Published in final edited form as:

Crit Care Med. 2018 July ; 46(7): e718–e719. doi:10.1097/CCM.0000000000003110.

Response to Letter by Beyoglu, Koksai, and Esquinas regarding “Association between partial pressure of arterial carbon dioxide and survival to hospital discharge among patients diagnosed with sepsis in the emergency department”

Brian W. Roberts, MD¹, Nicholas M. Mohr, MD, MS³, Enyo Ablordeppey, MD, MPH^{4,5}, Anne M. Drewry, MD, MSCI⁴, Ian T. Ferguson, MPH⁷, Stephen Trzeciak, MD, MPH^{1,2}, Marin H. Kollef, MD⁶, and Brian M. Fuller, MD, MSCI^{4,5}

¹The Department of Emergency Medicine, Cooper University Hospital, Cooper Medical School of Rowan University, Camden, New Jersey ²The Department of Medicine, Division of Critical Care Medicine, Cooper University Hospital, Cooper Medical School of Rowan University, Camden, New Jersey ³Departments of Emergency Medicine and Anesthesiology, Division of Critical Care Medicine, Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, Iowa ⁴Department of Emergency Medicine, Washington University School of Medicine in St. Louis, St. Louis, Missouri ⁵Department of Anesthesiology, Division of Critical Care, Washington University School of Medicine in St. Louis, St. Louis, Missouri ⁶Department of Medicine, Division of Pulmonary and Critical Care Medicine, Washington University School of Medicine in St. Louis, St. Louis, Missouri ⁷School of Medicine and Medical Science, University College Dublin, Dublin, Ireland

To the Editor

We would like to thank Dr. Beyoglu and colleagues (1) for their interest in our recent paper, “Association between partial pressure of arterial carbon dioxide and survival to hospital discharge among patients diagnosed with sepsis in the emergency department.”(2) In their letter to the editor they raise several important points regarding our results. First, they point out the value of including a wide range of patients and ask if patients with COPD were included in our cohort. As noted in our Table 1, patients with COPD were included and we did not find a statistically significant difference in the proportion of patients with COPD among survivors vs. non-survivors. In addition, on a sensitivity analysis not included in our paper, we performed a test of interaction using our original multivariable logistic regression model and did not find evidence that the association between PaCO₂ and survival to hospital

Address for correspondence: Brian W. Roberts, MD, Department of Emergency Medicine, Cooper University Hospital, One Cooper Plaza, K152, Camden, NJ 08103, roberts-brian-w@cooperhealth.edu, Telephone: 856-342-2351.

Declarations of interests: All authors declare no competing interests.

Copyright form disclosure: Drs. Roberts and Drewry received support for article research from the National Institutes of Health (NIH). Dr. Mohr disclosed that he has grants unrelated to this work with the US Department of Health and Human Services and the US Veterans Administration. Dr. Ablordeppey’s institution received funding from the BJH foundation and Washington University School of Medicine. Dr. Drewry’s institution received funding from the NIH. The remaining authors have disclosed that they do not have any potential conflicts of interest.

discharge differed between patients with and without COPD ($p = 0.283$). Second, they ask about the relationship between PaCO_2 and lung compliance. This is an important point, as one would expect a decrease in lung compliance to result in decreased minute ventilation and thus higher PaCO_2 , potentially confounding our results. Using Spearman correlation we found a modest negative correlation between PaCO_2 and lung compliance ($r = -0.22$) and when we added lung compliance to our original multivariable logistic regression model we did not find it to alter the association between PaCO_2 and survival to hospital discharge [aOR 1.03, 95% confidence interval (CI) 1.01–1.05, $p < 0.001$]. Third, Dr. Beyoglu and colleagues point out that we only found a modest correlation between PaCO_2 and arterial pH ($r = -0.48$). This low correlation is likely secondary to respiratory compensation for metabolic acidosis, which is common in this patient population, resulting in a low PaCO_2 in the setting of a low pH. Fourth, they point out that the high FiO_2 and low PEEP initially in the emergency department is not consistent with classical lung protective mechanical ventilation strategies.⁽³⁾ We agree that excessive FiO_2 should be avoided, but it is common for treating physicians to start with a FiO_2 of 100% immediately after intubation in an effort to prevent hypoxia. Our clinicians rapidly titrate down the FiO_2 from 100% and increase PEEP as needed to ensure prevention of excessive FiO_2 exposure. Our Table 2 demonstrates this reduction in FiO_2 , as the median (IQR) FiO_2 on arrival to the ICU was 0.44 (0.40–0.51).

In our study we found a higher PaCO_2 to have a positive association with survival to hospital discharge among patients diagnosed with sepsis in the emergency department after adjusting for corrected minute ventilation for a normal PaCO_2 , a surrogate for dead space volume. Our results suggest that hypercapnia may be well tolerated in this patient population and may even be a potential therapeutic target. Given the observational design of this study we can only describe associations and cannot suggest causal inference. However, we believe our results provide scientific rationale for clinical trials testing early manipulation of PaCO_2 in this patient population.

References

1. Beyoglu CA, Koksall GM, Esquinas AM. Association between partial pressure of arterial carbon dioxide and survival to hospital discharge among patients diagnosed with sepsis in the emergency department Is PaCO_2 a predictive parameter for hospital discharge? *Crit Care Med*. 2018 in press.
2. Roberts BW, Mohr NM, Ablordeppey E, et al. Association Between Partial Pressure of Arterial Carbon Dioxide and Survival to Hospital Discharge Among Patients Diagnosed With Sepsis in the Emergency Department. *Crit Care Med*. 2017
3. Gattinoni L, Chiumello D, Russo R. Reduced tidal volumes and lung protective ventilatory strategies: where do we go from here? *Curr Opin Crit Care*. 2002; 8(1):45–50. [PubMed: 12205406]