LETTER

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Prolonged corticosteroid treatment in acute respiratory distress syndrome: impact on mortality and ventilator-free days

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See related letter by Blot et al., https://ccforum.biomedcentral.com/articles/10.1186/s13054-017-1920-x

We read with interest the letter by Blot and colleagues recently published in Critical Care [1] which concluded that the recommendations of the Corticosteroid Guideline Task Force of SCCM and ESICM [2] for the use of adjunctive corticosteroids in early moderate to severe acute respiratory distress syndrome (ARDS) were based on insufficient evidence. In support of their view, the authors refer to the meta-analysis of Ruan et al. (reference [3] in Blot and colleagues' letter) also published in Critical Care in 2014. We respectfully disagree with their comments and offer the following observations. First, the meta-analysis by Ruan et al. did not take into account how current understanding of disease pathophysiology impacts the administration of corticosteroid treatment in ARDS. The meta-analysis by Ruan et al. incorporated four randomized trials from the 1980s that investigated short-term (24-48 h) massive daily corticosteroid doses (up to 120 mg/kg methylprednisolone equivalent), an intervention that is obsolete and discredited by the present pathophysiological understanding of ARDS [2]. Thus, the inclusion of these trials in the meta-analysis is mostly responsible for the inconsistency reported in their letter. Moreover, the conclusion by Ruan et al. that the benefits of corticosteroid treatment decreased over time are not supported by the actual findings of the cited trials (Figure 3 in [4], Figure 4 in [5] and Table 5 in [3]).

As the Corticosteroid Guideline Task Force state in the guideline, our recommendation for adjunctive use of corticosteroids in early moderate to severe ARDS is a conditional recommendation and not necessarily meant to imply a standard of care treatment. In our analysis [2] the pooled relative risk estimate for hospital mortality (Fig. 1)

¹Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Medicine, Memphis Veterans Affairs Medical Center, (111) - 1030 Jefferson Avenue Suite room #CW444 -, Memphis, TN 38104, USA Full list of author information is available at the end of the article with corticosteroids was 0.64 (95% confidence interval (CI) 0.46–0.89). Even if one excludes the four studies which Blot and colleagues appear to question [1], the pooled relative risk estimate for hospital mortality is 0.76 (95% CI 0.58–0. 99), which is not significantly different from 0.64 (0.46–0. 89). Independent of hospital mortality, the use of corticosteroids was associated with approximately a 7-day increase in ventilator-free days (mean difference 7.06 days, 95% CI 3.19–10.93) [2] (supplementary digital content in [5]). Given that our recommendation for adjunctive corticosteroids in ARDS is conditional in nature, ongoing and future prospective trials will certainly impact our future recommendations.

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Authors' contributions

GUM wrote the first draft and BR, SMP and DA reviewed, edited, and approved the final manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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	Corticost	eroid	Contr	ol		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% Cl
1.2.1 High Risk of B	ias							
Confalonieri 2005	0	15	7	19	1.3%	0.08 [0.01, 1.35]	2005	· · · · · · · · · · · · · · · · · · ·
Sabry 2011	2	26	6	34	4.1%	0.44 [0.10, 1.99]	2011	
Liu 2012	2	12	7	14	4.9%	0.33 [0.08, 1.31]	2012	
Rezk 2013	0	18	3	9	1.3%	0.08 [0.00, 1.32]	2013	·
Subtotal (95% CI)		71		76	11.7%	0.27 [0.11, 0.68]		\bullet
Total events	4		23					
Heterogeneity: Tau ² = 0.00; Chi ² = 2.05, df = 3 (P = 0.56); $l^2 = 0\%$								
Test for overall effect	t: Z = 2.81 (P = 0.00)5)					
1.2.2 Low Risk of Bi	as							
Meduri 1998	2	16	5	8	4.7%	0.20 [0.05, 0.81]	1998	
Annane 2006	15	66	23	66	16.8%	0.65 [0.37, 1.13]	2006	
Steinberg 2006	54	85	67	92	28.3%	0.87 [0.71, 1.07]	2006	
Meduri 2007	15	63	12	28	15.1%	0.56 [0.30, 1.03]	2007	
Tongyoo 2016	37	98	40	99	23.4%	0.93 [0.66, 1.32]	2015	
Subtotal (95% CI)		328		293	88.3%	0.76 [0.58, 0.99]		\blacklozenge
Total events	123		147					
Heterogeneity: Tau ² = 0.04; Chi ² = 7.20, df = 4 (P = 0.13); $l^2 = 44\%$								
Test for overall effect: $Z = 2.02$ (P = 0.04)								
Total (95% CI)		399		369	100.0%	0.64 [0.46, 0.89]		•
Total events	127		170		e () 12			
Heterogeneity: $ au^* = 0.09$; Chi* = 16.04, df = 8 (P = 0.04); I* = 50%								
lest for overall effect: $Z = 2.64$ ($P = 0.008$) Favours [control]								
lest for subgroup alterences: Cnl ⁻ = 4.46, at = 1 (V = 0.03), l ⁻ = 77.6%								
Fig. 1 Hospital mortality in ARDS subgroup before day 14. Comparison between randomized trials at high risk of bias versus those at low risk of								

FIG. I Hospital mortality in AKUS subgroup before day 14. Comparison between randomized trials at high risk of bias versus those at bias which investigated prolonged glucocorticoid (methylprednisolone or hydrocortisone) treatment in ARDS

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