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Reply to Borrelli *et al.*

From the Authors:

We thank the authors for calling attention to an important recent study on examining the use of pharmacotherapy with buspirone in patients with central sleep apnea related to heart failure with reduced ejection fraction (1) in our recent statement (2). As noted, the study found important decreases in chemoreflex sensitivity to carbon dioxide without changes in sensitivity to oxygen. These findings lend support to emerging evidence that central chemoreceptors play an important role in the pathogenesis of central sleep apnea in those with heart failure and stand in contrast to the traditional view that peripheral chemoreceptors are the sole important drivers in this context (3). Although the reductions in the apnea–hypopnea index in this study were modest, this work provides a foundation for much needed novel clinical investigations in addition to clarifying relevant underlying neurobiology. ■

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

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The 4DPRR Index and Mechanical Power: A Step Ahead or Four Steps Backward?

To the Editor:

We read with interest the manuscript by Costa and colleagues (1) showing that the combination of driving pressure and respiratory rate is significantly associated with mortality in patients with acute respiratory distress syndrome. Their analysis suggests that a simplified composite variable (driving pressure multiplied by four plus respiratory rate [4DPRR]) is as informative as the more comprehensive equation of mechanical power. Although we are delighted to see that respiratory rate, long neglected, has finally been considered (better late than never) as an essential determinant of ventilator-induced lung injury (VILI), we believe that some conceptual and methodological considerations need to be highlighted.

First, it is essential to make a clear distinction between a parsimonious epidemiological model that includes ventilatory variables associated with mortality and the more VILI-relevant *physical* concept of total energy transferred during mechanical ventilation—expressed as mechanical power (2). Regarding the latter, all elements of the ventilator's settings, including positive end-expiratory pressure (PEEP), should be included because all contribute to the total mechanical energy (3). Mechanical power is not intended to be the "unifying theoretical explanation" of VILI, but it is a more physiological way to summarize the physical contributions of the ventilator settings expressed in meaningful and understandable physical units (J/min) (2).

Although 4DPRR may help estimate the average trade-off between driving pressure and respiratory rate under purely theoretical isocapnic conditions, it is a population-associated statistical measure based entirely on the effect size derived from a mediation analysis; it does not describe a physical quantity or encapsulate total mechanical energy. Indeed, its 4:1 ratio may not apply under all conditions (e.g., when PEEP achieves lung

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