










Early complications in flexible bronchoscopy at a university hospital

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ABSTRACT

Objective: To analyze the complications related to flexible bronchoscopy (FB) and its collection procedures in outpatients and inpatients with various lung and airway diseases treated at a university hospital. **Methods:** This was a retrospective analysis of complications occurring during or within 2 h after FB performed between January of 2012 and December of 2013, as recorded in the database of the respiratory endoscopy department of a hospital complex in the city of São Paulo, Brazil. **Results:** We analyzed 3,473 FBs. Complications occurred in 185 procedures (5.3%): moderate to severe bleeding, in 2.2%; pneumothorax, in 0.7%; severe bronchospasm, in 0.8%; general complications (hypoxemia, psychomotor agitation, arrhythmias, vomiting, or hypotension), in 1.6%; and cardiopulmonary arrest, in 0.03%. There were no deaths related to the procedures. Specifically, among the 1,728 patients undergoing biopsy, bronchial brushing, or fine-needle aspiration biopsy, bleeding occurred in 75 (4.3%). Among the 1,191 patients undergoing transbronchial biopsy, severe pneumothorax (requiring chest tube drainage) occurred in 24 (2.0%). **Conclusions:** In our patient sample, FB proved to be a safe method with a low rate of complications. Appropriate continuing training of specialist doctors and nursing staff, as well as the development of standardized care protocols, are important for maintaining those standards.

Keywords: Bronchoscopy/adverse effects; Biopsy/adverse effects; Pneumothorax.

INTRODUCTION

Flexible bronchoscopy (FB) is a minimally invasive procedure that since its introduction in the 1960s has been widely used for direct visualization of the tracheobronchial tree in order to diagnose and treat lung and airway diseases. Although there have been reports of complications, the complication rate is low (ranging from 0.8% to 6.8%), confirming the safety of FB when preventive measures are employed, including adequate patient preparation, risk-benefit assessment, and the use of standardized protocols during the procedure.⁽¹⁻³⁾

Complications are generally due to sedation and topical anesthesia,⁽⁴⁾ but they can also be due to the following: introduction of the bronchoscope into the airway; sample collection procedures, such as BAL, endobronchial biopsy (EBB), transbronchial biopsy (TBB), and bronchial brushing (BB); and patient clinical status.^(4,5) Most complications occur during or within 2 h after the procedure, and only a minority of patients require hospitalization.^(4,6-8) Serious adverse effects requiring interruption of the procedure, including tension pneumothorax, heart/respiratory failure, and death, are rare and are generally related to the severity of underlying heart or lung disease, as well as to severe central airway obstruction.^(2,7,9) The objective of the present study was to analyze early complications of

FB in patients with various lung and airway diseases treated at a university hospital.

METHODS

We retrospectively analyzed complications occurring during or within 2 h after FB performed between January of 2012 and December of 2013, as recorded in the database of the Respiratory Endoscopy Department of the University of São Paulo School of Medicine *Hospital das Clínicas* Heart Institute, located in the city of São Paulo, Brazil. The present study was approved by the local research ethics committee (Protocol no. 4358/16/024).

All FBs were performed with patients receiving continuous monitoring (cardiac monitoring, noninvasive blood pressure monitoring, and oximetry) and supplemental oxygen via nasal cannula. Intravenous sedation was provided primarily with fentanyl and midazolam (with or without propofol), patients being maintained with mild or moderate sedation depending on the case.

We examined patient age, sex, and class (inpatient or outpatient), as well as indications for FB, sample collection methods, and potential complications.

Complications were divided into general complications and complications associated with collection procedures such as EBB, laryngeal biopsy, TBB, BB, and fine-needle

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aspiration biopsy (FNAB). General complications included persistent hypoxemia (an SpO₂ of < 90% throughout the procedure and in the postprocedural period, difficult to control despite raising the mandible and FiO₂), psychomotor agitation, arrhythmias, vomiting, bronchospasm, and cardiopulmonary failure. Specific complications included bleeding (during any sample collection procedure) and pneumothorax (during TBB only). Moderate to severe bleeding was defined as bleeding requiring interruption of the procedure or hemostatic measures such as wedging the flexible bronchoscope into the bleeding bronchial segment, using cold 0.9% saline, using an epinephrine solution (1:20,000), moving the patient to a lateral decubitus position with the bleeding side down, inserting a balloon catheter (bronchial blocker), and performing selective intubation to isolate the bleeding lung. A diagnosis of pneumothorax was made on the basis of clinical symptoms (pleuritic chest pain and dyspnea, with or without decreased SpO₂) and chest X-ray findings consistent with pneumothorax.

Before undergoing FB, all patients were informed of the risks of the procedure. They remained under observation until discharge by the medical and paramedical staff within 2 h after the procedure.

Statistical analysis

All statistical analyses were performed with the IBM SPSS Statistics software package, version 19.0 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were used in order to estimate the frequencies of the study variables. The only continuous variable, age, was summarized as a mean with standard deviation. The Student's t-test was used in order to analyze parametric data (age), and Pearson's correlation coefficient was used in order to correlate nonparametric data. The level of significance was set at 5% ($p < 0.05$).

RESULTS

We analyzed 3,473 FB procedures performed in outpatients, ward patients, ICU patients, ER patients, and operating room patients in our hospital. Endobronchial ultrasound, simple laryngoscopy, and therapeutic rigid bronchoscopy procedures were not included in the analysis.

The mean age of the patients was 52.58 ± 17.33 years, with a predominance of males (59.2%). In our patient sample, 2,061 (59.3%) were outpatients, 935 (27.0%) were ward patients, and 477 (13.7%) were ICU or ER patients (Table 1).

As can be seen in Table 1, reasons for undergoing FB included suspected infection, in 34.8%, suspected neoplasia, in 16.2%, post-lung transplant follow-up/surveillance, in 8.9%, esophageal cancer staging, in 7.6%, investigation/management of hemoptysis, in 5.4%, investigation of interstitial lung disease, in 4.6%, postoperative thoracic surgery, in 1.6%, and other reasons, in 20.9%.

A total of 3,701 sample collection procedures were performed; BAL was the most commonly performed procedure, followed by TBB and BB. Other procedures, including BB, FNAB, and laryngeal biopsy, were performed in 132 patients (3.6%). These results are shown in Table 2.

Complications occurred during or within 2 h after FB in 185 (5.3%) of the 3,473 procedures performed. Most of the complications occurred in patients undergoing sample collection procedures, particularly biopsy ($n = 99$; 53.5%).

General complications (hypoxemia, psychomotor agitation, arrhythmias, and vomiting) occurred in 56 patients (1.6%). Bronchospasm requiring interruption of the procedure occurred in 29 (0.8%). Cardiopulmonary arrest occurred in 1 (0.03%). There were no deaths related to the procedures. Bleeding occurred in 2.2% of the FBs, and pneumothorax occurred in 0.7%. Specifically, among the 1,728 patients undergoing a sample collection procedure (EBB, TBB, BB, or FNAB), moderate to severe bleeding occurred in 75 (4.3%). Among the 1,191 patients undergoing TBB, pneumothorax occurred in 24 (2.0%), all of whom required chest tube drainage. All complications are described in Table 2.

Complications were more common in patients > 50 years of age than in those ≤ 50 years of age (6.1% vs. 3.9%; $p = 0.002$). In addition, complications were most common in patients undergoing FB for the following reasons: investigation of interstitial lung disease, suspected neoplasia, suspected bronchopulmonary infection, postoperative thoracic surgery, investigation of hemoptysis, post-lung transplant follow-up/surveillance, and esophageal cancer staging. In patients undergoing FB for other reasons, including difficult airway management (difficult intubation or extubation), decannulation, burns, foreign body aspiration, and evaluation of airway malacia/fistula/stenosis, complications occurred in 2.8% (Table 1).

As can be seen in Table 1, there were no significant differences in the frequency of complications between outpatients and inpatients (including ward patients, ICU patients, and ER patients).

DISCUSSION

FB is a minimally invasive procedure that is used in various lung and airway diseases.^(5,10,11) The reported overall complication rate varies, being higher when biopsy is performed.^(5,12,13) To our knowledge, this is the first study in Brazil to report the overall complication rate of FB in a large number of patients, the reported rate (5.3%) being within the expected range.^(5,12,13) These data are important because of the need to improve patient safety by preventing or reducing risks, especially in a teaching hospital setting. In addition, it is important to know the risks of the procedure in order to develop informed consent forms that clearly explain to patients and their families the expected complication rate.

Table 1. Characteristics of the study patients (N = 3,473), reasons for undergoing flexible bronchoscopy, and complications of the procedure.^a

Characteristic	Complications		p
	No (n = 3,288)	Yes (n = 185)	
Age, years	52.36 ± 17.83	56.45 ± 15.75	0.002
Sex			
Male (n = 2,056)	1,965 (95.6)	91 (4.4)	0.004
Female (n = 1,417)	1,323 (93.4)	94 (6.6)	
Patient class			
Outpatient (n = 2,061)	1,939 (94.1)	122 (5.9)	NS
Ward patient (n = 935)	882 (94.3)	53 (5.7)	
ICU/ER patient (n = 477)	467 (98.0)	10 (2.0)	
Reason for undergoing flexible bronchoscopy			
Interstitial lung disease (n = 159)	142 (89.3)	17 (10.7)	NS
Neoplasia (n = 564)	508 (90.1)	56 (9.9)	
Infection (n = 1,207)	1,127 (93.4)	80 (6.7)	
Postoperative thoracic surgery (n = 57)	55 (96.5)	2 (3.5)	
Hemoptysis (n = 187)	183 (97.9)	4 (2.1)	
Lung transplantation (n = 308)	303 (98.4)	5 (1.6)	
Esophageal cancer staging (n = 264)	263 (99.6)	1 (0.4)	
Other (n = 727) ^b	707 (97.2)	20 (2.8)	

NS: not significant. ^aValues expressed as n (%) or mean ± SD. ^bDifficult intubation/extubation, evaluation of airway malacia/fistula/stenosis, atelectasis, decannulation, burns, and foreign body aspiration.

Table 2. Diagnostic procedures performed during flexible bronchoscopy and complications thereof.

	Procedure	n (%)
Diagnostic procedures (n = 3,701)	BAL	1,973 (53.3)
	Transbronchial biopsy	1,191 (32.2)
	Endobronchial biopsy	405 (10.9)
	Bronchial brushing	37 (1.0)
	Fine-needle aspiration biopsy	62 (1.7)
	Laryngeal biopsy	33 (0.9)
Complications (n = 185)	Bleeding ^a	75 (4.3)
	Pneumothorax ^b	24 (2.0)
	Bronchospasm ^c	29 (0.8)
	Other ^d	57 (1.63)

^aAmong the 1,728 patients undergoing biopsy. ^bAmong the 1,191 patients undergoing transbronchial biopsy.

^cAmong the 3,473 patients undergoing flexible bronchoscopy. ^dHypoxemia, arrhythmias, cough, agitation, need for endotracheal intubation, and cardiopulmonary arrest.

In the present study, the most common complications were bleeding and pneumothorax. Other complications, such as bronchospasm, hypoxemia, hypotension, arrhythmias, and cardiopulmonary arrest, were less common, being related to respiratory and cardiovascular comorbidities, as well as to the passage of the bronchoscope through the airway and the drugs used for sedation and anesthesia.

We found no significant differences in the complication rates across patients, regardless of their origin or underlying respiratory disease. However, because this was a retrospective observational study, we used no severity scales or complication prediction scores; in addition, we did not analyze single comorbidities. Nevertheless, we found that patients with interstitial lung disease, cancer, or respiratory infection had a higher number of complications. Given these findings

and the profile of our patients, we believe that hospitalization is required for patients with underlying hypoxemia and those at risk of hypoxemia or other types of decompensation during or after the procedure, including patients with COPD, severe asthma, and heart disease. The primary goal of this approach is to perform a clinical evaluation of patients before the procedure and minimize procedure cancellation rates.

The complication rate was low in our study because FB is performed in accordance with international standards at our institution. In addition, all FB procedures are performed by qualified professionals trained and with technical experience in performing FB and in diagnosing and managing complications, supervision being mandatory when a physician in training performs the procedure.⁽³⁾ Physician training

in FB should also focus on the periods before and after the procedure.

Adequate patient preparation prior to FB is essential for identifying and preventing complications.⁽³⁾ Careful history taking is required in order to identify clinical contraindications to FB, including signs of respiratory failure (including hypoxemia, tachypnea, and hypercapnia), bronchospasm during the procedure, decompensated arrhythmias, and recent hemodynamic instability or myocardial infarction (less than six weeks before the procedure).^(4,5,10,11,14,15) All of these parameters should be interpreted within the clinical scenario of individual patients, the risks and benefits of the procedure being weighed.

Critically ill patients undergoing diagnostic FB require ventilatory support, multidisciplinary care, and full monitoring in order to minimize risk and facilitate early identification of complications, thus allowing timely management. In COPD or asthma patients experiencing bronchospasm, it is important to control the underlying disease before the procedure is performed.^(4,15) In individuals at high risk of developing bronchospasm during or shortly after FB, a β_2 agonist and an intravenous corticosteroid can be administered before the procedure. If BAL is required, 0.9% saline at 37°C should be used in order to prevent bronchospasm.⁽¹⁶⁾

To prevent aspiration of gastric contents, patients undergoing FB at our institution are required to abstain from solid/semisolid foods for 8 h before the procedure; breast milk for 4 h before the procedure; and a clear or strained liquid diet for 2 h before the procedure. However, in intubated patients who are on mechanical ventilation and have a nasogastric feeding tube in place, fasting times can vary depending on how urgent the need for FB is and should be discussed on a case-by-case basis. In such patients, the following is recommended: better control of endotracheal tube cuff inflation pressure, fasting before the procedure, and nasogastric tube drainage.^(4,15,17) In our study, there were no cases of bronchial aspiration during or after FB.

Before FB, it is essential to inquire about drug allergies, complications of previous surgeries or procedures, and the presence of cardiovascular diseases, endocrine disorders, and respiratory comorbidities, including the drugs and doses used.^(1,12,15)

Because of the risk of bleeding, coagulation disorders and the use of anticoagulants should be carefully examined in patients requiring biopsy, BB, or FNAB during FB. Clinical history taking is important to identify signs of active bleeding. In addition, antiplatelet and anticoagulant drug use should be discontinued for as long as recommended, adjustments being required for patients with hepatic or renal failure. A platelet count $> 50,000/\text{mm}^3$ and a prothrombin time/international normalized ratio of < 1.5 are considered safe in patients undergoing biopsy. A platelet count

of $< 20,000/\text{mm}^3$ is a contraindication to FB, even without biopsy.⁽⁴⁾ Such patients should undergo platelet replacement therapy before undergoing FB.^(4,9,14,18-21) Other laboratory data, such as urea and creatinine levels, should be assessed before biopsy.

In our study, all patients received supplemental oxygen (1-5 L/min, as needed) during and after FB. In intubated ICU patients, FiO_2 was set to 100% during the procedure, other ventilator settings being adjusted as needed.^(4,15) Thus, the rate of oxygen saturation decrease was low in our study.

Sedatives and their doses should be chosen on a case-by-case basis. The sedatives used in our study included midazolam, fentanyl citrate, and, in some cases, propofol.⁽⁴⁾ The medical staff should receive appropriate training in dosing and managing potential complications.

According to Brazilian Federal Medical Council Resolution no. 2,174/2017, a second physician should be present in the examination room, being responsible for administering sedation. In patients at risk of cardiovascular or respiratory decompensation, FB can be performed with endotracheal intubation in the ICU (if necessary).

It is also important to be familiar with benzodiazepine and opioid antagonists (flumazenil and naloxone, respectively). They can have adverse effects and should only be used in specific situations, in order to prevent complications such as convulsion, psychomotor agitation, and respiratory distress.⁽¹²⁾ In addition, naloxone use can result in pain, especially in cancer patients receiving treatment with opioids.

With regard to the use of topical lidocaine for cough control during FB, the maximum total dose, including all doses of the three formulations (i.e., gel, 2%; spray, 10%; and liquid, 2%), should be 7-9 mg/kg.^(5,12,15) Care must be taken when using lidocaine in elderly patients and patients with heart failure, as well as in those with upper/lower airway candidiasis, infection, or inflammation, because of the possibility of increased absorption and, consequently, toxicity. Major complications of excessive lidocaine include nausea, vomiting, metallic taste, mental confusion, cardiac arrhythmias, and seizures.

In patients undergoing biopsy, it is important to adopt measures to facilitate the management of bleeding complications and minimize the risk of pneumothorax. It is difficult to quantify bleeding risk in patients undergoing FB, and reports of bleeding during FB are very subjective. Hemostatic measures such as wedging the flexible bronchoscope into the bleeding bronchial segment, using cold 0.9% saline, using an epinephrine solution (1:20,000), moving the patient to a lateral decubitus position with the bleeding side down, and inserting a balloon catheter (in cases of bleeding that is massive or difficult to control with the aforementioned measures) are essential and possible to perform.⁽⁴⁾ In our study, the first four measures were adopted during diagnostic FB. Future studies

should quantify bleeding risk in patients undergoing FB, correlating bleeding with bronchoscopic measures to manage it, as well as with clinical worsening after the procedure.

Whenever possible, fluoroscopy can be used in order to guide biopsy of lung nodules and infiltrates, improving safety in patients with pulmonary emphysema and at increased risk of pneumothorax.⁽⁴⁾ However, there is a lack of consistent data regarding other patient groups. Given that fluoroscopy is not available for all FB procedures performed at our institution, we did not analyze the role of fluoroscopy in guiding bronchoscopic sample collection. Nevertheless, the rate of pneumothorax in the present study (2%) is consistent with that in the literature (1-6%).^(1,3,22,23)

For bronchoscopists, appropriate continuing training is essential to improve knowledge and practice, including management of complications.^(1,12,13,15,24) Training is also essential for paramedical and nonmedical staff. Resuscitation equipment and adequate physical space are also important.

With regard to postprocedure care, patients should be monitored in the recovery room until regaining full consciousness.⁽²⁴⁾ At discharge, patients and their companions should be alerted to the possibility

of accidental falls, fever, bleeding, and symptoms suggestive of pneumothorax.⁽⁴⁾ Minor bleeding can occur 2-3 days after the procedure, rest therefore being important. In cases of persistent bleeding, patients are advised to return for further evaluation. It should be noted that pneumothorax can go unnoticed on examination at discharge. Patients experiencing chest pain or dyspnea should return for medical evaluation and, if necessary, a chest X-ray.

Imaging tests are reserved for patients with clinical symptoms suggestive of pneumothorax.^(4,6-8,10) Although it has been reported that only a minority of cases require intervention,⁽¹⁾ nearly all cases of pneumothorax in our study required chest tube drainage.

In order to develop best-care practices that prioritize patient safety and health care efficiency, it is essential to know the complication rates at a given medical institution. Our study showed low rates of early FB complications. However, it has limitations inherent to its retrospective nature, including the use of database records, written reports of FB procedures, and complication notes, all of which are subject to problems such as missing or incorrectly recorded data. Therefore, the complication rates might have been underestimated. Prospective studies are needed in order to address this issue.

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