EDITORIAL

Indications of BAL, lung biopsy, or both in mechanically ventilated patients with unexplained infiltrations

L. Papazian, M. Gainnier

The diagnosis of unexplained infiltrations in mechanically ventilated patients is a major problem in intensive care unit (ICU) patients.

In this issue of the *European Respiratory Journal*, BULPA *et al.* [1] report the results of 38 mechanically ventilated patients who underwent bronchoalveolar lavage (BAL) combined with transbronchial biopsy (TBB) for the diagnosis of lung infiltrates. They obtained a diagnosis in 74% of the patients, which altered the treatment in 63% of the patients. The diagnostic performance was equally effective in both immunocompetent and immunosuppressed patients.

BAL is a firstline examination with many advantages, including a large sampled lung area and sufficient fluid return to perform multiple analyses. Indeed, cytology (percentage of neutrophils, siderophages, eosinophils and presence of malignant cells), a Gram stain, and numerous cultures (bacteriology, mycology, virology) can be performed. BAL is one of the best tools to establish the diagnosis of bacterial ventilator-associated pneumonia. BAL was evaluated in mechanically ventilated patients by AUBAS *et al.* [2], who found a sensitivity of 89% and a specificity of 83% when using clinical and radiological criteria. When compared with histological criteria, at a threshold of 10^4 colony forming units (cfu)·mL⁻¹, BAL exhibited a sensitivity of 47–58% [3–5]. Its sensitivity can reach 91% in patients not receiving antibiotics [6]. The specificity of BAL varies from 45–100% when compared with histological examination [3–6].

When diffuse infiltrates are present, a definite diagnosis can be difficult to establish, especially in acute respiratory distress syndrome (ARDS) patients. Therefore, histological diagnosis could be useful when BAL does not contribute to the diagnosis in the following two situations. The first is usually at the initial phase of acute respiratory failure, when the aetiology remains unclear, with a lack of improvement despite an empirical treatment. The second is more delayed (after at least 7–10 days of evolution), when there is a possible indication for corticosteroids in ARDS patients. Indeed, corticosteroids can improve the oxygenation status and the outcome of ARDS at the fibroproliferative phase [7, 8]. While determination of type III procollagen peptide in BAL fluid is highly correlated with an increased risk of fatal outcome [9], no study has demonstrated a correlation between the presence of fibrosis assessed by lung histology and the level of type III procollagen peptide in BAL fluid in ARDS patients. Biopsies not only establish the diagnosis of fibrosis, but also provide valuable information to rule out pulmonary infection as the continuing cause of respiratory distress. It is well recognised that nosocomial pneumonia is a major complication of

ARDS, and the use of corticosteroids, if sepsis was the cause of continuing ARDS, would be contraindicated.

Open lung biopsy (OLB) is accepted as being a safe and useful technique in ventilated ARDS patients before prescribing corticosteroids [10]. However, not all ARDS patients exhibited histological signs characterising fibrosis. Indeed, in 38 ARDS patients presenting an established ARDS with a potential indication for corticosteroids, fibrosis was present in only 41% of the lung specimens obtained by OLB [10]. While OLB is potentially associated with underestimation of bacterial lung infection (due to the small area investigated), viral infections and fibrosis are less heterogeneous and could be diagnosed by a single lung tissue sample. Few studies have been devoted to the use of OLB in immunocompromised patients [11–13]. However, all of these studies showed that the procedure can be carried out with a low mortality rate even in seriously ill patients. The question of the performance and tolerance of OLB in mechanically ventilated patients has been poorly investigated. This surgical technique can be performed at the bedside in the ICU especially when oxygenation status contraindicates any transport of the patient. In a previous study [10], no deaths from this procedure were reported and the only morbidity was a minor haemothorax and the development of a low-grade air leak in five patients. One of these five patients presented a pneumothorax necessitating pleural space drainage. To minimise these complications, the patient was disconnected from the ventilator during the stapling procedure and two pleural chest tubes rather than one were used. There was no mortality related to OLB or minimal morbidity in the series by ASHBAUGH and MAIER [14]. The same result was noted by MEDURI *et al.* [15] who reported only one persistent air leak after OLB in 13 patients. On the contrary, POTTER *et al.* [16] noted a high incidence of complications (71%), which they attributed directly to the need for general anaesthesia, mechanical ventilation, and the surgical procedure in patients undergoing OLB. All of the patients investigated in this latter study were spontaneously breathing prior to OLB. However, the principal finding of these studies is that OLB is an acceptably safe and useful technique in a disease process as serious as ARDS.

Nevertheless, while OLB is undoubtedly of value in making or confirming diagnoses, the designs of these studies do not demonstrate that this information improves overall survival rates of mechanically ventilated patients. The video-assisted thoracic surgery (VATS) has recently gained popularity in the diagnostic strategy of diffuse inflammatory lung disease. However, at bedside and in the context of severe pulmonary dysfunction, the open technique may be safer since single-lung ventilation is not required. Samples of lung tissue that are a few centimetres in diameter can usually be obtained with little difficulty.

An alternative approach for invasive diagnosis, fibroscopic TBB, has commonly been limited to autonomously ventilating patients. Only a few reports [17–19] have evaluated

Service de Réanimation Médicale, Hôpitaux Sud, Marseille, France.

Correspondence: L. Papazian, Réanimation Médicale, Hôpital Sainte-Marguerite, 13274 Marseille Cedex 9, France. Fax: 33 491745435. E-mail: laurent.papazian@ap-hm.fr

the feasibility of TBB during mechanical ventilation. However, there are factors that may limit the utility of TBB. These factors are generally believed to be related to its small size or the lack of representation of the tissue specimen or both. FRAIRE *et al.* [20] identified a statistically significant association between the specific pathological diagnosis of infection and biopsy specimens containing a greater number of alveoli. Moreover, BURT *et al.* [21] performed synchronous TBB and OLB in 20 patients. They showed that OLB yielded a diagnosis in 94% versus 59% for TBB. Recently, RAO *et al.* [19] compared *post mortem* TBB with standard *post mortem* histological examination of lung tissue specimens. The sensitivity and specificity of TBB for making a specific diagnosis were 57 and 100%, respectively, suggesting that TBB may be of limited value in mechanically ventilated patients, due to its low sensitivity. Furthermore, haemorrhage and pneumothorax are the potentially life-threatening complications of TBB. For example, two cases of pneumothorax (15%) were encountered in the study of PINCUS *et al.* [17], one by PAPIN *et al.* [18] in their series of 15 patients, and 10 (14.3%) in the study of O'BRIEN *et al.* [22]. In a previous study [23], no pneumothorax was observed in a series of 25 patients undergoing TBB. However, no lung tissue was obtained in three patients.

While BULPA *et al.* [1] do not report any mortality related to the procedure, they note that four out of nine ARDS patients presented a pneumothorax. This is probably an important limitation of this approach in the most severely hypoxaemic patients (*i.e.* ARDS patients). Moreover, BULPA *et al.* [1] report that at least five biopsies are necessary. In this context, it is probably wiser to perform a BAL first and, if this proves inconclusive, an OLB should be performed. It is also important to note that OLB can be performed in the ICU at the patient's bedside, especially in the most severely hypoxaemic patients [10].

The impact of diagnostic delay on mortality is an important emerging general theme in the care of seriously ill patients, particularly as it affects the adequacy of initial therapy. Finally, bronchoalveolar lavage and histology are two complementary diagnostic procedures in this context. However, it is not known if their use (either combined or biopsy only when bronchoalveolar lavage is not conclusive) improved the prognosis of mechanically ventilated patients (acute respiratory distress syndrome or not, immunocompetent or not). Large randomised multicentre trials are required but they are difficult to plan owing to the heterogeneity in the practice of lung biopsies from one centre to another.

References

1. Bulpa PA, Dive AM, Mertens L, *et al.* Combined bronchoalveolar lavage and transbronchial lung biopsy: safety and yield in ventilated patients. *Eur Respir J* 2003; 21: 489–494.
2. Aubas S, Aubas P, Capdevila X, Darbas H, Roustan JP, Du Cailar J. Bronchoalveolar lavage for diagnosing bacterial pneumonia in mechanically ventilated patients. *Am J Respir Crit Care Med* 1994; 149: 860–866.
3. Marquette CH, Copin MC, Wallet F, *et al.* Diagnostic tests for pneumonia in ventilated patients: prospective evaluation of diagnostic accuracy using histology as a diagnostic gold standard. *Am J Respir Crit Care Med* 1995; 151: 1878–1888.
4. Papazian L, Thomas P, Garbe L, *et al.* Bronchoscopic or blind sampling techniques for the diagnosis of ventilator-associated pneumonia. *Am J Respir Crit Care Med* 1995; 152: 1982–1991.
5. Torres A, el-Ebiary M, Padro L, *et al.* Validation of different techniques for the diagnosis of ventilator-associated pneumonia. Comparison with immediate *postmortem* pulmonary biopsy. *Am J Respir Crit Care Med* 1994; 149: 324–331.
6. Chastre J, Fagon JY, Bornet-Lecso M, *et al.* Evaluation of bronchoscopic techniques for the diagnosis of nosocomial pneumonia. *Am J Respir Crit Care Med* 1995; 152: 231–240.
7. Meduri GU, Headley AS, Golden E, *et al.* Effect of prolonged methylprednisolone therapy in unresolving acute respiratory distress syndrome: a randomized controlled trial. *JAMA* 1998; 280: 159–165.
8. Hooper RG, Kearl RA. Established adult respiratory distress syndrome successfully treated with corticosteroids. *South Med J* 1996; 89: 359–364.
9. Clark JG, Milberg JA, Steinberg KP, Hudson LD. Type III procollagen peptide in the adult respiratory distress syndrome. Association of increased peptide levels in bronchoalveolar lavage fluid with increased risk for death. *Ann Intern Med* 1995; 122: 17–23.
10. Papazian L, Thomas P, Bregeon F, *et al.* Open-lung biopsy in patients with acute respiratory distress syndrome. *Anesthesiology* 1998; 88: 935–944.
11. Warner DO, Warner MA, Divertie MB. Open lung biopsy in patients with diffuse pulmonary infiltrates and acute respiratory failure. *Am Rev Respir Dis* 1988; 137: 90–94.
12. White DA, Wong PW, Downey R. The utility of open lung biopsy in patients with hematologic malignancies. *Am J Respir Crit Care Med* 2000; 161: 723–729.
13. Miller RF, Pugsley WB, Griffiths MH. Open lung biopsy for investigation of acute respiratory episodes in patients with HIV infection and AIDS. *Genitourin Med* 1995; 7: 280–285.
14. Ashbaugh DG, Maier RV. Idiopathic pulmonary fibrosis in adult respiratory distress syndrome. Diagnosis and treatment. *Arch Surg* 1985; 120: 530–535.
15. Meduri GU, Chinn AJ, Leeper KV, *et al.* Corticosteroid rescue treatment of progressive fibroproliferation in late ARDS. Patterns of response and predictors of outcome. *Chest* 1994; 105: 1516–1527.
16. Potter D, Pass HI, Brower S, *et al.* Prospective randomized study of open lung biopsy versus empirical antibiotic therapy for acute pneumonitis in nonneutropenic cancer patients. *Ann Thorac Surg* 1985; 40: 422–428.
17. Pincus PS, Kallenbach JM, Hurwitz MD, *et al.* Transbronchial biopsy during mechanical ventilation. *Crit Care Med* 1987; 15: 1136–1139.
18. Papin TA, Grum CM, Weg JG. Transbronchial biopsy during mechanical ventilation. *Chest* 1986; 89: 168–170.
19. Rao VK, Ritter J, Kollef MH. Utility of transbronchial biopsy in patients with acute respiratory failure: a *post-mortem* study. *Chest* 1998; 114: 549–555.
20. Fraire AE, Cooper SP, Greenberg SD, Rowland LP, Langston C. Transbronchial lung biopsy. Histopathologic and morphometric assessment of diagnostic utility. *Chest* 1992; 102: 748–752.
21. Burt ME, Flye MW, Webber BL, Wesley RA. Prospective evaluation of aspiration needle, cutting needle, transbronchial, and open lung biopsy in patients with pulmonary infiltrates. *Ann Thorac Surg* 1981; 32: 146–153.
22. O'Brien JD, Ettinger NA, Shevlin D, Kollef MH. Safety and yield of transbronchial biopsy in mechanically ventilated patients. *Crit Care Med* 1997; 25: 440–446.
23. Martin C, Papazian L, Payan MJ, Saux P, Gouin F. Pulmonary fibrosis correlates with outcome in adult respiratory distress syndrome. A study in mechanically ventilated patients. *Chest* 1995; 107: 196–200.