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Reply to Schwarz *et al.*

From the Authors:

We are very grateful to Schwarz and colleagues for reading our article (1) and their fruitful comments, which we wish to address below.

First, Schwarz and colleagues point out that any causal relationship between low odds ratio product (ORP) levels and weaning failure cannot be established from our data. They also highlight that the ORP level evaluation was made "at a single time point" and that potentially important information (previous sleep deprivation and previously diagnosed sleep disorders) was missing. Given the observational and exploratory nature of our study, we acknowledge that the design was not intended to reveal any causal relationship between the ORP findings and weaning outcomes. This study investigating ORP is the first to be conducted in an ICU setting, and further studies will have to determine whether the association between low ORP or interhemispheric ORP correlation and poor weaning outcome results from causality. Nevertheless, in a recent study, Thille and colleagues reported that patients with weaning failure were more likely to have pathological wakefulness (2). We actually observed an association between a low level of right-/left-brain hemisphere ORP correlation and reaching a normal ORP level (Figure 6 in our article). We therefore believe that there might be a possible link between a low level of ORP and poor weaning outcome. It is true that ORP—as reported in our study—reflects the average ORP in the whole study period, from 5 P.M. to 8 A.M. Consequently, we may have missed some relevant changes that occurred during the night. In a sensitivity analysis not shown in the article, we addressed this issue by assessing ORP over tertiles of the night and did not observe different findings. Of note, we had excluded patients with known sleep-disordered breathing.

Second, Schwarz and colleagues raise concerns about the weaning process and the process used in deciding to extubate. They also questioned the reasons for patients' failure to wean. However, Table E1 in the online supplement of our article provides the reasons for spontaneous breathing trial (SBT) failures and for not extubating patients who passed the SBT. Regarding the weaning process, all details are provided in the METHODS section of our article, but we totally agree that the evaluation of success (or failure) of the SBT remains subjective. However, as stated in METHODS, predefined criteria were used by the clinical team (3). Another important point is that the same SBT protocol was used for all of the patients (4). We believe that this approach may have reduced the subjective bias of the clinical evaluation. In addition, we also provide in the online supplement the results from an analysis of two groups: successful SBT and failed SBT. This analysis provided the same findings as the primary analysis.

Third, Schwarz and colleagues suggest some further areas of research that we think are highly relevant, including the effects of various analgosedation regimes. The assessment of ORP levels in combination with neuroimaging and neurofunctional data certainly deserves attention, and further studies are needed to consider this important objective. Schwarz and colleagues indicate some interesting leads in this regard. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Erratum: Acute Respiratory Distress Syndrome Subphenotypes Respond Differently to Randomized Fluid Management Strategy [Additional Corrections]

The authors of an article published in the February 1, 2017, issue of the *Journal* (1) have identified two additional errors that require correction (an erratum had been previously published for this article [2]). In the article's online supplement, the values provided for two plasma biomarkers (tumor necrosis factor receptor-1 and angiopoietin-2) had not been corrected for assay dilution. In addition, driving pressure was mislabeled as plateau pressure in online supplement Tables E1 and E2 and on the *x*-axis in Figure 1. In the judgment of the authors, these errors do not affect the study's main results or conclusions.

Clinical data for this study are publicly available through the NHLBI's Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC); the authors are happy to share the biological data from this analysis with researchers with the requisite BioLINCC approval.

A corrected version of the manuscript and online supplement have been posted, and the copy of the original article with corrections indicated in red has been updated in the supplemental materials tab. The authors apologize for these errors. ■

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2. Erratum: Acute respiratory distress syndrome subphenotypes respond differently to randomized fluid management strategy. *Am J Respir Crit Care Med* 2018;198:1590.