I read with interest the article by Kao and colleagues [1] in which the authors investigated the role of open lung biopsy in patients with early-stage acute respiratory distress syndrome (ARDS) of suspected non-infectious origin.

A point that merits attention is the need to differentiate between ARDS and acute interstitial pneumonia (AIP). AIP is a rapidly progressive idiopathic interstitial pneumonia characterized by the presence of an organizing form of diffuse alveolar damage on histopathological examination of lung specimens. Although the histological pattern is indistinguishable from that found in ARDS, the term AIP is reserved for cases of unknown cause [2]. In fact, exclusion of a precipitating or etiological agent (which is usually identifiable in patients with ARDS) is one of the diagnostic criteria for AIP. The mortality from AIP is about 70% and is higher than that from ARDS [3].

Although there are no established therapies for AIP, parenteral corticosteroids, often at high doses, are used frequently. Recently Suh and colleagues [4] reported survival rates of 80% in a small series of ten patients with AIP, all of whom required mechanical ventilation (with a median positive end-expiratory pressure of 11 cmH₂O) and underwent open lung biopsy (on median hospital day 4). In these patients, high-dose corticosteroid pulse therapy had been initiated (on median hospital day 3.5) after respiratory infection had been ruled out by means of an aggressive diagnostic workup (including bronchoalveolar lavage performed on median hospital day 2). The authors had postulated that the approach of aggressive diagnostics, mechanical ventilation with lung-protective strategy, and early institution of high-dose immunosuppressive therapy could have led to the improved clinical outcome [4].

In the present study, diffuse alveolar damage was seen in most of the patients who had a non-specific pathological diagnosis. Moreover, this group, in comparison with the group with a specific diagnosis, had a higher rate of treatment alteration (87% versus 56%) as well as a higher rate of hospital survival (61% versus 33%). It is possible that the trend toward improved survival that was seen in this group was a reflection of the possibility that some of these patients had AIP (rather than ARDS) and benefited from the early administration of high-dose corticosteroids.

---

**Authors’ response**

Kuo-Chin Kao, Ying-Huang Tsai and Chung-Chi Huang

We appreciate Dr Singh’s interest in our article [1] and his comments. The term ‘acute interstitial pneumonia (AIP)’ is reserved for ARDS of unknown cause. The critical point in the diagnosis of AIP is to exclude all possible etiologies using the available methods. However, there is no standard laboratory protocol for investigating all possible etiologies. Actually, the diagnostic rate for AIP depends on how aggressive the diagnostic approach is, such as open lung biopsy in ARDS patients.

Some studies have found that the survival rate for AIP was higher than for non-AIP ARDS patients [4,5]. Furthermore, high-dose pulse corticosteroid treatment combined with a lung-protective mechanical strategy could improve the clinical outcome in AIP [4]. Recently the ARDS Clinical Trials Network reported that there was no survival benefit when corticosteroid was administered to ARDS patients beyond 7 days, but there was an improvement in cardiopulmonary physiology [6]. However, in the subgroup in whom

AIP = acute interstitial pneumonia; ARDS = acute respiratory distress syndrome.
corticosteroid treatment was begun 7 to 13 days after the onset of ARDS, the mortality rate was 25% lower than in the placebo group, although this did not have statistical significance. In that study [6], the percentage of patients with ARDS due to unknown causes was not mentioned and should have been very low (the category ‘other’ was only 12%). It is reasonable to assume that different etiologies should be treated with different strategies in heterogeneous ARDS patients, such as AIP and non-AIP patients.

In conclusion, AIP should be identified as soon as possible in ARDS patients. In patients with disease due to unknown causes, the corticosteroid response and outcome seem better than in the ‘known cause’ ARDS patients. Open lung biopsy is therefore indicated to diagnose AIP in some selected early-stage ARDS patients. We recommend that a prospective, randomized controlled trial be performed to confirm this contention.

Competing interests
The author declares that they have no competing interests.

References
1 Kao K-C, Tsai Y-H, Wu Y-K, Chen N-H, Haieh M-J, Huang S-F, Huang C-C: Open lung biopsy in early-stage acute respiratory distress syndrome. Critical Care 2006, 10:R106.
2 American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. Am J Respir Crit Care Med 2002; 165:277-304.
3 Vourlekis JS: Acute interstitial pneumonia. Clin Chest Med 2004; 25:739-747.
4 Suh GY, Kang EH, Chung MP, Lee KS, Han J, Kitaichi M, Kwon OJ: Early intervention can improve clinical outcome of acute interstitial pneumonia. Chest 2006, 129:753-761.
5 Quefatieh A, Stone CH, DiGiovine B, Toews GB, Hyzy RC: Low hospital mortality in patients with acute interstitial pneumonia. Chest 2003, 124:554-559.
6 Steinberg KP, Hudson LD, Goodman RB, Hough CL, Lanken PN, Hyzy R, Thompson BT, Ancukiewicz M; National Heart, Lung, and Blood Institute Acute respiratory Distress Syndrome (ARDS) Clinical Trials Network: Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. N Engl J Med 2006, 354:1671-1684.