Flexible Bronchoscopy and its Role in the Staging of Non–Small Cell Lung Cancer

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KEYWORDS

• Flexible bronchoscopy • Transbronchial needle aspiration
• Endobronchial ultrasound • Electromagnetic navigation

The first ever bronchoscopy was performed in 1887 by Gustav Killian of Freiburg, Germany.[1] During the early years of the development of bronchoscopy, the indications for the procedure were primarily therapeutic: removal of foreign bodies and dilation of strictures from tuberculosis and diphtheria. In the early part of the twentieth century, Chevalier Jackson, the father of American bronchoesophagology, further advanced bronchoscopic techniques and designed modern rigid bronchoscopes.[2] Again, the primary indication was often therapeutic.

The flexible bronchoscope was developed in the late 1960s by Ikeda[3] and has become the mainstay investigation in the evaluation of patients suspected of lung cancer. It is used mainly as a diagnostic tool providing tissue to determine the histologic type of tumor. Bronchoscopy also has a role in disease staging and an extended role in delivering therapeutic modalities. Flexible bronchoscopy (FB) is easier to perform and is safe and well tolerated by patients. The requirement of only a moderate sedation makes it an acceptable outpatient procedure. It has almost completely replaced rigid bronchoscopy in the initial assessment. The development of video bronchoscopes has the added advantage of facilitating teaching and rendering the procedure more interesting for the observers in the bronchoscopy suite.

The flexibility of the bronchoscope allows the operator to inspect most of fourth order and often up to sixth order bronchi. In addition, the operator may directly assess mucosal details, such as color and vascularity. Relative contraindications to the procedure are few and include hypoxemia refractory to supplemental oxygen, intractable bleeding diathesis, severe pulmonary hypertension, cardiovascular instability, and acute hypercapnia.[4]

FB is safe with a complication rate of 0.12% and a mortality rate of 0.04%.[5] The dangers of hemorrhage and pneumothorax relate to the biopsy procedure used and are discussed later. In all patients, the bronchoscope causes a temporary increase in airflow obstruction, which may result in hypercapnia.[6] Inappropriate sedation with benzodiazepines or opiates increases the likelihood of respiratory complications and high-risk patients could be identified by prior measurement of arterial blood gases.[5–7] Supplemental oxygen should be provided and patients monitored throughout the procedure with pulse oximetry. Cardiac monitoring should be used for those patients with a history of ischemic heart disease and resuscitation equipment immediately available.

Although FB has largely replaced rigid bronchoscopy in the initial assessment of the patient, the rigid scope has advantages in certain situations.[8] It may provide more accurate information regarding the endobronchial location of a tumor before resection. Additionally, manipulation of the scope allows assessment of the mobility of the proximal airways providing an indirect

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Clin Chest Med 31 (2010) 87–100
doi:10.1016/j.ccm.2009.08.006
0272-5231/10/$ – see front matter

evaluation of mediastinal nodal involvement. Airway obstruction is less and the rigid scope may be preferable in exploring patients with tracheal narrowing in whom the flexible scope may produce critical airway narrowing. It provides superior suction, facilitating the assessment and biopsy of potentially hemorrhagic lesions and the debulking of large tumors.[8–10] In addition, many physicians are now acquiring skills in this technique to facilitate endobronchial laser therapy and stent placement.[11]

THE DIAGNOSTIC YIELD OF FB

The expected diagnostic yield from FB depends on the location and the size of the lesion. Central endobronchial lesions yield the highest diagnostic return (>90%), whereas small peripheral lesions often prove more elusive unless more demanding and time-consuming techniques are used. The question of which combination of cytologic and histologic procedures provides the optimum diagnostic yield has not been conclusively answered but probably depends on the expertise available in any individual center. The routine techniques include bronchial washings, brushings, and biopsies but these may be augmented by the use of transbronchial needle aspiration (TBNA) and bronchoalveolar lavage (BAL).[12]

More than 70% of lung carcinomas can be approached with FB and although the yield is dependent on operator's experience, a high level of diagnostic accuracy can be achieved by taking between three and five biopsy specimens and a combination of brushing, biopsy, and bronchial washes can expect to establish a diagnosis in more than 60% of cases.[6,7,13,14] When the tumor is visible but is intramural rather than endobronchial in distribution the diagnostic yield falls to 55% and is reduced further when the tumor lies beyond the bronchoscopist's vision.[6,7,12]

The main role of BAL in patients with lung cancer is the diagnosis of opportunistic infections, especially in patients undergoing chemotherapy. BAL may have an extended role, however, in the diagnosis of malignancy itself. A high diagnostic yield has been shown in the detection of pulmonary hematologic malignancies, primary bronchoalveolar cell carcinoma, and metastatic adenocarcinoma of the breast.[15–17]

Information on the role of BAL in the diagnosis of primary lung cancer remains sparse. Examination of BAL from 55 patients with a peripheral lung lesion demonstrated a diagnostic yield of around 30% with no false-positive results and only one instance of incorrect cell typing. Additionally, in combination with bronchial washings and postbronchoscopy sputum analysis BAL increased the yield to 56%.[18] Examination of BAL in 162 patients with malignant lung infiltrates revealed improved sensitivity in cases of bronchoalveolar cell carcinoma (93%) and lymphangitic carcinomatosis (83%). Forty-five percent of non-Hodgkin lymphoma could be detected and immunocytochemistry is of value in identification and classification.[19]

BAL is safe; bleeding and pneumothorax are uncommon and the fever and transient loss of lung function reported are rarely serious and there is no need for fluoroscopy. Furthermore, the diagnostic yield is high in diseases other than cancer, such as pulmonary tuberculosis. Advances in cell and molecular biology may complement the technique of BAL to improve the rate of tumor diagnosis in peripheral lesions (particularly adenocarcinoma) and may also provide a useful tool to explore the molecular mechanisms governing the genesis of lung cancer.[20–22]

VISIBLE ENDOBRONCHIAL LESIONS

Central tumors can present as exophytic mass lesions, with partial or total occlusion of the bronchial lumen, as peribronchial tumors with extrinsic compression of the airway, or with submucosal infiltration of tumor. The changes with peribronchial tumors or with submucosal infiltration are often subtle. The airways should be examined closely for characteristic changes, such as erythema, loss of bronchial markings, and nodularity of the mucosal surface. Central lesions are usually sampled with a combination of bronchial washes, bronchial brushings, and endobronchial biopsies. The yield of endobronchial biopsies is highest for exophytic lesions, with a diagnostic yield of approximately 90%.[23–25] Three to four biopsies are likely adequate in this situation. Attempts should be made to obtain the biopsies from areas of the lesion that seem viable (**Fig. 1**).

For submucosal lesions, TBNA can be performed by inserting the needle into the submucosal plane at an oblique angle, and in patients with peribronchial disease and extrinsic compression, the needle should be passed through the bronchial wall into the lesion.[26,27] It is particularly frustrating when apparently adequate biopsy specimens from visible endobronchial disease fail to achieve a diagnosis (**Fig. 2**). Reasons for this include the presence of surface necrosis or the presence of crush artifact (particularly common with samples from small cell carcinoma). In these circumstances, TBNA may improve diagnostic yield.[28,29]