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Safety of Bronchoscopy in Elderly

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Abstract Flexible bronchoscopy (FB) is a commonly performed procedure for diagnostic and therapeutic interventions of pulmonary disorders. Due to high prevalence of lung diseases especially lung cancer in the aging population, there is an increasing demand for FB in elderly patients. Flexible bronchoscopy is a well-tolerated procedure with low complication rate and mortality while providing valuable diagnostic and staging information. However, due to age-related decline in cardiopulmonary reserves and frequent presence of comorbid conditions, procedural safety is the most critical issue in any elderly patient undergoing FB. A thorough understanding of these cardiopulmonary limitations and a careful assessment of medical issues, functional status and social support are essential in every elderly patient before performing bronchoscopy. Several studies have shown that age has no major effect on procedure-related complications or tolerance to bronchoscopy even with recent addition of increasingly complex and longer procedures. Advanced age by itself is not a contraindication to bronchoscopy.

Keywords Flexible bronchoscopy · Bronchoscopy safety · Lung cancer · Elderly

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"Old age hath yet his honor and his toil." Alfred Lord Tennyson (1809–1892)

Introduction

Pulmonary disorders are highly prevalent in elderly patients [1]. Bronchoscopy is often needed for appropriate diagnosis and management of respiratory diseases in these patients. Procedural safety is the most immediate concern every time bronchoscopy is performed in elderly subjects. The following case illustrates several important issues relevant to a safe and optimal bronchoscopy in an elderly patient.

Case Report

An 81-year-old man was referred for a new 3.5×3.0 cm right lower lobe lung mass. Past medical history was significant for chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in 1 s (FEV_1) of 0.70 l (25 % of predicted), myocardial infarction (MI) needing a drug-eluting stent, type II diabetes, peripheral vascular disease, an infra-renal abdominal aortic aneurysm, extensive degenerative joint disease and chronic anxiety disorder. On echocardiogram, the ejection fraction (EF) was 40 %. The patient had chronic stable angina. He had no problems with gait, balance, or memory. He lived alone and had managed his activities of daily living with minor difficulties. He was not driving for past 2 years. His medications were inhaled tiotropium, budesonide-formoterol combination, oral metoprolol, clopidogrel, aspirin, metformin, theophylline, lorazepam, nitroglycerine, and long-term oxygen treatment at 3 L/min. Chest examination showed prolonged expiration with bilateral expiratory wheezes. Cardiovascular examination was normal. Laboratory data was unremarkable.

There was no evidence for mediastinal or extra-thoracic disease on fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET).

Many factors in our patient increase the risk of flexible bronchoscopy (FB). The patient had advanced COPD, coronary artery disease, and left ventricular dysfunction. He had resting hypoxemia and poor exercise tolerance. He was receiving clopidogrel, which increases the risk of bleeding during bronchoscopy. He had no social support and there was a serious concern about his safety at home after the procedure.

To perform bronchoscopy in an elderly patient with many co-morbid conditions is a complicated decision. At the outset, perhaps the most pressing issue at hand is the procedural safety. Although this is a valid concern, it is felt that many elderly patients are inappropriately denied the procedure due to ill-perceived safety considerations and therapeutic nihilism.

The last decade has witnessed a revolution in the field of bronchoscopy. Several advanced diagnostic techniques such as endobronchial ultrasound and electromagnetic navigation have emerged and become integral parts of everyday practice of bronchoscopy [2, 3]. There can be no question that these procedures have increased the diagnostic reach of bronchoscopy and it is clear that elderly patients stand to gain substantially from these techniques. However, application of these techniques frequently demands a longer procedure time and deeper level of sedation during bronchoscopy. In fact, many operators routinely perform these procedures under general anesthesia [4]. With the anticipated demographic changes and these evolving interventions, it has become more important than ever to meticulously analyze the safety and complications associated with FB in elderly.

In this review, we discuss the issues surrounding safety of bronchoscopy in elderly patients. We will discuss the reasons for concern, review the existing literature on this subject and provide a practical approach to improve the safety of bronchoscopy in elderly patients.

Scope of the Problem

At what age an adult becomes qualified to be called elderly or old is not well-defined. World Health Organization (WHO) considers anyone to be old after the age of 60 [5]. European Medicines Agency uses chronological age of 65 years or more to define old age [6]. Oncologists draw this line at a chronological age of more than 70 years [7]. Gerontologists have many different views [8].

Most bronchoscopists do not have much interest in this debate. Irrespective of age, every patient who requires bronchoscopy has a serious respiratory disorder that has important implication for survival and quality of life. In some circumstances, there is no choice but to perform the procedure regardless of age. For example, age is not a consideration when bronchoscopy is needed in an asphyxiating patient with foreign body inhalation [9]. Fortunately, such situations are uncommon. Usually, the need for bronchoscopy is less imminent and there is time for a detailed evaluation as well as risk assessment prior to bronchoscopy. However, in this context, it is important for the bronchoscopists to assess the functional age of a patient which requires a thorough assessment of health, medical conditions, nutrition, cognition, functional status, and psychosocial aspects instead of dwelling too much on the chronological age of the patient.

The need for bronchoscopy in elderly is expected to increase with aging of population worldwide. In USA, the number of people with age 65 or older is projected to double from 35 million in 2000 to 71 million in 2030 [10]. The proportion of people aged 85 years or older is growing even faster. It was estimated to be 5.8 million in 2010 and is projected to be 15.8 million in 2050 [11]. Global trends of population statistics paint a similar picture. Between 2000 and 2050, the proportion of the world's population over 60 years is projected to double from about 11 to 22 % [12].

Bronchoscopy is an important procedure in elderly due to high prevalence of lung cancer in older patient population. Majority of new cases of non-small cell lung cancers (NSCLC) are diagnosed in patients older than 65 years of age [13]. The peak incidence of lung cancer is observed at age 70 [14]. According to the surveillance epidemiology end result (SEER) program, there were estimated 224,210 new cases of lung cancer in 2014 in the USA [15]. Given these alarming statistics, an increasing future demand for bronchoscopy is to be expected in elderly patients.

Age has a strong influence on how lung cancer is diagnosed and treated [16]. In a study of 25,261 lung cancer patients in the UK by the National Lung Cancer Audit (NLCA), only 68 % of patients had histological confirmation and only 57 % of patients received anticancer treatment [17•]. After adjusting for the tumor stage, comorbidities, and performance status, there was a progressive decline in receipt of histological diagnosis and anti-cancer treatments as age advanced. Compared with patients aged 60–69 years, the odds ratio (OR) of histological confirmation in this study was 0.71 for 70–79 years and 0.36 for 80–89 years. What is more, patients with at least one co-morbid condition had lower odds (OR 0.75) of histological confirmation.

Lower treatment rate for lung cancer in elderly patients is a formidable problem. Most likely, it is due to the belief that elderly patients cannot tolerate and receive little benefit from lung cancer treatments. This commonly held view is not based on evidence since elderly patients are shown to receive substantial benefit from all modalities of lung cancer treatments such as surgery, radiation therapy, and chemotherapy [13, 18].

It is important to understand why histological diagnosis of lung cancer is not pursued aggressively in elderly patients. We

can think of four potential reasons. First is an inaccurate belief that elderly patients do not benefit from treatment and therefore it is not appropriate to expose them to the risks associated with diagnostic testing. Second, many elderly patients may choose not to undergo diagnostic testing or therapies due to their own personal experience, beliefs, and values. The role of clinicians in this situation is to provide patients with accurate and relevant information in order to facilitate an appropriate informed decision. Third, it is possible that primary care physicians are more liberal in referring younger patients but are more selective in referring older patients to pulmonary consultants for bronchoscopy and other advanced procedures such as endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) [19••]. The fourth and perhaps most important reason for not pursuing diagnosis is the concern regarding safety of bronchoscopy in elderly patients. In other words, denial of bronchoscopy due to safety concerns may be an important impediment to appropriate care of an elderly patient with lung cancer.

Although a decision not to perform bronchoscopy due to safety concerns is largely ill-advised, a cautious approach in elderly patients is not without merits. In the following section, we discuss why clinicians must approach elderly patients with caution before subjecting them to bronchoscopy.

Reasons for Safety Concerns in Elderly

Generally, flexible bronchoscopy has an excellent safety record. In a large survey in 1976, the major complication rate was 0.3 % and procedure-related mortality rate was under 0.04 % [20]. In a prospective study in 1978, the major complication rate after FB was 1.7 % and mortality rate was 0.1 % [21]. In a more recent retrospective study of more than 4,000 cases, the major complication rate was 0.5 % and there were no procedure-related deaths [22]. In a retrospective study of 16,814 patients with diagnostic and 5,921 with therapeutic bronchoscopies from China, the major complication rate was 0.637 % and a mortality rate was 0.013 % [23]. While these safety data are reassuring, caution is warranted before applying these results to elderly patients undergoing bronchoscopy. None of aforementioned studies give adequate demographic information to separately analyze the complication rates among elderly patients. Also, there is an emerging evidence for a higher complication rates with bronchoscopy performed for patients with suspected lung cancer; the most common indication for which bronchoscopy is performed in elderly patients. For example, in one study, adverse events were reported in 35 % of 300 patients who underwent diagnostic bronchoscopy for lung cancer [24]. Although, majority of procedure related complications were minor, 10 % of patients developed severe adverse events needing hospital admission and 2 % of patients died due to procedure-related complications. The results from this study stand in contrast to prior studies and suggest need to re-examine the long-held views about safety of FB procedures at least in certain groups of patients.

There are other reasons to be cautious. Alteration in cardiopulmonary physiology in elderly may increase the risk of complications and impair the ability to tolerate a complicating event during bronchoscopy. Further, it is usual for these patients to have many associated co-morbid conditions which may increase the procedure-related risk. Of particular concern is significant burden of undiagnosed co-morbid conditions such as COPD [25], heart failure [26], and obstructive sleep apnea [27] that are commonly overlooked in elderly patients. A failure to recognize and optimize these conditions has important safety implications during bronchoscopy. Finally, the cognitive function and social circumstances assume a critical importance in elderly patient undergoing bronchoscopy. Administration of sedatives and even a minor stress on cardiopulmonary physiology may have important implications on gait, cognitive function, and functional status for several hours after completion of the procedure. A sound knowledge of these factors is essential for a safe bronchoscopy in elderly patients. In following sections we discuss some of the most pertinent issues in this regard.

Altered Cardiopulmonary Physiology

Many structural and functional alterations occur in pulmonary and cardiovascular physiology with aging that increase the risk of peri-operative complications [28, 29]. A detailed discussion of this topic is beyond the scope of this review but we will highlight a few points pertinent to safety of bronchoscopy in elderly.

The chest wall compliance decreases [30] and the lung compliance increases with age [31]. Overall effect is a decrease in respiratory system compliance with aging. A reduction of elastic recoil of the lung also reduces small airway caliber and causes expiratory flow limitation in elderly. A combination of lower respiratory system compliance and a higher airway resistance increases the work of breathing. To make the matter worse, respiratory muscles are weakened with advancing age, which limits the ability of an elderly patient to respond appropriately to an increased ventilatory demand [32].

Gas exchange is also altered in elderly patients. There are many reasons for it. With advancing age, there is progressive enlargement of airspaces and an increase in residual volume somewhat similar to that seen in emphysema [33]. Some contribution also comes from a modest age-related decline in diffusing capacity [34]. However, the most important factor contributing to abnormal gas exchange is small airway closure in the lower portions of lung during tidal breathing in elderly

patients. There is a linear increase in closing volume with age that increases ventilation perfusion mismatching in elderly patient [35]. The result is a modest decrease in partial pressure of oxygen (PaO_2) and a slight increase in alveolar–arterial oxygen difference (A-aDO_2) with age [36].

The closing volume exceeds functional residual capacity (FRC) around age 65 in the upright position and age 44 in supine position [35]. As a consequence, transition from upright to supine position in an elderly patient further increases mismatching of ventilation and perfusion due to under-ventilation and over-perfusion of the dependent portions of the lung. This has potential to create problems with gas exchange during bronchoscopy in a supine position. The problem is likely to be compounded in presence of additional patient-related factors such as obesity, CHF, and COPD and procedure-related factors such as over-sedation, hypoventilation, and excessive suction during bronchoscopy.

Both hypoxic and hypercapnic ventilatory drives are blunted with advancing age [37]. It can lead to an inadequate ventilatory response to hypoxia and hypercapnia during bronchoscopy. Cough reflex is also decreased in elderly patients [38]. To some extent, it is helpful during bronchoscopy because it allows operators to achieve better control of cough with lower doses of topical lidocaine in these patients [39]. On the down side, it decreases the ability to clear the respiratory secretions, thereby increasing the risk of aspiration during and immediately after the bronchoscopy.

Aging also has important effects on cardiovascular structure and function. The physiological changes in cardiovascular system reduce the ability of elderly patients to tolerate hemodynamic changes which can occur during bronchoscopy. With normal aging, central blood vessels develop increased thickness of intima and media, impaired endothelial function and increased vascular stiffness due to arteriosclerosis [40]. Increase in blood pressure and left ventricular after-load that results from these vascular changes [41] causes a progressive increase in the left ventricular wall thickness and impairment in ventricular relaxation with age [42]. As a result, the cardiac output in elderly patients becomes highly dependent on preload and diastolic filling time. Furthermore, early diastolic filling rate is significantly decreased in elderly patients compared to young individuals [43]. To compensate, an increase in late diastolic filling is needed in order to maintain left ventricular end diastolic volume and the stroke volume. This is accomplished by a forceful contraction of left atrium in late diastole [44]. These alterations in cardiovascular physiology cause elderly patients to have a poor tolerance to hemodynamic stress imposed by hypovolemia, tachycardia, and loss of atrial contraction due to atrial fibrillation. Any such event in an elderly patient becomes an issue of immediate concern during bronchoscopy.

Autonomic regulation is also altered with aging process [45]. While the heart is less responsive to chronotropic or inotropic effects of β-adrenergic agents, the α-mediated arterial constriction is maintained or even augmented in elderly subjects [46]. Apparently, this has potential to cause excessive vasoconstriction with topical application of adrenergic agents sometimes used to control bleeding during bronchoscopy in elderly patients.

Co-Morbid Conditions

Elderly patients who require bronchoscopy have a high burden of co-morbid conditions. For example, in a study of 61 patients >75 years of age who underwent bronchoscopy, 64 % had COPD, 39 % had CAD, 25 % had CHF, and 18 % were receiving home oxygen therapy [47]. Presence of multiple co-morbid conditions clearly raises a safety concern during bronchoscopy.

The incidence of COPD increases with age [48]. Many elderly patients who require bronchoscopy have an advanced COPD. Bronchoscopy can cause a further decline in lung function in COPD patients. For example, a 23 % increase in airway resistance has been reported in patients with COPD but not in control subjects after the procedure [49]. In one study, complications of FB in 91 patients with severe airflow obstruction (defined as FEV1<1 lit and FEV1/FVC ratio <69 %, or FEV1/FVC ratio <50 %) was compared with 162 patients with normal pulmonary functions [50]. Patients with COPD were older (65.8±8.0 years) than those with normal pulmonary functions (57.1±15.6 years). The complication rate of 5 % in the COPD patients was significantly higher than the 0.6 % in patients with normal pulmonary functions. However, only one patient in COPD group required mechanical ventilation and there were no procedure-related deaths. Although the complication rate was higher, it is reassuring that bronchoscopy was safe in the vast majority of patients with severe COPD in this study. Data are also available on safety of bronchoscopy in COPD patients with hypercapnia. In a study of 26 such patients, bronchoscopy was feasible but was associated with bronchospasm in 62 % and oxygen desaturation in 26 % of patients [51]. Although the operators were forced to terminate the procedure before completion in 4 of 26 (15 %) of patients, there were no life-threatening complications. A recent study has also suggested feasibility of performing bronchoscopy in acutely ill COPD patients under assistance of non-invasive positive pressure ventilation (NIPPV) via a full-face mask [52]. Larger prospective studies are required to validate these preliminary findings. Short-term NIPPV support may also be helpful in an occasional patient in immediate post-bronchoscopy period.

Age is a strong risk factor for cardiovascular diseases. The prevalence of hypertension, coronary artery disease, heart failure, and atrial fibrillation increases with advancing age. In the Framingham study, hypertension was present in 71.6 %,

coronary artery disease in 27.7 %, heart failure in 9.1 %, and atrial fibrillation in 8.8 % of persons from 80 to 89 years of age [53]. A majority of elderly patients undergoing bronchoscopy have one or more of these cardiovascular morbidities. Safety of bronchoscopy becomes an important consideration in such patients. Unfortunately, very limited data are available to guide the physicians in this regard. It is generally felt that most patients with stable coronary artery disease and medically treated heart failure can undergo bronchoscopy without experiencing major adverse events [54]. However, most experts agree that bronchoscopy is contraindicated in patients with unstable angina and uncontrolled cardiac arrhythmia. Retrospective studies have found bronchoscopy to be safe in patients with recent myocardial infarction but the indications and usefulness of bronchoscopy in these patients are poorly defined [55, 56]. Without a doubt, a rigorous indication must be established before considering bronchoscopy in such patients.

Another safety matter of great concern is appropriate management of anti-platelet agents and oral anticoagulants in elderly patients undergoing flexible bronchoscopy. It is essential to withhold many of these agents before the procedure due to increased risk of bleeding complications during bronchoscopy. However, interruption of anticoagulants for the procedure is a complicated issue because it places these patients at a higher risk of thrombotic event. For example, in a large study, the 30-day incidence of stroke was 1.06 % in atrial fibrillation patients who required adjustment of anticoagulants prior to endoscopic procedures including bronchoscopy [57]. Age >80 was identified as one of the factor associated with increased risk of stroke in this study.

Aspirin does not increase the risk of bleeding during bronchoscopy [58]. Withdrawal of aspirin prior to bronchoscopy is therefore not warranted as it would unnecessarily place these patients at a higher risk of adverse cardiovascular events. In contrast, clopidogrel is associated with a high risk of bleeding and therefore it needs to be stopped 5 days prior to a planned bronchoscopic lung biopsy [59]. A cardiology consultation is strongly recommended before interrupting clopidogrel for a diagnostic procedure in any patient who has received a drug-eluting coronary stent. It is becoming increasingly common to encounter elderly patients who are receiving newer anticoagulants and require bronchoscopic lung biopsy. Although there are no bronchoscopy studies to guide physicians in this regard, the suggested duration between the last doses of the medication prior to bronchoscopic lung biopsy for different anti-thrombotic and anti-platelet agents is listed in Table 1 [60].

Anti-coagulant use for atrial fibrillation, prosthetic cardiac valves and prior pulmonary thromboembolism is common in elderly patients. Every such patient merits a thorough risk-assessment and a close collaboration across different specialties is often needed to manage anticoagulants in these patients [60].

Table 1 Recommended interval between last dose of anti-thrombotic or anti-platelet agent and bronchoscopic lung biopsy

Medication	Interval
Warfarin	Till PT-INR is <1.5
Unfractionated heparin	2–6 h
Low molecular weight heparin	24 h
Fondaparinux	36–48 h
Dabigatran	1–2 days for creatinine clearance ≥50 ml/min 3–5 days for creatinine clearance <50 ml/min
Rivaroxaban	1 day for creatinine clearance >90 ml/min 2 days for creatinine clearance 60–90 ml/min 3 days for creatinine clearance 30–59 ml/min 4 days for creatinine clearance 15–29 ml/min
Apixaban	1–2 days for creatinine clearance 60–90 ml/min 3 days for creatinine clearance 50–59 ml/min 5 days for creatinine clearance ≤30–49 ml/min
Aspirin/dipyridamole	7–10 days
Cilostazole	2 days
Clopidogrel and ticagrelor	5 days
Prasugrel	7 days
Ticlopidine	10–14 days

Cardiopulmonary Changes During Bronchoscopy

Many important changes in respiratory and cardiac parameters take place during bronchoscopy. A deep understanding of these changes is essential for a safe bronchoscopy in elderly patients. It is known for a while that bronchoscopy is associated with a decline in arterial P_aO_2. In one study, the average decline in arterial P_aO_2 was 20 mmHg with a range of 4–38 mmHg [61]. A transient decrease in oxygen saturation <85 % has been observed in as many as 35 % of patients undergoing bronchoscopy [62]. Age has some correlation with hypoxemia during bronchoscopy. In one report, oxygen desaturation (oxygen saturation <90 % for >10 s) occurred in 55 % of patients over 80 years of age compared to 27 % of younger patients [63]. An associated pulmonary fibrosis significantly increased the risk of hypoxemia among elderly patients during bronchoscopy in this study.

A decline in arterial P_aO_2 to <60 mmHg is shown to increase the risk of cardiac arrhythmia during bronchoscopy, which is an important concern in elderly patients [64, 65]. Fortunately, most of the rhythm disturbances during bronchoscopy are self-limiting and have no major adverse clinical consequences. It is also noteworthy that arterial hypoxemia

persists in some patients for a variable duration after completion of the procedure [66]. Therefore, routine oxygen supplementation should be continued after completion of bronchoscopy until patients have fully recovered.

Transcutaneous carbon dioxide levels increase due to alveolar hypoventilation during flexible bronchoscopy [67, 68]. This is most likely due to respiratory depression secondary to sedative use during bronchoscopy. In the majority of instances, the elevation of CO_2 level has no major implication. It is proposed that transcutaneous monitoring of CO_2 may improve the safety of bronchoscopy in patients with severe COPD and allow more effective titration of sedative medications during the procedure [69]. The matter remains open to debate and at present there are limited data to support this view.

Many hemodynamic changes are observed during routine bronchoscopy, which may have deleterious effects in elderly patients with underlying cardiac disease. In one study, the mean arterial pressure increased by 30 %, heart rate by 43 %, cardiac index by 28 %, and mean pulmonary artery occlusion pressure by 86 % during bronchoscopy under topical anesthesia [70]. Reflex sympathetic discharge due to mechanical irritation of larynx and bronchi is proposed to be the major mechanism behind these hemodynamic changes. There is also evidence for silent myocardial ischemia during bronchoscopy. In a study of 29 patients 50 years or older, ischemic changes were found in 17 % of patients on continuous electrocardiographic (ECG) monitoring [71]. Similar findings were reported in another study in which 7 of 45 patients developed important ECG changes during bronchoscopy [72]. These included ischemic changes in 4 patients, and bundle branch block in three patients. The patients with ECG changes were older (mean age 72±5 years versus 61±15 years) and had more tachycardia during the procedure than those who did not have ECG changes. The bronchoscopist must vigilantly watch the patient for an excessive rise of double-product during bronchoscopy as it may precipitate myocardial ischemia in some patients [73]. β-adrenergic blocking agents are shown to attenuate the increase in double product and their use should be considered in every elderly patient with ischemic heart disease undergoing bronchoscopy [74].

Bronchoscopy Studies in Elderly

Several studies have directly addressed the indications, diagnostic yield, safety and complications of FB in elderly patients (Table 2) [19••, 39, 75–77, 79–85]. Before we discuss the findings, it is important to point out several limitations of these studies. A majority of these studies had a retrospective design. That raises a serious concern about a selection bias that would naturally favor inclusion of relatively healthy patients and exclusion of frail elderly patients. Even in prospective studies, it is difficult to exclude this possibility due to a referral bias. With few exceptions, the majority of studies do not provide details on comorbidities or functional status of elderly patients undergoing bronchoscopy. Comparison of safety data may not be valid because complications were not uniformly defined in different studies. Retrospective design also raises concerns about under-reporting of complications due to inadequate documentation. Some studies did not have a control group. The choice of sedation and sampling procedures varied widely in different studies. This is especially noticeable for high risk sampling procedures such as transbronchial biopsies. Despite all the inadequacies, these publications provide valuable information on safety and efficacy of bronchoscopy in the elderly.

Suspicion for lung cancer is the most common indication for performing bronchoscopy in elderly patients (Table 2). Nearly two third of all bronchoscopy procedures is performed for this indication in elderly patients. Other common reasons for performing bronchoscopy are atelectasis, retained secretions, hemoptysis, and non-resolving infiltrates. With availability of EBUS-TBNA technology, mediastinal staging of lung cancer is emerging as an important indication for bronchoscopy in elderly patients [19••].

Flexible bronchoscopy provides useful diagnostic information in the majority of elderly patients undergoing the procedure. The diagnostic yield has varied from 27 to 75 % in different studies. The diagnostic yield of bronchoscopy among elderly patients is similar to that in younger patients [76, 77]. Flexible bronchoscopy is also found to be useful in the removal of airway foreign bodies in elderly patients. For instance, in one study, flexible bronchoscopy was 87.5 % effective in removal of airway foreign bodies in elderly patients [9]. No difference was noted in procedure related complications between elderly and young patients in this study.

A small retrospective study of 18 patients addressed the clinical utility of rigid bronchoscopy in the octogenarian patients [78]. In addition to rigid bronchoscopy, several interventional procedures were performed for treatment of malignant airway obstruction or benign strictures in this study. All subjects experienced relief in dyspnea after the procedure. Despite the advanced age, multiple comorbidities, and high-risk interventions, rigid bronchoscopy was well-tolerated. Transient hypoxemia and intra-operative hypotension were common but there was no peri-operative mortality.

Two recent studies have addressed usefulness and safety of EBUS-TBNA in elderly patients. In the first study from Japan, a diagnostic yield of 79 % among 34 elderly patients (>70 years) was similar to 71 % yield among 75 younger patients [79]. Elderly patients tolerate the procedure without difficulty and the procedure-related complication rate was similar in both groups. In a large prospective study, EBUS TBNA was safe and highly effective in mediastinal staging, pathological confirmation, and morphological sub-typing of tumor in 198 elderly patients [19••]. The specimens were sufficient for molecular testing in the majority of patients. Elderly

Table 2 Key studies on bronchoscopy in elderly patients

Author (year)	Ref no.	Design	Number	Age (years)	Indications	Setting	Sedation	Procedures	Diagnostic yield	Complications
Macfarlane (1981)	82	Retrospective	204	>70	Lung mass (51 %) Atelectasis (32 %) Pneumonia (14 %) Others (13 %)	Inpatient 52 % Outpatient 48 %	Atropine Papaveretum Fentanyl Droperidol	EBB TBB (n=3)	71 %	Respiratory distress (0.5 %)
Brandstetter (1984)	84	Prospective	100	>65	Retained secretions (37 %) Infiltrates (36 %) Tumor (8 %) Hemoptysis (6 %) Others (13 %)	Inpatient	Promethazine Meperidine Atropine	BAL Brushing EBB TBB (n=28)	N/A	Overall (23 %) Bleeding (17 %) Fever (10 %) Arrhythmia (8 %) Mortality (1 %) Others (5 %)
O'Hickey (1987)	75	Retrospective	423	>65	Atelectasis (48 %) Hemoptysis (17 %) Lymphadenopathy (7 %) Other (28 %)	Outpatient	Atropine Papaveretum	BW BAL EBB TBB (n=33)	46 %	Bleeding needing lobectomy (0.25 %) Inability to tolerate (1 %)
Knox (1988)	80	Retrospective	60	>80	N/A	Inpatient Outpatient	Atropine Fentanyl Diazepam	BW BB EBB	42 %	Respiratory depression (1.6 %)
Costello (1997)	39	Prospective	47	>66	Lung cancer (68 %) Suspected TB (23 %) Others (9 %)	Outpatient	Atropine Midazolam	EBB TBB (n=1)	N/A	Desaturation (15 %) Bleeding (2 %)
Hehn (2003)	81	Prospective	219	>70	SPN Lung mass Focal infiltrates	N/A	Fentanyl Midazolam	BAL BB TBB (n=80) TBNA (n=71)	N/A	Pneumothorax (3.2 %) Bleeding (3.7 %) Desaturation (6 %) Hypotension (1.8 %) Arrhythmia (1 %)
Allan (2003)	76	Retrospective	120	>80	Lung mass (55 %) Infiltrates (28 %) Hemoptysis (8 %) Others (19 %)	Outpatient Inpatient	Fentanyl Midazolam Meperidine Promethazine	EBB TBB (n=47) TBNA (n=26)	27 %	Oversedation (2.5 %) Hypoxemia (1 %)
Kanemoto (2006)	85	Prospective	165	≥70	Lung mass (67 %) Others (33 %)	N/A	N/A	BW BAL BB FBx (n=81)	75 %	Fever (3.6 %) Pneumonia (4.2 %)
Rokach (2008)	83	Retrospective	150	>80	Lung mass Infection	Inpatient Outpatient	Midazolam Pethidine	BAL EBB TBB (n=18)	63 %	Overall 11.5 % Bleeding (4 %) Hypoxemia (6.3 %) Arrhythmia (1.7 %) Pneumothorax (1.2 %) Others (1.2 %) Mortality (1.2 %)
Sarinc Ulasli (2013)	77	Retrospective	367	≥65	Lung mass (69 %) Others (31 %)	N/A	Midazolam	BW BAL EBB	51 %	Overall 11.2 % Cough (4.6 %) Bleeding (3.8 %)

Table 2 (continued)

Author (year)	Ref no.	Design	Number	Age (years)	Indications	Setting	Sedation	Procedures	Diagnostic yield	Complications
								TBB (n=19) TBNA (n=18)		Agitation (1.1 %) Respiratory depression (0.8 %) Bronchospasm (0.3 %) Death (0.3 %)
Okachi (2013)	79	Retrospective	34	>70	Mediastinal lymphadenopathy (100 %)	N/A	Midazolam	EBUS-TBNA	79.4 %	Atrial fibrillation (2.9 %)
Evison (2014)	19••	Prospective	198	≥70	Nodal staging (66 %) Others (34 %)	Outpatient	Midazolam Afentanyl	EBUS-TBNA	51.9 %	Overall 5.1 % Bleeding (2 %) Hypoxemia (0.5 %) Poor tolerance (2 %) Hypotension (0.5 %)

BAL bronchoalveolar lavage, *BW* bronchial washing, *EBB* endobronchial biopsy, *EBUS* endobronchial ultrasound, *FBx* forceps biopsy, *N/A* not available, *Ref No.* reference number, *TBB* transbronchial biopsy, *TBNA* transbronchial needle aspiration

patients tolerated the procedure better than younger patients. Once again, the complications were minor and were unrelated to age in this study.

There is limited information on how often a bronchoscopic procedure in elderly patients leads to change in management or outcome. In an older study, majority of octogenarians diagnosed to have lung cancer on bronchoscopy received only supportive therapy [80]. However, in a more recent study, important management changes occurred in 29 of 61 (48 %) of elderly patients (>75 years) who underwent FB over a 4-year period. These included initiation of radiation therapy, chemotherapy, or lung cancer surgery after diagnosis of lung cancer [47]. We believe that greater application of minimally invasive techniques such as EBUS-TBNA is going to have a very positive influence on lung cancer outcome in elderly patients. Future studies must look into this issue.

Elderly patients tolerate bronchoscopy as well as younger patients do. Age has no influence on the perception of pain with the procedure [81]. Overall, 67 to 90 % of elderly patients are willing to return for a repeat procedure if necessary [39, 81, 82]. In one study, 86 % of patients reported being sleepy on the day of the procedure but the majority (82 %) felt as well as usual the following day after bronchoscopy [82].

Bronchoscopy is generally found to be safe in elderly patients. The complication rate in different studies has varied from 1 to 23 %. (Table 2) Studies which included both inpatients and outpatients generally have a higher complication rate, most likely due to a higher proportion of acutely ill patients in these studies [83, 84]. There is a slight trend toward a higher bronchoscopy-related complication rate among octogenarians. However, this finding is not a sufficient reason to deny appropriately indicated bronchoscopy to octogenarians [76, 80, 81, 83].

The majority of bronchoscopy-related complications in elderly patients are minor and self-limiting. In the studies reviewed, life-threatening bleeding, hypoxemia, respiratory failure, and cardiac arrhythmia were exceedingly uncommon. There is no evidence for a higher risk of pneumonia in elderly patients than in younger patients after bronchoscopy [85]. As shown in Table 2, there were four reported deaths among a total of 2087 procedures in elderly patients, for a mortality rate of 0.19 %. Overall, our analysis of the literature in this area strongly suggests that age has little impact on the safety or tolerance of FB.

Sedation in Bronchoscopy

No discussion of safety can be considered comprehensive without addressing issues surrounding sedation during FB in elderly patients. Although bronchoscopy is possible without sedation, the majority of operators perform bronchoscopy with sedation, as it improves patient comfort and tolerance to the procedure [86–88]. Better patient cooperation with

adequate sedation is very helpful as it reduces the procedure duration and improves physician satisfaction [87]. However, sedative use in elderly patients increases the risk of respiratory depression during bronchoscopy [76, 77, 80].

In recent years, benzodiazepines have become the most commonly used agents for sedation during bronchoscopy [89]. Appropriate dose adjustment is needed in patients with advanced age and liver disease because these patients are more prone to adverse effects such as drowsiness, confusion, gait disturbances, and falls [90]. Older patients who receive benzodiazepines require longer time to recover after the bronchoscopy [82]. Midazolam is the most preferred benzodiazepine agent for bronchoscopy because of its rapid onset of action, and relatively short duration of effect [91]. Compared to young patients, studies in elderly subjects have consistently needed a lower dose of midazolam for a comparable level of sedation during bronchoscopy [19••, 79, 81]. In one study, the mean dose of midazolam during endoscopy was 4.65 mg in patients younger than 70 years and 1.89 mg in patients older than 70 years [92]. Lower dose requirement in elderly is largely due to greater sensitivity to the pharmacodynamic effects of midazolam rather than the alterations in the pharmacokinetic properties [93].

Opioids are used during bronchoscopy for their analgesic and cough suppressant action. Fentanyl is the most commonly used drug in this setting due to its rapid onset and short duration of action. Randomized studies have reported better comfort and tolerance and improved cough control with the combination of benzodiazepines and opiates over benzodiazepines alone [94]. The main danger with opioids use is decrease in central ventilatory drive and attendant respiratory depression. This risk is more pronounced when opioids are used in conjunction with benzodiazepines [95]. Elderly patients are particularly sensitive to opioids and studies have shown that elderly patients require significantly lower doses of fentanyl or similar opioids than younger patients [19••, 76].

Cough control is essential during bronchoscopy. Effective cough control improves patient comfort and provides more optimal working conditions for the bronchoscopists. Uncontrolled cough increases the risk of complications such as pneumothorax and prolongs the duration of bronchoscopy. Lidocaine is the topical anesthetic of choice to control cough during flexible bronchoscopy owing to its short half-life, wide therapeutic window, and minimal tissue toxicity [96]. However, patients with advanced age, impaired liver function, or congestive heart failure are at increased risk for lidocaine toxicity [97]. Features of lidocaine toxicity such as circumoral paraesthesia, seizures, and cardiac arrhythmias can occur if the total topical dose exceeds 7 mg/kg or serum lidocaine level exceeds 5 mg/L [98]. Careful monitoring of the total dose of lidocaine including that applied to the upper airways and the tracheobronchial tree is warranted in every elderly patient.

Anti-cholinergic agents are no longer favored during bronchoscopy. In a large randomized trial, the use of atropine or glycopyrrolate had no effect on cough, patient comfort, oxygen desaturation, or procedure time [99]. On the contrary, their use was associated with a significant increase in heart rate and blood pressure. Use of anti-cholinergic agents in the elderly is not without risks. Hence, there is no reason to use these agents during bronchoscopy.

Recommendations

Performing a bronchoscopy in elderly patients is an art as much as it is a science. Key is to understand the altered physiology in elderly subjects and use that knowledge to improve

Table 3 Suggested approach to bronchoscopy in elderly patients

Pre-bronchoscopy
- Detailed history and physical examination
- Identify and optimize the co-morbid conditions
- Assess functional status
- Assess social support and living conditions
- Define the overall goal of diagnostic tests and future treatments
- Review all medications
- Adjust anti-platelet agents and anticoagulants
- Obtain baseline electrocardiogram, chest radiograph and oxygen saturation
- Obtain appropriate consultations as deemed necessary
- Carefully plan sampling techniques ahead of procedure
- Obtain informed consent

During bronchoscopy
- Monitor vital signs, ECG and oxygen saturation
- Use supplemental oxygen as a routine
- Maintain oxygen saturation>90 % throughout the procedure as much as possible
- Consider use of end-tidal CO_2
- Have resuscitation equipment available
- Consider performing procedure in semi-recumbent position
- Control cough with minimum doses of lidocaine
- Carefully titrate desired level of sedation with minimal doses of sedatives
- Avoid unnecessary suction
- Limit the duration of procedure to minimum necessary
- Minimize the use of topical epinephrine. Preferably use 1:50,000 or 1:100,000 dilution
- Terminate the procedure if deemed unsafe

Post-bronchoscopy
- Continue supplemental oxygen until full recovery
- Monitor vital signs and oxygen saturation
- Maintain semi-recumbent position
- Assess swallowing, gait and balance before discharge
- Reassess safety of home environment
- Have low threshold for overnight admission if patient lives alone
- Provide clear instructions and contact information

the safety of bronchoscopy. An optimal bronchoscopy in an elderly patient requires comprehensive clinical assessment and planning. At the outset, the goal of the procedure must be clearly defined. Every effort must be made to achieve the goal with maximum comfort and minimum risk to the patient. Table 3 lists the important considerations for improving the safety and efficacy of bronchoscopy in elderly patients. We recognize that some of the suggestions listed here may not have gone through scrutiny of strict scientific inquiry, but evidence-base is not always needed to practice common sense. Each elderly patient undergoing bronchoscopy poses unique challenge to the health care workers. This challenge can only be met with a carefully planned individualized approach with full involvement of patient in every aspect of the procedure.

Our Case

The patient had witnessed several of his relative succumbing to advanced and metastatic lung cancer. He had realistic assessment of his prognosis and life-expectancy but he wanted to aggressively pursue the diagnosis and treatment of lung cancer in order to reduce the future risk of developing metastatic disease. After a thorough discussion, a decision was made to pursue the tissue diagnosis with FB. Clopidrogel was discontinued for 5 days. Transbronchial biopsies with radial probe ultrasound using guide sheath method under fluoroscopic guidance were performed. The total duration of procedure was 21 min. There were no procedure related complications. However, due to concerns regarding his safety, he was asked to stay in the hospital for overnight observation. A diagnosis of squamous cell lung cancer was made on transbronchial biopsies. The patient received external beam radiation therapy and responded well to treatment without experiencing any major adverse effects.

Conclusions

According to British Thoracic Society (BTS) guidelines, advanced age by itself is not the contraindications for FB [100••]. We agree. Bronchoscopy is safe in the majority of elderly subjects. There should be strict indication to perform bronchoscopy and there must be a good chance that a successful procedure would lead to a meaningful change in patient management and outcome. A thorough assessment of comorbid conditions, functional status and social support is essential before bronchoscopy. The procedure must be carefully planned and executed with clear goals and expectations. Advanced chronological age is not a contraindication for bronchoscopy.

Compliance with Ethics Guidelines

Conflict of Interest Sarah Hadique and Prasoon Jain declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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