion, purulent discharge, mucus plug, and blood clot. The absolute contraindication of the procedure is persistent desaturation throughout the procedure. Various relative contraindications require preparation and medication before, during, and after the procedure. Patient, equipment, personnel, and facility preparation before FFB procedure in patients with COVID-19 emphasizes modification and application of infection control standards to prevent infection transmission between patient and doctor and contamination of equipment.

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Conflict of Interest

None declared.

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Authors' Contributions

Principal manuscript writer and data collector: IPP. Co-investigators and data collectors: HB, IM, and NP. Manuscript reviewers: DS, P, and KT. Manuscript writers and proofreaders: TK and AF.

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