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Safety of Diagnostic Bronchoscopy in Patients with Pulmonary Hypertension

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Key Words

Pulmonary hypertension · Bronchoscopy · Transbronchial biopsy · Hemorrhage

Abstract

Background: Patients with pulmonary hypertension (PH) are considered to be at risk for complications associated with flexible bronchoscopy (FB). Although previous reports suggest that transbronchial biopsies increase the risk for hemorrhage in this population, data are limited to survey analyses and isolated reports. ***Objectives:*** It was the aim of this study to describe our experience with FB and to determine if bronchoscopic procedures are associated with adverse events in this population. ***Methods:*** We conducted a retrospective review of patients with diagnosis of PH who underwent FB at the Cleveland Clinic between 2002 and 2005. Patients without PH who underwent FB by the same pulmonary physician were used as controls. ***Results:*** A total of 90 patients, PH (n = 45) versus controls (n = 45), were included. The mean systolic pulmonary artery pressure in patients with PH was 58 ± 7 mm Hg. Patients with PH had higher oxygen requirements at baseline (FiO_2 0.42 vs. 0.3%; p = 0.01). The total number of procedures was similar between the groups (95 vs. 102). Procedures performed were bronchoalveolar lavage (21 vs. 13), transbronchial biopsies (24 vs. 32) and transbronchial needle aspiration (7 vs. 6). There were no hemodynamic complications or episodes of respiratory failure associated with the procedures. None of the patients had significant hemorrhage and only 2 developed mild bleeding which resolved spontaneously. Similarly, none required hospitalization or transfer to an intensive care unit. ***Conclusions:*** FB can be performed safely in patients with mild to moderate PH. Transbronchial biopsies are not associated with worsening hypoxemia or an increased risk of hemorrhage. Prospective studies with hemodynamic measurements are necessary to confirm these findings.

Introduction

Flexible bronchoscopy (FB) is one of the most common invasive procedures performed by pulmonologists [1]. Typically performed under topical anesthesia and conscious sedation, the procedure is considered to be safe, effective and well tolerated in patients with a wide variety of pulmonary diseases [2]. Complications associated with the procedure are rare and studies have estimated an incidence of 0.5–4% [3]. The most commonly recognized complications include hypoxia, bleeding, bronchospasm, cardiac dysrhythmias, pneumothorax, and vagal reactions [4]. Several conditions increase the risk of complications including pre-existent hypoxemia, use of mechanical ventilation, uremia, profound thrombocytopenia, coagulopathy and pulmonary hypertension (PH) [5].

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Studies have shown that patients with PH are at increased risk for adverse hemodynamic events after noncardiac surgery [6] and at low risk for invasive procedures that require intravenous sedation [7]. The risk appears to be highest among patients with severe PH [8]. FB has been shown to affect central hemodynamics, including a significant increase in pulmonary capillary wedge pressure during bronchial suctioning [9]. Furthermore, an acute pulmonary hypertensive response has been described in mechanically ventilated patients undergoing FB [10]. It is unknown if these hemodynamic alterations result in clinically significant adverse events.

Given these findings, patients with PH are generally considered to be at an increased risk of complications with FB, particularly if transbronchial lung biopsies (TBLB) are performed. Among pulmonary physicians, there is a general notion that PH increases the risk of bleeding, although available reports to support this concept are scant and contradictory [11]. Furthermore, there is no consensus regarding levels of pulmonary artery pressure (PAP) considered to be safe for invasive diagnostic interventions such as TBLB or transbronchial needle aspiration.

We conducted this study to assess the safety of FB in patients with PH and to study the occurrence of complications associated with different diagnostic bronchoscopic procedures.

Materials and Methods

The study was approved by the institutional review board. We performed a review of computerized hospital records to identify patients with PH who underwent bronchoscopy between January 2002 and December 2005. A retrospective review of medical records and bronchoscopy reports was performed to investigate the occurrence of complications.

Study Subjects

The study included patients with a diagnosis of PH defined as (1) mean PAP (mPAP) >25 mm Hg measured by right heart catheterization (RHC), or (2) right ventricular systolic pressure (RVSP) >40 mm Hg estimated by Doppler echocardiography and clinical evidence of right heart failure. Patients that did not meet criteria for PH and who underwent bronchoscopy by the same physician within 48 h of the study patients were used as controls. Patients were matched by duration of bronchoscopy and number of procedures performed.

Outcome Measures

The primary outcome was the incidence of complications after FB. Complications were defined as hypoxemia (SpO_2 <90% and need of supplemental oxygen within 30 min of completed procedure), hypotension (mean arterial pressure <60 mm Hg or systolic blood pressure <90 mm Hg for more than 5 min and/or need for administration of intravenous solution or vasopressors), cardiac dysrhythmias (new onset of arrhythmia or worsening of underlying arrhythmia that caused hemodynamic instability or required urgent intervention), bleeding, and death.

The amount of bleeding was estimated as: no bleeding – minimal bleeding that does not require suctioning; mild bleeding – the need to continually suction the airways; moderate bleeding – the need to wedge FB in the segment involved; severe bleeding – the need for additional interventions or transfusion.

Procedural Conduct

All procedures were performed at the outpatient bronchoscopy suite of the Pulmonary Department of the Cleveland Clinic. Fluoroscopy was available for all procedures when needed. FB was performed by a pulmonary fellow under the supervision of a staff physician. Prior to the procedure, patients required evaluation by a clinician to determine hemodynamic stability and at least 6 h of fasting. Oxygen was administered to all patients to ensure SpO_2 >90% prior to the introduction of the bronchoscope. Continuous pulse oximetry, electrocardiogram and noninvasive blood pressure monitoring were obtained throughout the procedure. Sedation was achieved using midazolam and morphine sulfate (fentanyl was used in patients with a history of morphine allergy). Topical anesthesia was obtained using 2% lidocaine at the discretion of the physician up to a maximum of 600 mg.

Interventions during FB included bronchoalveolar lavage, endobronchial brushings, TBLB, endobronchial biopsies and transbronchial needle aspiration. These procedures were performed as deemed necessary by the staff physician present.

Statistical Analysis

Results are expressed as the mean ± SD for continuous variables. Qualitative data are expressed as the percentage of patients with a 95% confidence interval. Nominal variables were compared with Pearson's χ^2 or Fisher's exact test. Continuous outcome variables were compared using Student's t test or rank-sum tests as appropriate. Statistical significance was defined as $p < 0.05$. Statistical analysis was performed using a statistical software package (SPSS, version 13.0; SPSS Inc., Chicago, Ill., USA).

Results

Forty-five consecutive patients with PH were included in the study (group A). An additional 45 patients without clinical or echocardiographic evidence of PH were included as controls (group B). Baseline demographics were similar between the groups. The median age was 63 ± 14 versus 58 ± 16 years, respectively (p = 0.12). The majority of patients were of Caucasian descent (82%) and male gender (55%). Causes of PH varied: idiopathic pulmonary arterial hypertension (n = 15), interstitial lung disease (n = 14), chronic obstructive pulmonary disease (n = 11), left heart disease (n = 4) and sarcoidosis (n = 1).

Table 1. Baseline characteristics of patients with PH

Parameters	Patients, n	Mean ± SD
Age, years		62.8 ± 14.5
Gender		
Male	25	
Female	20	
Race		
White	37	
African American	8	
Severity of PH by RVSP, mm Hg		57.9 ± 15.7
Mild (40–50 mm Hg)	16	44.5 ± 3.6
Moderate (51–60 mm Hg)	13	54.6 ± 3.7
Severe (>60 mm Hg)	14	76.3 ± 13.3
RHC	13	
mPAP, mm Hg		45.5 (14.9)
PCWP, mm Hg		17.1 (7.2)
Cardiac index, l/min/m^2		2.7 (1.8)
PVR, Wood units		4.7 (1.9)
NYHA class		
I	15	
II	13	
III	10	
IV	7	
BNP, ng/l	24	351.9 (448)
6MWT	18	
Distance, m		230 (102)
SpO_2, % at rest		90.4 (7)
SpO_2, % lowest		87.2 (6)
O_2 needed, l/min		5.9 (3)

Figures in parentheses are SD. PCWP = Pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; NYHA = New York Heart Association; BNP = brain natriuretic peptide; 6MWT = 6-min walk test.

Table 2. PH versus controls: summary of indications and diagnostic interventions[1]

Parameters	Group A	Group B
Age, years	62.8 ± 14.1	58.1 ± 15.6
Males	25	27
Caucasians	37	40
Indications		
Pulmonary infiltrates	23	13
Hemoptysis	8	3
Lung mass	6	14
Airway evaluation	5	3
Shortness of breath	2	1
Fever	1	1
Surveillance[2]	0	9
Cough	0	1
Duration of FB[3], min	20.8 ± 12	25.7 ± 11
Midazolam, mg	11.2 ± 2.3	10.7 ± 2.7
Morphine, mg	10.4 ± 1.6	11.6 ± 2.4
Procedures[4]		
BAL/washings	15	8
BAL/brush ± EBB	6	5
TBLB	17	26
TBLB + TBNA	3	2
Multiple (TBLB + TBNA + brush)	4	4
Total number of TBLB	24	32
Complications	7 (15.6)	4 (8.8)

Figures in parentheses are SD. BAL = Bronchoalveolar lavage; EBB = endobronchial biopsy; TBNA = transbronchial needle aspiration.

[1] All comparisons, p = not significant.

[2] Lung allograft recipients;

[3] p = 0.06.

[4] Number of patients according to different bronchoscopic procedures.

Hemodynamics and baseline characteristics of patients with PH are depicted in table 1. The mean RVSP for group A was 58 ± 7 mm Hg. RHC data were available in 13 patients (mPAP was 43 ± 9 mm Hg). Indications and summary of interventions are described in table 2. There was no difference in need for sedative agents, topical anesthesia or duration of the procedure between the 2 groups. Vital signs as well as oxygen requirements before, during and after the procedure are described in table 3. Patients in group A had higher oxygen requirements, respiratory rate and heart rate at baseline. There was no statistically significant difference in noninvasive hemodynamics between the groups before or after the procedure.

Complications were uncommon and similar between the groups. Fifty-six patients underwent TBLB. More patients underwent TBLB in the control group, although this difference was not statistically significant (24 vs. 32; p = 0.12); there were no episodes of moderate or significant hemorrhage, and only 2 patients developed mild bleeding (both in group A). Table 4 describes complications associated with TBLB according to PH severity. Only 4 patients (8.9%) in group A developed hypoxemia compared with 3 (6.7%) among the controls. Hypoten-

sion was rare (1 patient in each group). No patients developed hemodynamically significant dysrhythmias. There were no deaths attributable to the procedure. All the patients who underwent FB in the bronchoscopy suite were discharged approximately 2 h after the procedure was finished and none required hospitalization or transfer to an intensive care unit.

Table 3. Noninvasive monitoring during FB

Parameters	Group A	Group B	p value
Before the procedure			
SpO_2, %	96.3 ± 3.2	97 ± 2.4	0.16
FiO_2, %	0.42 ± 0.04	0.29 ± 0.1	0.001
RR, breaths/min	20.7 ± 4.1	18.9 ± 2.3	0.02
HR, beats/min	88.9 ± 18.8	82.5 ± 14	0.07
Systolic BP, mm Hg	132.4 ± 20.6	139.3 ± 21.7	0.15
Diastolic BP, mm Hg	73.6 ± 15	79.8 ± 13.5	0.05
At the end of the procedure			
SpO_2, %	97 ± 2.9	97.8 ± 2	0.18
FiO_2, %	0.57 ± 0.3	0.45 ± 0.3	0.10
RR, breaths/min	20.7 ± 3.8	19.8 ± 3.2	0.21
HR, beats/min	89.9 ± 22.3	87.3 ± 18.4	0.53
Systolic BP, mm Hg	130 ± 21	135.9 ± 24	0.27
Diastolic BP, mm Hg	72.5 ± 15	79.7 ± 12.1	0.025
1–2 h after the procedure			
SpO_2, %	95.9 ± 3	96.7 ± 2.5	0.20
FiO_2, %	0.38 ± 0.20	0.27 ± 0.17	0.0058
RR, breaths/min	20.3 ± 3.4	19 ± 2.5	0.06
HR, beats/min	87.5 ± 19.3	81 ± 14.4	0.08
Systolic BP, mm Hg	122.9 ± 17.7	129.1 ± 21	0.16
Diastolic BP, mm Hg	68.8 ± 14.4	74.5 ± 13.4	0.10

Data are mean ± SD. SpO_2 = Pulse oximetry saturation; FiO_2 = inspired fraction of oxygen; RR = respiratory rate; HR = heart rate; BP = blood pressure.

Discussion

The main findings of this study are that FB can be performed safely in patients with PH, and that bronchoscopic diagnostic procedures, including transbronchial biopsies, are not associated with an increased risk of hemorrhage. Importantly, patients with PH do not have a high risk of cardio-respiratory complications such as hypoxemia, hypotension or cardiac arrhythmias as a result of FB.

Bronchoscopy is considered a safe procedure associated with a very low complication rate and negligible mortality [2]. Several studies and survey analyses have estimated the rate of major complications among experienced pulmonary physicians to be <2% [12, 13]. Moreover, reports have suggested that FB can be performed safely in patients considered at risk for complications, such as patients with chronic obstructive lung disease, asthma and thrombocytopenia, as well as after myocardial infarction [14].

Several features present in patients with PH are thought to increase the risk of complications with FB. For example, chronic venous PH may cause dilation of submucosal bronchial veins and their plexuses [15]. The presence of elevated pulmonary capillary pressure has been related with significant hemorrhage after transbronchial biopsies [5, 16, 17]. Additionally, patients with severe PH often have right ventricular dysfunction and may be at risk for cardiac ischemia, arrhythmias and hypotension [12, 18–20]. Finally, FB can also be associated with transient hypoxemia [21] which may be a particular concern in patients with PH who may be hypoxic at baseline and frequently have poor cardio-respiratory reserve [22].

In our study, the majority of the patients (60%) had evidence of moderate to severe PH (RVSP >50 mm Hg),

Table 4. Complications associated with TBLB according to PH severity

Parameters	PH	TBLB	Complications
Clinical severity by NYHA			
No evidence of CHF	8		none
I	7		1 minimal bleeding
II	13		1 hypoxia
III	10		1 hypotension
IV	7		3 hypoxia, 1 minimal bleeding
Severity of PH by RVSP			
Mild (40–50 mm Hg)	16	8	1 hypoxia, 1 minimal bleeding
Moderate (51–60 mm Hg)	13	10	2 hypoxia, 1 hypotension
Severe (>60 mm Hg)	14	6	1 hypoxia, 1 minimal bleeding

NYHA = New York Heart Association; CHF = congestive heart failure.

and more than a third had a poor functional class (New York Heart Association class III–IV). Despite evidence of PH severity, no major complications occurred: there were no incidents of moderate or severe hemorrhage, none of the patients developed refractory hypotension or hemodynamic instability, there were no fatalities, and none required hospitalization or developed respiratory failure.

The rate of minor complications in patients with PH was higher than in the control group; nevertheless, this difference did not reach statistical significance. Use of sedatives may have contributed to the development of minor complications such as hypoxemia or hypotension. One study showed an 8% incidence of transient hypoxia associated with the use of midazolam [23]. Similarly, and despite the use of higher doses of sedatives, we found a low incidence of transient hypoxemia (9%) in patients with PH. Although the rate of minor complications is high compared with prior survey analyses and retrospective reviews [3, 4, 24, 25], the discrepancy between our results and prior findings may be a consequence of differences of the definition of complications and ascertainment bias across studies rather than an effect associated with PH.

Significant bleeding after FB is infrequent and occurs more commonly after transbronchial biopsies. It has been suggested that PH is associated with an increased risk of hemorrhage and should be considered a contraindication for TBLB [26]. Evidence to support the concept of elevated pressure at the capillary level increasing the risk of bleeding in patients with PH is limited. Despite the lack of available studies, a survey reported that up to 40% of pulmonary physicians considered PAPs of ≥40 mm Hg unsafe for TBLB [24].

Schulman et al. [27] prospectively studied the occurrence of bleeding in heart transplant recipients that underwent TBLB for the evaluation of parenchymal lung disease. The incidence of moderate hemorrhage (25–100 ml) was 15% when mPAP was >16 mm Hg. Other reports have found lower rates of hemorrhage. In an animal model of induced PH, an increase in PAPs (12–33 mm Hg) did not increase the risk of bleeding [28]. Morris et al. [29] investigated the risk for hemorrhage in 21 patients with interstitial lung disease and echocardiographic evidence of PH who underwent TBLB and found evidence of bleeding in only 1 patient.

We report a low rate of bleeding complications occurring after TBLB (8.3%) in patients with PH. A relevant observation is that TBLB was performed less frequently in patients with PH compared with controls (24 vs. 32). Unfortunately, we could not find enough documentation to explain for the difference between the groups; therefore, we cannot exclude the possibility of operator bias. Additionally, although analysis of the rate of complications related to TBLB alone did not reach statistical significance, small numbers preclude further conclusions in patients with severe PH.

FB can also be associated with cardiovascular complications such as hypotension, dysrhythmias and cardiac arrest [20, 30, 31]. A study of FB performed under topical anesthesia found significant increases in mean arterial pressure and heart rate and an 86% increase in pulmonary capillary wedge pressure; these hemodynamic changes were similar during passage through the larynx and during suctioning [9]. Hemodynamic complications after FB appear to be rare. A recent study that included more than 20,000 procedures reported an incidence of cardiac arrhythmias of 1%, including 3 deaths from cardiopulmonary arrest (0.013%) [13]. In our study, invasive hemodynamic monitoring was not performed; however, there were no episodes of arrhythmia or electrocardiographic evidence of cardiac ischemia. Similarly, despite more frequent use of oxygen at baseline, patients with PH did not develop more hypoxemia compared with controls, and none of the patients developed respiratory failure associated with the procedure.

The study has several limitations. First, data were collected retrospectively and are subject to charting errors and/or paucity of event recordings. Second, not all of the patients with echocardiographic evidence of PH underwent RHC; therefore, underestimation or overestimation of PAPs is possible. Third, definition of bleeding was subjective, and although all patients had appropriate documentation of hemorrhagic complications, we could not find information regarding the amount of blood suctioned during the procedure. Finally, we included only 6 patients with clinically severe PH who underwent TBLB; thus, the risk of hemorrhagic complications from TBLB in this group may be underestimated.

In conclusion, our study suggests that FB can be performed safely in patients with mild to moderate PH. Patients with PH were able to tolerate sedation and suctioning without hemodynamic consequences. The risk of hemorrhage does not appear to be elevated when transbronchial biopsies or transbronchial needle aspirations are performed; nevertheless, caution must be used in patients with severe PH as data are limited in this subgroup of patients. Finally, despite higher use of oxygen at baseline, patients with PH did not have an increased risk for respiratory failure or refractory hypoxemia after FB. Prospective studies with hemodynamic measurements are needed to confirm these preliminary findings.

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