Corticosteroid Therapy for Severe Community-Acquired Pneumonia: A Meta-Analysis

To the Editor:

I have read with interest the original article entitled "Corticosteroid Therapy for Severe Community-Acquired Pneumonia: A Meta-Analysis" by Cheng et al.[1] The authors decided to use the fixed-effects model despite the heterogeneity of the studies included in the meta-analysis (populations, doses, and antibiotics were different in each study). If the random-effects model had been used, which seems more appropriate in this case, the conclusion would have been different (Fig. 1). Another choice that seems inadequate was the decision to use the Peto odds ratio. The Peto odds ratio method usually works well in cases in which the odds ratio is close to 1.[2] This is not what happened in 2 studies. Thus, if the odds ratio had been used, even if using the fixed-effects model, there would have been no difference between the corticosteroid and placebo groups (Fig. 2).

Thus, I believe that this meta-analysis should be interpreted with caution.

Dimitri Gusmao-Flores MD PhD
Intensive Care Unit
Hospital Universitário
Professor Edgar Santos
Salvador, Brazil

The author has disclosed no conflicts of interest.

REFERENCES

1. Cheng M, Pan ZY, Yang J, Gao YD. Corticosteroid therapy for severe community-acquired pneumonia: a meta-analysis. Respir Care 2014;59(4):557-563.
2. Higgins JP, Green S, editors. Cochrane handbook for systematic reviews of interventions version 5.1.0. Updated March 2011. The Cochrane Collaboration, 2011. www.cochrane-handbook.org. *Accessed June 6, 2014.*

Corticosteroid Therapy for Severe Community-Acquired Pneumonia: A Meta-Analysis–Reply

In Reply:

We thank Dr Gusmao-Flores for the interest in our recent article "Corticosteroid therapy for severe community-acquired pneumonia: a meta-analysis."[1] We appreciate the opportunity to respond to the concerns raised with regard to our article.

According to Cochrane recommendations, the chi-square test measures the heterogeneity of observed effect sizes from an underlying overall effect. This test has low power in detecting true heterogeneity when studies have a small sample size or are few in number.[2,3] Hence, we used a *P* value of .10 to determine statistical significance. When *P* was > .10, a fixed-effects model was used.

The Peto odds ratio (OR) method works well when intervention effects are small, events are rare, and the studies have similar numbers in 2 groups.[2,4] Bradburn et al[4] found that the Mantel-Haenszel OR method using

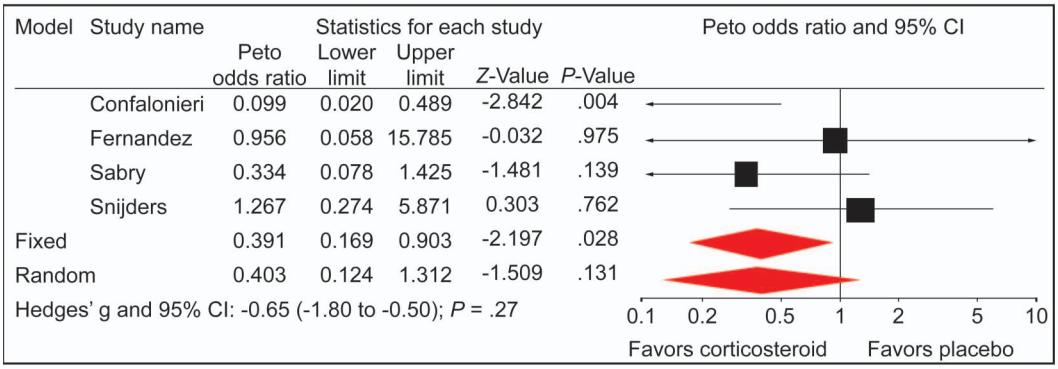

Fig. 1. Correlation between mortality and corticosteroid treatment using the random-effects model.

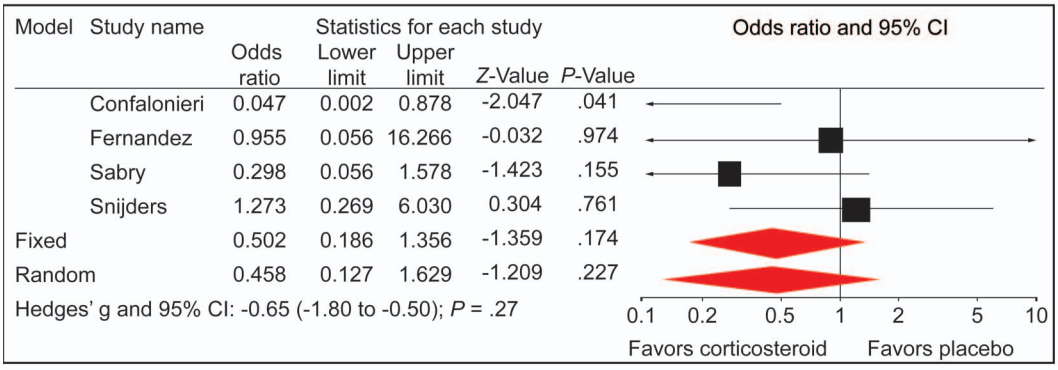

Fig. 2. Correlation between mortality and corticosteroid treatment using the odds ratio.

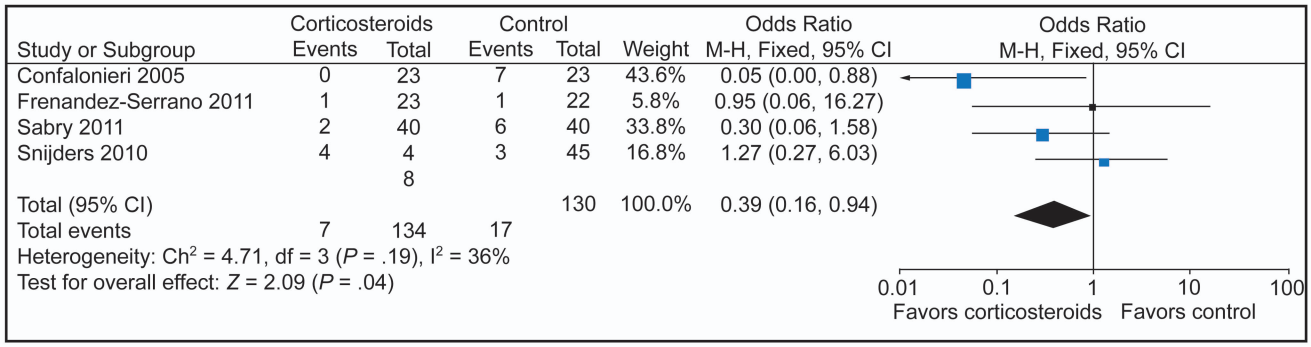

Fig. 1. Correlation between mortality and corticosteroid treatment using the odds ratio.

a 0.5 zero-cell correction produces great bias, whereas the Peto method needs no correction. Therefore, mortality was analyzed using the Peto method to calculate the OR and 95% CI in our meta-analysis. Even if the OR was used, the *P* value from the heterogeneity test was .19 (I^2 = 36%), and the fixed-effects model could be used. A significant difference still existed between the corticosteroid and control groups (OR = 0.39, 95% CI 0.16–0.94) (Fig. 1).

Ming Cheng MD
Jiong Yang PhD
Ya-dong Gao PhD
Department of Pneumology, Zhongnan Hospital of Wuhan University, Wuhan, People's Republic of China

Zhi-yong Pan MD
Department of Neurosurgery
Zhongnan Hospital of Wuhan University
Wuhan, People's Republic of China

The authors have disclosed no conflicts of interest.

REFERENCES

1. Cheng M, Pan ZY, Yang J, Gao YD. Corticosteroid therapy for severe community-acquired pneumonia: a meta-analysis. Respir Care 2014;59(4):557-563.
2. Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. Updated March 2011. http://www.cochrane-handbook.org. *Accessed June 19, 2014.*
3. Deeks JJ, Higgins JPT, Altman DG. Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions. Version 5.0.1. Updated September 2008. http://www.cochrane-handbook.org. *Accessed June 19, 2014.*
4. Bradburn MJ, Deeks JJ, Berlin JA, Russell Localio A. Much ado about nothing: a comparison of the performance of meta-analytical methods with rare events. Stat Med 2007;26(1):53-77.

Expiratory Rib Cage Compressions to Improve Secretion Clearance During Mechanical Ventilation: Not Only a Matter of Squeezing the Chest

To the Editor:

We read with interest the manuscript by Guimarães et al,[1] who assessed in humans the pulmonary effects of manual rib cage compressions (MRCCs). The authors found a mild increase in the amount of cleared airway secretions with the use of MRCCs and no effects on respiratory mechanics. Some of their results are in line with previous evidence from clinical[2] and laboratory[3-5] studies; nevertheless, we would like to comment on a few critical methodological aspects of previous works.

First, there is a lack of consistency in the applied methods in previous studies. Unoki et al[2-4] applied gentle and gradual rib cage compressions during the expiratory phase and demonstrated marginal effects on mucus clearance and respiratory mechanics, as in the study by Guimarães et al.[1] Conversely, in our previous study,[5] we applied two different techniques (Fig. 1): (1) soft MRCCs to prolong the late expiratory phase through gentle and gradual chest compressions; and 2) hard MRCCs consisting of brief and strong compressions synchronized with the early expiratory phase to increase peak expiratory flow. Interestingly, soft MRCCs did not influence mucus clearance and worsened the static lung elastance. Conversely, hard MRCCs significantly improved mucus clearance and did not cause any deleterious pulmonary effect. Unfortunately, in the study by Guimarães et al, the applied technique is not fully elucidated. The significant increase in peak expiratory flow (> 16 L/min) indicates that they used a technique comparable to hard MRCCs. Nonetheless, given the expiratory flow limitation found in a limited number of subjects, it is possible that compressions were applied throughout the expiratory phase. Our previous investigation clearly demonstrated that the beneficial effects of MRCCs may vary based on the applied forces, synchronization with the expiratory phase, and the time of application.[5] In particular, it seems that very brief compressions synchronized with the early expiratory phase could be the best option to improve mucus clearance during controlled mechanical ventilation.

Second, Guimarães et al[1] suggested that the expiratory flow limitation found in their study was probably due to the increased transmural pressure associated with the compressions, which ultimately led to peripheral airway collapse. In our study, we found a significant increase in static elastance, likely related to a decrease in expiratory lung volume, as corroborated by the significant loss of PEEP (~3 cm H_2O) (see Fig. 1). However, this was associated with prolonged compressions only up to the late expiratory phase. Another possible explanation for the findings of Guimarães et al is that the subjects were not fully sedated (3 subjects were not sedated, and 16 presented a Ramsay Sedation Scale score of 2–4). Consequently, the subjects might have modulated the expiratory flow and opposed the thoracic compressions. Thus, uncertainty exists as to the feasibility of the technique in lightly sedated patients