



Defining low-dose corticosteroid: the pendulum still oscillates



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To the Editor:

TAGAMI *et al.* [1], in their retrospective analysis, have contributed to further understanding of the use of corticosteroids in severe community-acquired pneumonia (CAP) and put forth an inference on the current dispute. Some issues, however, need further discussion.

The patients with severe CAP and sepsis may have adrenal insufficiency. In this retrospective analysis, neither the cortisol level at baseline nor the response to corticotrophin testing has been mentioned, to assess for possible adrenal insufficiency. Therefore, the role of corticosteroids in management of severe CAP should be based on the assessment for adrenal reserve before drawing any conclusions.

The dosage of low-dose corticosteroid used in this study [1] is intravenous infusion of methylprednisolone $0.5\text{--}2.5\text{ mg}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ (an equivalent dose of hydrocortisone is $2.5\text{--}12.5\text{ mg}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$). Therefore, an average person weighing 60 kg would require up to 750 mg hydrocortisone. However, according to the sepsis guidelines, $200\text{--}300\text{ mg}\cdot\text{day}^{-1}$ of hydrocortisone is considered a low-dose steroid, which is indicated in patients with septic shock [2].

Patients with comorbidities like asthma or chronic obstructive pulmonary disease are more likely to benefit with systemic corticosteroids. It is unclear if there was any indication bias with patients having any acute associated condition requiring corticosteroids [3].



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Defining low-dose corticosteroid in severe community-acquired pneumonia <http://ow.ly/OazzW>

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From the authors:

We would like to thank P.R. Mohapatra and colleagues for their comments and interest in our study [1]. We also appreciate the editors of the *European Respiratory Journal* for giving us the opportunity to reply. The points made by P.R. Mohapatra and colleagues regard the following: 1) the corticotrophin test, 2) the dosage of corticosteroid, and 3) comorbidities as confounding factors for the use of corticosteroid.

We agree that some patients with community-acquired pneumonia (CAP) in the present study [1] might have had adrenal insufficiency. However, we possessed no data on how many patients were responders or



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nonresponders to the adrenocorticotropic hormone stimulation test, which was suggested for the evaluation of septic shock patients a decade ago (grade E recommendations in the Surviving Sepsis Campaign international guidelines for management of severe sepsis and septic shock, from 2004 [2]). Meanwhile, this stimulation test is no longer recommended (rather, is recommended not to be performed) for the identification of septic shock patients who should receive corticosteroid, in the revised guidelines (grade 2B recommendations in the Surviving Sepsis Campaign guidelines from 2008 [3] and 2012 [4]). Thus, we do not necessarily agree with the opinion that “the role of corticosteroids in management of severe CAP should be based on the assessment for adrenal reserve”, as far as the recent evidence is concerned [3, 4].

Although the current guidelines for severe sepsis and septic shock recommend hydrocortisone at a dose of 200 mg·day⁻¹ [4], the present study [1] evaluated CAP patients with mechanical ventilation. Most of the major studies and systematic review studies on CAP (with acute lung injury) have used the criteria of methylprednisolone 0.5–2.5 mg·kg⁻¹·day⁻¹ (or an equivalent dose of other steroids) [5–8]. Therefore, we defined low-dose corticosteroid use as intravenous infusion of methylprednisolone 0.5–2.5 mg⁻¹·kg⁻¹·day⁻¹ (or an equivalent dose of dexamethasone, hydrocortisone, prednisolone or betamethasone), and any higher dose was defined as high-dose corticosteroid use in the present study [1].

We strongly agree that comorbidities may work as important confounding factors for the treatment of CAP with corticosteroid. In particular, the comorbidities would include asthma and chronic obstructive pulmonary disease (COPD), because these diseases are also often treated by corticosteroid administration. Therefore, we implemented these factors in the estimation of the propensity scores, and these confounders were well balanced after propensity score matching. Moreover, we performed an instrumental variable analysis as a confirmatory analysis of the propensity score analyses. Using hospitals’ preference as an instrumental variable, we computed the differences in the 28-day mortality risk between the groups with and without corticosteroid, using a two-stage least-squares method adjusted for the patient characteristics (*i.e.* all variables listed in tables 1 and 2 of our study [1], including asthma and COPD). We believe that these analyses are appropriate and useful for treating measured and unmeasured confounders.

We cannot yet draw robust conclusions regarding the effect of low-dose corticosteroid for CAP patients in general, at least from our retrospective analysis [1]. We believe that further studies are required to evaluate the optimal doses and types of corticosteroids for treating CAP. Our results provide basic data for future prospective trials to lead to the “end of the story” [9] and stop the “pendulum”.



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Low-dose corticosteroids for severe CAP: further studies are required to evaluate the optimal doses and types <http://ow.ly/OazFp>

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Computed tomography in the diagnosis of bronchiectasis



To the Editor:

We read with great interest the article by HURST *et al.* [1], who discussed the overlap between chronic obstructive pulmonary disease (COPD) and bronchiectasis, and provided the position statement from the BRONCH-UK Consortium.

Bronchiectasis is defined as abnormal, persistent bronchial dilatation, usually associated with inflammation in the bronchial tree and lung parenchyma. The disease remains a common cause of significant morbidity and mortality, especially when associated with COPD. Computed tomography (CT) is now the diagnostic modality of choice and may also contribute to clinical management. However, we would like to highlight some technical aspects of diagnosis.

Bronchial dilatation remains the most important CT finding to establish a diagnosis of bronchiectasis, and its detection typically relies solely on simple visual identification [2]. Although generally accurate, visual inspection may lead to the overestimation of airway dilatation, as a result of a subtle optical illusion in which the diameters of hollow circles appear larger than those of solid circles, despite their identical size, a phenomenon that only occurs when airways are sectioned at right angles. Several quantitative metrics, most including lumen diameter and broncho–arterial ratio (ring sign), have been proposed for the diagnosis of this condition. Care should be taken to avoid misinterpretation of physiologically dilated airways as bronchiectatic, which occurs, for example, in individuals who live at high altitudes [3], in elderly patients [2], or on images obtained through the lung bases in the prone position. In one study of high-resolution CT (HRCT) findings in 85 subjects without cardiopulmonary disease divided into three age groups, a significant correlation between the broncho–arterial ratio and age was noted ($r=0.768$, $p<0.0001$), with broncho–arterial ratios >1 identified in 41% of individuals aged >65 years [2]. With ageing, morphological changes occur in the lung, which include: increased alveolar duct air; decreased complexity of the alveolar surface or surface-to-volume ratio; loss of alveolar wall tissue, elastic tissue, and bronchiolar muscle; and increased frequency of emphysema [4]. The relationships between ageing and morphological changes of the lung have also been investigated radiographically. LEE *et al.* [5] detected age-related increases in the frequency and severity of air trapping on HRCT images of the lung. Air trapping is induced by occlusion or narrowing of the airway. LEE *et al.* [5] suggested that age-related occlusion or luminal narrowing occurred at the lobular bronchiole level. HANSELL *et al.* [6] showed a clear relationship between the extent of bronchiectasis and CT attenuation values, which suggests that involvement of the small airways is an integral part of bronchiectasis. Although the relationship between small airways involvement and the development of bronchodilation has not yet been clearly established, these reports provide some support for a relationship between bronchodilation and age. That relationship might be another reason for the increase in the broncho–arterial ratio that occurs with age.

These important technical parameters and physiological variations should be evaluated critically, as they may dramatically influence the diagnosis and determination of the significance of bronchiectasis.



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Bronchiectasis diagnosis and significance can be influenced by technical parameters and physiological variations <http://ow.ly/OatKb>

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