
Response

To the Editor:

Meduri et al highlight the nature of the ongoing debate over the value of corticosteroids in acute lung injury/ARDS. The study by Confalonieri and colleagues¹ was not included in our review because the study population had severe pneumonia, not ARDS. The retrospective study by Annane et al² was a secondary analysis of a randomized controlled trial of corticosteroids in septic shock; benefit was noted in the subgroup of patients with sepsis-associated ARDS who failed to respond to a corticotropin stimulation test. The benefits of corticosteroids in this group likely derive from their beneficial effects in the overall population of nonresponders in this study rather than from an effect specific to ARDS; no statistical test of interaction between corticosteroid therapy and ARDS was reported in the article. In addition, while post hoc subgroup analysis may be useful for hypothesis generation, generalizing the findings to patient treatment can be perilous.³ The 2007 study by Meduri et al was not published at the time of our review; however, this trial³ has significant limitations as well. For one, the majority of patients randomized to placebo who remained on mechanical ventilation at day 9 of the study were crossed over to open-label methylprednisolone, making outcomes analysis after that point (such as mortality and ventilator-free days) very difficult to interpret. In our review,⁵ we focused on the largest and most rigorous trial on this issue: the prospective, randomized controlled trial performed by the ARDS Network, which demonstrated no mortality benefit to corticosteroids.⁶ We agree that the size of the subgroup of patients randomized after day 14 in this study is small, and that conclusions drawn from this subgroup, albeit a prespecified one, should be tempered by this consideration; however, most of the baseline imbalances cited by the letter were not statistically significant.

We also question the validity of the authors’ approach of pooling data from the five studies cited in their letter. Since the trials did not have similar inclusion criteria (ie, ARDS vs pneumonia, early vs late ARDS), they would be poor candidates for a traditional metaanalysis.⁷ Moreover, the authors do not describe their meta-analysis methods (ie, fixed vs random-effects model, statistical tests for heterogeneity). For these reasons, we also disagree with their calculation of a number needed to treat based on this data. The heterogeneity of prior studies was a primary driving force behind the creation of the ARDS Network’s large randomized controlled trial, which has rendered the most definitive verdict in this field.

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Steroids in Early ARDS

To the Editor:

We admire the endurance of Dr. Meduri et al¹ in completing their ARDS study (April 2007). However, during the 10 years that passed after the start of this study there have been important changes in daily ICU practice. In the control arm, with 46% catecholamine-dependent patients, no steroids were administered in the first week. With the spread of the Surviving Sepsis Campaign,² most patients in the control arm and probably several in the treatment arm would nowadays have received low-dose steroids (100 to 300 mg/24 h). We wonder how much of the beneficial results of the study are attributable to undertreatment of the control patients. Surprisingly Dr. Annane, one of the advocates of low-dose steroid treatment in septic shock, did not mention this item in the accompanying editorial.³ We can image the enthusiasm for steroids, but the study by Meduri et al¹ does not justify the unconditional title of the editorial. Even Dr. Meduri advises a further study with stratification to minimize the risks of mismatching as occurred in this study.

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DOI: 10.1378/chest.07-0927

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