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Lung Recruitment in Patients with ARDS

TO THE EDITOR: In the April 27 issue, Gattinoni et al.[1] suggest that the potential for lung recruitment in patients with acute lung injury is generally low and extremely variable among patients. We believe that a suboptimal recruitment maneuver explains such results, contradicting investiga-

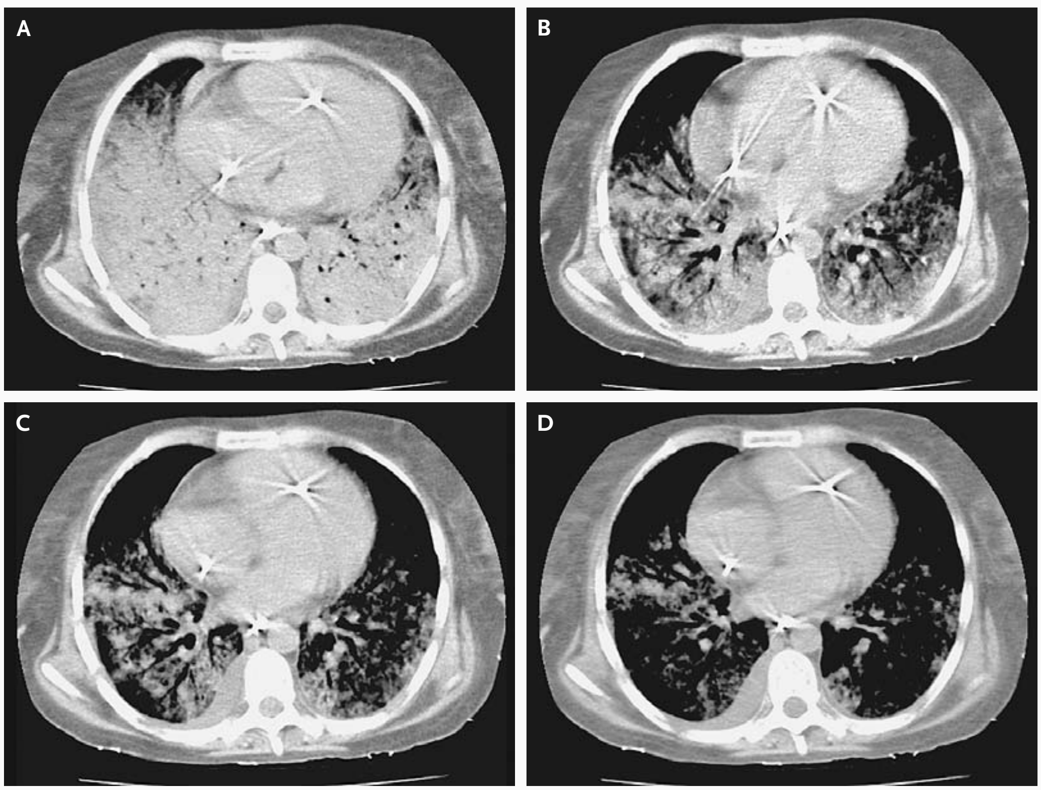

Figure 1. Computed Tomographic Images Obtained at the End-Expiratory Pause in a Patient with Pneumocystosis and the Acute Respiratory Distress Syndrome.

The images were obtained under different ventilatory conditions: a positive end-expiratory pressure (PEEP) of 5 cm of water and a plateau pressure of 20 cm of water (Panel A), a PEEP of 17 cm of water and a plateau pressure of 40 cm of water (Panel B, similar to the strategy used by Gattinoni et al.), a PEEP of 25 cm of water and a plateau pressure of 40 cm of water (Panel C), and a PEEP of 25 cm of water and a plateau pressure of 60 cm of water (Panel D). The corresponding potential for recruitment (relative to the conditions in Panel A) was 35 percent for the conditions in Panel B, 67 percent for the conditions in Panel C, and 87 percent for the conditions in Panel D. At the same plateau pressures (Panels B and C), the application of a higher PEEP (25 cm of water in Panel C) improved the efficacy of the maneuver. A further increase in inspiratory plateau pressure (Panel D) revealed the full potential for recruitment.

tions[2-4] that demonstrate a much larger potential for recruitment and greater homogeneity of response. Gattinoni et al. used an inspiratory plateau pressure of 45 cm of water, a pressure certainly below the critical opening pressures reported in recent studies[2-4] in humans. The investigators also allowed expiratory pressures to repeatedly fall to 5 cm of water, a pressure certainly below the closing pressures of most lung units.[5] This procedure is likely to have cyclically forced the energy provided by the next pulse of inspiratory pressure to be wasted in the opening of the recollapsed units, instead of promoting the recruitment of units. The application of the same inspiratory pressures but a higher expiratory pressure (e.g., 20 to 25 cm of water) could greatly enhance the efficacy of the maneuver (Fig. 1), thus affecting the main conclusion.

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TO THE EDITOR: We were surprised by the level of lung recruitment observed by Gattinoni et al. We would have expected a higher percentage of recruitable lung, on the basis of the known response to recruitment maneuvers.[1-3] One explanation for this lack of response may have been the length of time for which patients received ventilation (5±6 days) before being studied. A large percentage of patients must have received ventilation for more than one week and some for more than two weeks. Grasso et al.[1] demonstrated virtually no lung recruitment in patients who received ventilation for an average of 7±1 days, as compared with a significant response in patients who received ventilation for only 1±0.3 day at the time of lung recruitment. Most recommend that lung recruitment be performed as early as is feasible in the course of the acute respiratory distress syndrome.[1-3]

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TO THE EDITOR: In the Supplementary Appendix of the article by Gattinoni et al., I believe the formula provided to determine the alveolar dead-space fraction was not correct. The value of this variable was automatically computed by a CO_2SMO monitor (Novametrix). This monitor calculates the areas generated by the partial pressure of carbon dioxide curve against the expired volume curve to determine the alveolar dead-space fraction.[1] The monitor therefore does not use the formula stated.

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1. Riou Y, Leclerc F, Neve V, et al. Reproducibility of the respiratory dead space measurements in mechanically ventilated children using the CO2SMO monitor. Intensive Care Med 2004;30:1461-7.

TO THE EDITOR: The article by Gattinoni et al. replicates, in principle, previously published data[1-3] and conclusions.[4] Patients with a higher or lower "percentage of potentially recruitable lung" are, in fact, patients with a diffuse or focal loss of aeration, involving predominantly the lower lobes.[1-3] As previously demonstrated, as compared with patients with a lower percentage of potentially recruitable lung, patients with a higher percentage of potentially recruitable lung (diffuse loss of aeration) have a lower ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, lower respiratory compliance, and a higher mortality rate and rate of direct lung injury and can be identified on the basis of an initial bedside chest radiograph that shows bilateral and diffuse infiltrates.[2]

The expression of lung overinflation as a percentage of hyperinflated lung tissue conceals the fact that many patients had regions of severely overdistended lung during the study. For example, if 10 percent of lung tissue is hyperinflated and lung tissue weighs 1500 g, the overinflated lung volume exceeds 1300 ml. This critical issue is not discussed by Gattinoni et al.; they overlook the fact that our group demonstrated that patients with focal loss of aeration who receive ventilation with a PEEP of 10 cm of water or more are at risk for lung overdistention.[4] The authors should provide the overall volume of overinflated lung (in milliliters) identified on computed tomography (CT) in each patient at a pressure of 45 cm of water.

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THE AUTHORS REPLY: Dr. Borges and colleagues illustrate that plateau pressures of up to 60 cm of water associated with a PEEP of 25 cm of water could be used to increase lung recruitment. However, data from the most recent study by Borges et al.[1] clearly indicate that the level of recruitment between plateau pressures of 45 and 60 cm of water is negligible, accounting for no more than 2 to 3 percent of nonaerated tissue. The price paid to obtain this result, which is of questionable clinical importance,[2] is the retention of carbon dioxide (partial pressure of arterial carbon dioxide, 95±34 mm Hg), severe acidosis (pH, 6.94±0.11), and most important, the need for the infusion of a remarkably large volume to sustain hemodynamic function, right before the recruitment maneuver. We wonder whether the unusually homogeneous and large densities observed at a PEEP of 5 cm of water in Figure 1A of their letter (given that severe pneumocystosis is usually characterized by interstitial infiltrates and low levels of recruitment[3]) reflects increased edema owing to the sudden overload of fluid (up to 2 liters of colloids[1]) in inflamed, leaking lung parenchyma, as observed after a few minutes in experiments in animals.[4] We believe that the risks associated with the use of pressures of 60 and 25 cm of water — possible barotrauma and volume overload[5] — largely outweigh the modest increment in the level of potentially recruitable lung.

Drs. Kacmarek and Villar wonder about the recruitment–time dependency, referring to reports in which the amount of potentially recruitable lung was assessed on the basis of physiological variables. In our study (see the Supplementary Appendix for our article), which used whole-lung CT, we could not find any relationship between the number of days of mechanical ventilation before the study and lung recruitability.

We thank Dr. Dixon for his correct observation. Actually, in our study, we computed the physiological and alveolar dead-space fractions, including in the standard formulas the mixed expired partial pressure of carbon dioxide and the end-tidal carbon dioxide, respectively.

We disagree with Dr. Rouby and colleagues that in our study many patients had regions of severely overdistended lung. In fact, the volume of overdistended lung is not the correct tool to assess overdistention on CT, because the volume includes both gas volume and lung-tissue volume. The issue of lung injury during mechanical ventilation lies in the amount of tissue (not gas) subjected to excessive stress and strain. Indeed, the volume of overdistended lung at a PEEP of 15 cm of water was 198±514 ml (5±11 percent of lung volume) among patients with a lower amount of potentially recruitable lung and 145±469 ml (3±9 percent of lung volume) among those with a higher amount of potentially recruitable lung, but these volumes included 183±482 and 135±434 ml of gas, respectively, and only 14±32 and 11±35 g of tissue, respectively, accounting for 1±3 percent and 1±2 percent of the total lung tissue.

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Hepatitis B Virus with Primary Resistance to Adefovir

TO THE EDITOR: Schildgen et al. (April 27 issue)[1] describe the results of tenofovir treatment in three patients infected with adefovir-resistant variant hepatitis B virus (HBV) that had a valine at position 233 of the reverse-transcriptase domain instead of isoleucine (rtI233V). We recently published the results of two trials in which entecavir demonstrated superiority over lamivudine in patients with chronic hepatitis B that was positive for antibody against hepatitis B e antigen (HBeAg)[2] and in patients with HBeAg-negative chronic hepatitis B.[3]

Four of the patients with HBeAg-positive chronic hepatitis B and four of those with HBeAg-

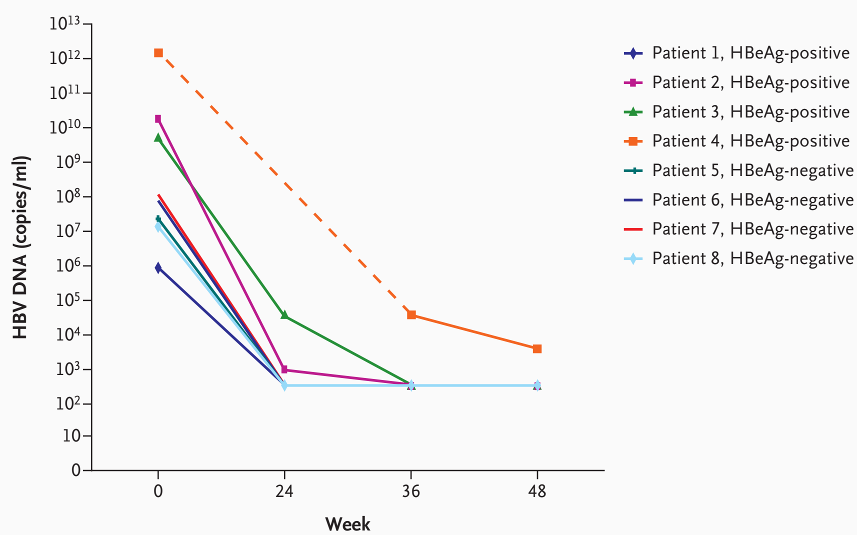

Figure 1. Decrease in HBV DNA Levels during 48 Weeks of Entecavir Therapy in Eight Patients with an rtI233V Mutation in HBV Conferring Primary Resistance to Adefovir.

The limit of detection of the polymerase-chain-reaction assay was 300 copies per milliliter. Data on the HBV DNA burden at 24 weeks were not available for Patient 4.