Is bronchoscopic lung biopsy helpful in the management of patients with diffuse lung disease?

S.A. Ensminger and U.B.S. Prakash

ABSTRACT: Few studies have evaluated how the results of bronchoscopic lung biopsy (BLB) affect clinical management. The objective of the present study was to evaluate the clinical usefulness of BLB in the overall management of patients with diffuse pulmonary diseases.

The study was a retrospective analysis of patients who underwent fluoroscopy-guided BLB over a 2-yr period. Patients whose biopsy was of a lung mass or single dominant lung nodule were excluded. The usefulness of BLB was assessed to determine whether the results affected the clinical management of these patients.

During the study period, 603 patients underwent 651 BLB procedures. The results of BLB were clinically helpful in 494 (75.9%) out of 651 procedures. No diagnostic abnormality was identified in 107 (16.4%) out of the 651 biopsy procedures. This finding was clinically helpful in 59 (55.1%) out of 107 procedures, as the results excluded specific processes suspected before BLB. In 52 procedures (8% of all BLB), no lung parenchyma was obtained.

In conclusion, bronchoscopic lung biopsy is a clinically useful test in ~75% of procedures. In the 25% of bronchoscopic lung biopsies that were clinically unhelpful, the reason for failure in approximately one-third of patients was the failure of the procedure to obtain an adequate quantity of lung parenchyma for a meaningful histological analysis.

KEYWORDS: Bronchoscopic lung biopsy, bronchoscopy, diffuse lung disease, interstitial lung disease, transbronchial biopsy, transbronchoscopic biopsy

Biopsies of the lung have been obtained *via* bronchoscopy for >40 yrs [1–3]. Several studies have reported the diagnostic yield and complications of bronchoscopic lung biopsy (BLB) in various patient populations [4, 5]. The purpose of the present study was to determine whether information obtained from BLB is useful to clinicians, and how this information is used in the management of patients with diffuse pulmonary disorders.

Many of the published reports have focused on the role of BLB in the diagnosis of diffuse pulmonary diseases and the accuracy of histological diagnosis. The present study, in contrast to earlier studies, was designed to evaluate how BLB results are used by clinicians. The main aim of the study was to assess whether the results of the BLB were clinically useful in the management of patients with diffuse pulmonary disorders.

METHODS

The study was a retrospective analysis of patients who underwent BLB at the Mayo Clinic

(Rochester, MN, USA) between July 1, 2002 and June 30, 2004. Subjects were identified through a medical records database by searching for the term “closed lung biopsy”. All patients authorised their records to be reviewed. The institutional review board approved the study. BLB was defined as a biopsy performed *via* bronchoscopy with the intention of obtaining adequate parenchymal lung tissue for meaningful histological analysis. By this definition, attempts to biopsy a lung mass, solitary nodule or lung cavity were excluded. Indication for BLB was obtained from the bronchoscopy report. All BLBs were performed with fluoroscopic guidance. Procedures were performed or supervised by a group of experienced, dedicated bronchoscopists. Medical records were reviewed to determine how the results of BLB impacted upon patient care. BLB was considered useful if: 1) it resulted in a specific clinical diagnosis; 2) a specific management decision was made based on the biopsy result; or 3) certain pathological processes were excluded on the basis of the biopsy result and other clinical information. BLB

AFFILIATIONS

Mayo Clinic College of Medicine,
Mayo Medical Center, Rochester,
MN, USA.

CORRESPONDENCE

U.B.S. Prakash
Pulmonary and Critical Care Division
East-18
Mayo Building
Mayo Medical Center
Rochester
MN 55905
USA
Fax: 1 5072664372
E-mail: prakash.udaya@mayo.edu

Received:

January 27 2006

Accepted after revision:

July 26 2006

SUPPORT STATEMENT

Neither author has any type of
conflict of interest regarding the
subjects discussed in this paper.

was considered unhelpful in patients who had a specific diagnosis from other procedures or biopsies, or those in whom the procedure failed to obtain lung tissue. Radiographic reports and clinical notes following bronchoscopy were reviewed for evidence of post-procedure pneumothorax.

RESULTS

During the study period, 603 patients underwent a total of 651 BLBs. During this period, ~3,300 bronchoscopies were carried out at the Mayo Medical Center. The median (range) patient age was 60 (10–93) yrs, and there were 355 females (54.5%). Indications for BLB are shown in table 1. A total of 54 BLBs were performed in 16 lung transplant recipients for the indications of pulmonary infiltrate or transplant surveillance. Histopathological diagnoses are shown in table 2. Biopsy results were considered helpful in 494 (75.9%) out of the 651 procedures. Of these, 249 (38.2% of all BLBs) provided clinically useful histopathological diagnoses and the remainder were helpful in excluding certain disorders. In total, 157 (24.1%) of the biopsies were considered not helpful. In 52 (8% of all BLBs), no lung parenchyma was obtained.

No specific diagnostic abnormality was identified in 107 (16.4%) of all biopsies. This finding was considered helpful in 59 (55.1%) out of the 107, as the clinician felt that specific pathological processes were ruled out and no further work-up was pursued. A total of 48 biopsies in 47 patients that identified no diagnostic abnormality were felt to be unhelpful (48 out of 107; 44.9%). Of these patients, 34 had additional diagnostic tests performed that resulted in a specific diagnosis (34 out of 47; 72.3%).

When the BLB result was considered unhelpful, open lung biopsy was performed in 44 (28.6%) out of 154 patients. A specific diagnosis was established by a bronchoscopic procedure performed at the time of BLB (cytology, transbronchial needle aspiration, endobronchial biopsy, cultures of bronchoalveolar lavage fluid or bronchial washings) in 23 out of the 157 BLB procedures with unhelpful results (14.6%).

Malignancy was ultimately diagnosed in 94 (15.6%) out of the 603 patients who underwent BLB. In 66 out of 94 (70.2%), the diagnosis was provided by BLB. Primary lung cancer was diagnosed in 66 (10.9%) out of 603 patients, and metastatic malignancy in 28 (4.6%) out of 603. The diagnostic rate of BLB was 72.7% for primary lung cancer and 64.3% for metastatic malignancy.

TABLE 1 Indications for bronchoscopic lung biopsy in 651 procedures

Pulmonary infiltrate[#]	533 (81.9%)
Multiple pulmonary nodules	59 (9.1%)
Lung transplant recipient surveillance	22 (3.4%)
Suspected interstitial lung disease	18 (2.8%)
Mediastinal or hilar lymphadenopathy	18 (2.8%)
Cough	1 (0.15%)

Data are presented as n (%). [#]: diffuse or patchy.

TABLE 2 Histopathological findings from bronchoscopic lung biopsy in 651 procedures

Pulmonary parenchyma without diagnostic abnormality	107 (16.4)
Malignancy	94 (14.4)
Organising pneumonia	80 (12.3)
Non-necrotising granulomas	67 (10.3)
No lung parenchyma	52 (8.0)
Bronchiolitis	40 (6.1)
Nonspecific fibrosis or interstitial thickening	36 (5.5)
Nonspecific inflammation	31 (4.8)
Chronic interstitial pneumonitis	25 (3.8)
Diffuse alveolar damage	19 (2.9)
Transplant rejection	19 (2.9)
Acute bronchopneumonia	16 (2.5)
Hemosiderosis or lung haemorrhage	13 (2.0)
Lymphoid/lymphoma/leukaemia	12 (1.8)
Eosinophilic pneumonia	8 (1.2)
Pneumocystis pneumonia	8 (1.2)
Fungal infection	8 (1.2)
Necrotising granulomas	6 (0.92)
Lipoid pneumonia	3 (0.46)
Amyloid	2 (0.31)
Alveolar proteinosis	2 (0.31)
Obliterative bronchiolitis	2 (0.31)
Langerhans cell histiocytosis	1 (0.15)

Data are presented as n (%).

Of all BLB procedures, pneumothorax occurred in eight (1.2%) out of 651. Other complications including bleeding and death were not specifically identified as part of this study.

DISCUSSION

BLB, also known as transbronchoscopic or transbronchial lung biopsy, refers to the bronchoscopic technique of obtaining pulmonary parenchymal tissue for histological analysis. At the Mayo Clinic in 1965, ANDERSEN *et al.* [1] described the rigid bronchoscopic technique of BLB in 13 patients. Subsequent studies reported the results of BLB using the rigid bronchoscope [2–8]. Among the first 450 cases of BLB performed *via* the rigid bronchoscope, lung tissue was obtained in 84% of patients with diffuse lung diseases [3]. The introduction of the flexible bronchoscope in the late 1960s increased the popularity of the technique and demonstrated that BLB with the flexible instrument could be obtained with minimal mortality and morbidity [4, 9–13].

The initial experience reported positive biopsy results in 60% of patients who had BLB *via* flexible bronchoscopy for diffuse bilateral shadows or multiple opacities [5]. Subsequent experience described in several studies reported positive results in 82% of cases [9, 10, 14]. The substantial clinical usefulness and safety of BLB in diffuse pulmonary disorders has been demonstrated in many studies [15, 16]. As a result, BLB is a well-established diagnostic technique used by almost all bronchoscopists, and the flexible bronchoscope is used almost exclusively. In a survey of 1,800 North American

bronchoscopists, nearly 70% reported that they performed BLB routinely in diffuse lung disease in nonimmunocompromised patients [17].

By definition, BLB denotes biopsy of lung or pathological processes occurring within the pulmonary parenchyma. Biopsy of peripheral nodules originating in the bronchial wall does not represent BLB. Nevertheless, the term BLB is loosely used in clinical practice as well as literature to describe biopsy of any bronchoscopically invisible lesion. As a result, the interpretation of diagnostic yield from "BLB" of diffuse and localised lesions becomes difficult [18]. In the current authors' analysis, results of biopsies of solitary nodules were excluded and patients who had radiological features of patchy or widespread diffuse parenchymal disease were included. Most, if not all, patients in the present study underwent chest computed tomography evaluation prior to bronchoscopy to guide BLB. However, a standardised algorithm was not used for work-up prior to bronchoscopy.

There is variability in defining the term "diffuse lung disease". In some cases, this term is used to describe bilateral, multilobar parenchymal changes; however, the present authors' analysis included any ill-defined radiographic lesion, reasoning that a pathological process can be diffuse in a localised area of pulmonary parenchyma. As mentioned previously, BLBs of these types of lesions are performed with the intent to obtain parenchymal lung tissue.

Diffuse interstitial lung disease caused by either benign or malignant processes is a common indication for BLB [19–22]. The most common indication for BLB in the current authors' study was pulmonary infiltrate (patchy or widespread) in 81.9% of cases, followed by multiple pulmonary nodules or nodular infiltrate in 9.1%. Patients with interstitial lung disease were frequently included in the pulmonary infiltrate group, as this was the main indication for BLB listed on the procedure report. Similarly, lung transplant recipients whose indication for BLB was "pulmonary infiltrate" were also included in the group, and those without specific radiographic abnormalities were included in the "lung transplant recipient surveillance" group.

When BLB was introduced into clinical practice, a positive biopsy using the BLB technique was defined as diagnostic histology, histology that supported a diagnosis, or histology consistent with the final diagnosis [4]. Indeed, most of the published studies have focused on the diagnostic accuracy of histological analysis of BLB in patients with diffuse lung disorders. In contrast to the earlier reports on BLB, the present study focused on how BLB results are used by clinicians. The main aim of the current study was to assess whether the results of the BLB were clinically useful in the management of patients with diffuse pulmonary disorders. The results of the present study indicate that BLB is a clinically useful test in ~75% of procedures. The current analysis showed that of the 25% of BLBs that were clinically unhelpful, the main reason for failure in approximately one-third of these patients was the absence of pulmonary parenchyma, or an inadequate quantity of lung parenchyma, in the biopsy specimen for a meaningful histological analysis. While it is difficult to enumerate every factor underlying this failure, various factors may have

contributed to the failure in obtaining adequate lung parenchyma. Some of the common reasons mentioned by the bronchoscopists included excessive patient cough, bleeding, and inadequate placement of biopsy forceps.

Inability to obtain optimal or adequate pulmonary parenchymal specimens is a common problem even when fluoroscopic guidance is used. Proper equipment, technique and use of fluoroscopy will enhance the chance of collecting good biopsy specimens [15]. Previous studies also noted the problem of inadequate lung tissue from BLB in up to 20% of patients [1, 3].

Bronchoscopic biopsy of very localised lesions yields a diagnostic rate of ~60% in primary lung cancer and of ~50% in metastatic cancer, when these tumours present as peripheral lung nodules [18]. Biopsy of lesions >2.0 cm in diameter provides a diagnostic yield in >60% of cases, whereas lesions <2.0 cm in diameter yield a diagnosis in <25% of cases [18]. Diagnostic rates are likely to be lower if nodular or localised lesions are caused by nonmalignant processes. In the present cohort of patients with patchy or widespread diffuse parenchymal disease, malignancy was ultimately diagnosed in 15.6%. The diagnostic rate of BLB was 72.7% in primary lung cancer and 64.3% in metastatic cancer.

It is not uncommon for BLB pathology results to return without diagnostic abnormality. It can be difficult to know whether this is due to sampling error, or whether there truly is an absence of significant pathology. In the current study, an adequate lung parenchymal biopsy without a specific diagnostic abnormality was considered clinically helpful in 55% of the patients.

The current study is limited by its retrospective nature, and the difficulty in determining how results from BLB were used. The present authors attempted to follow strict criteria for definitions of usefulness or unusefulness; however, in some cases a degree of subjectivity was required. The bronchoscopy reports did not uniformly report the number of biopsies taken, so the current authors were unable to comment on the relationship between number of biopsies and diagnostic yield or clinical utility.

Since the 1990s, high-resolution computed tomography and video-assisted thoracoscopic lung biopsy have been emerging techniques in establishing the diagnosis of diffuse lung disorders. Bronchoalveolar lavage has also emerged as an important diagnostic tool that has obviated the need for bronchoscopic lung biopsy in many clinical conditions. Further improvements in these and other techniques may lead to a decline in the need for bronchoscopic lung biopsy. In the USA alone, >500,000 bronchoscopies are performed each year [23], and ~15% of these procedures include bronchoscopic lung biopsy [24, 25]. It is clear that bronchoscopic lung biopsy remains an important diagnostic method for the evaluation of patients with diffuse lung diseases [15, 16].

REFERENCES

- 1 Andersen HA, Fontana RS, Harrison EG Jr. Transbronchoscopic lung biopsy in diffuse pulmonary disease. *Dis Chest* 1965; 48: 187–192.

- 2 Andersen HA, Fontana RS, Sanderson DR, Harrison EG Jr. Transbronchoscopic lung biopsy in diffuse pulmonary disease: results in 300 cases. *Med Clin North Am* 1970; 54: 951–959.
- 3 Andersen HA, Fontana RS. Transbronchoscopic lung biopsy for diffuse pulmonary diseases: technique and results in 450 cases. *Chest* 1972; 62: 125–128.
- 4 Andersen HA. Transbronchoscopic lung biopsy for diffuse pulmonary diseases. Results in 939 patients. *Chest* 1978; 73: 734–736.
- 5 Mitchell DM, Emerson CJ, Collins JV, Stableforth DE. Transbronchial lung biopsy with the fiberoptic bronchoscope: analysis of results in 433 patients. *Br J Dis Chest* 1981; 75: 258–262.
- 6 Andersen HA. Transbronchial lung biopsy in diffuse pulmonary disease. *Ann Thorac Surg* 1977; 24: 1.
- 7 Palojoki A, Sutinen S. Transbronchoscopic lung biopsy as aid in pulmonary diagnostics. *Scand J Respir Dis* 1972; 53: 120–124.
- 8 Mitchell DM, Mitchell DN, Collins JV, Emerson CJ. Transbronchial lung biopsy through fiberoptic bronchoscope in diagnosis of sarcoidosis. *BMJ* 1980; 280: 679–681.
- 9 Levin DC, Wicks AB, Ellis JH Jr. Transbronchial lung biopsy via the fiberoptic bronchoscope. *Am Rev Respir Dis* 1974; 110: 4–12.
- 10 Joyner LR, Scheinhorn DJ. Transbronchial lung biopsy through the fiberoptic bronchoscope in diffuse lung disease. *Ann Otol Rhinol Laryngol* 1975; 84: 596–601.
- 11 Joyner LR, Scheinhorn DJ. Transbronchial forceps lung biopsy through the fiberoptic bronchoscope. tdiagnosis of diffuse pulmonary disease. *Chest* 1975; 67: 532–535.
- 12 Scheinhorn DJ, Joyner LR, Whitcomb ME. Transbronchial forceps lung biopsy through the fiberoptic bronchoscope in *Pneumocystis carinii* pneumonia. *Chest* 1974; 66: 294–295.
- 13 Hanson RR, Zavala DC, Rhodes ML, Keim LW, Smith JD. Transbronchial biopsy via flexible fiberoptic bronchoscope; results in 164 patients. *Am Rev Respir Dis* 1976; 114: 67–72.
- 14 Ellis J Jr. Transbronchial lung biopsy via the fiberoptic bronchoscope. Experience with 107 consecutive cases and comparison with bronchial brushing. *Chest* 1975; 68: 524–532.
- 15 Prakash UBS, Utz JP. Bronchoscopic lung biopsy. In: Wang KP, Mehta AC, Turner JF Jr, eds. *Flexible Bronchoscopy*. Malden, Blackwell Publishing, 2004; pp. 89–102.
- 16 Prakash UBS. Bronchoscopy. In: Mason RJ, Broaddus VC, Murray JF, Nadel JA, eds. *Murray and Nadel's Textbook Respiratory Medicine*. 4th Edn. Philadelphia, Elsevier Saunders, 2005; pp. 1617–1650.
- 17 Prakash UBS, Offord KP, Stubbs SE. Bronchoscopy in North America: the ACCP survey. *Chest* 1991; 100: 1668–1675.
- 18 Cortese DA, McDougall JC. Bronchoscopy in peripheral and central lung lesions. In: Prakash UBS, ed. *Bronchoscopy*. New York, Raven Press, 1994; pp. 135–140.
- 19 Collard HR, King TE Jr. Demystifying idiopathic interstitial pneumonia. *Arch Intern Med* 2003; 163: 17–29.
- 20 Baughman RP, Drent M. Role of bronchoalveolar lavage in interstitial lung disease. *Clin Chest Med* 2001; 22: 331–341.
- 21 Raghu G, Mageto YN, Lockhart D, Schmidt RA, Wood DE, Godwin JD. The accuracy of the clinical diagnosis of new-onset idiopathic pulmonary fibrosis and other interstitial lung disease: A prospective study. *Chest* 1999; 116: 1168–1174.
- 22 American Thoracic Society, Idiopathic pulmonary fibrosis: diagnosis and treatment. International consensus statement. American Thoracic Society (ATS), and the European Respiratory Society (ERS). *Am J Respir Crit Care Med* 2000; 161: 646–664.
- 23 Owings MF, Kozak LJ. Ambulatory and inpatient procedures in the United States, 1996. Vital and health statistics. Series 13. No. 139. DHHS publication no. (PHS) 99–1710. Hyattsville, National Center for Health Statistics, 1998.
- 24 Prakash UBS, Colt HG. Bronchoscopy survey by the American Association for Bronchology; does it reveal anything new? *J Bronchol* 2000; 7: 1–4.
- 25 Colt HG, Prakash UBS, Offord KP. Bronchoscopy in North America: survey by the American Association for Bronchology, 1999. *J Bronchol* 2000; 7: 8–25.