

# Modifiable risk factors and the role of driving pressure in acute respiratory distress syndrome

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Comment on: Laffey JG, Bellani G, Pham T, *et al.* Potentially modifiable factors contributing to outcome from acute respiratory distress syndrome: the LUNG SAFE study. *Intensive Care Med* 2016;42:1865-76.

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In the December 2016 issue of *Intensive Care Medicine* (1), Laffey *et al.* published their analysis of potentially modifiable risk factors of mortality in patients with acute respiratory distress syndrome (ARDS) enrolled in the LUNG SAFE prospective cohort study.

Laffey and colleagues included 2,377 patients in their analysis and stratified them based on the Berlin Criteria. The etiology of ARDS was also identified, dividing patients in to having a pulmonary etiology versus non-pulmonary etiology. The LUNG SAFE study has multiple strengths including use of the Berlin criteria to classify patients and the stratification of patients into pulmonary etiology ARDS and non-pulmonary etiologies. Given it is a prospective cohort study it allowed for retrospective comparison of patients based on treatment provided.

ARDS continues to be associated with significant inpatient mortality, ranging from 24–46% and occurs in approximately 10% of ICU patients hospitalized worldwide (2-4).

Multiple non-modifiable predictors of ARDS associated mortality including older age, active neoplasm, immunosuppression, and chronic liver failure were identified and correspond with previous studies. Additionally, lower pH, lower PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and higher non-pulmonary sequential failure assessment (SOFA) score were identified as predictors of mortality. Of note, in the LUNGSAFE cohort mortality did not differ between patients with pulmonary versus extra-pulmonary

etiology of ARDS.

Given the multiple associated non-modifiable predictors of ARDS associated mortality, identifying modifiable factors related to outcome can help to develop new treatment strategies and to potentially decrease in-hospital mortality.

This study identified several modifiable factors associated with in-hospital mortality including lower PEEP (<12 mmHg), higher peak inspiratory pressure, higher plateau pressure, higher driving pressure, and increased respiratory rate (1). Driving pressure was defined as plateau pressure minus PEEP and calculated for patients with no evidence of spontaneous ventilation (N=742). Amato *et al.* demonstrated that driving pressure was strongly associated with survival and increased driving pressure was associated with mortality by using a multilevel mediation analysis to analyze individual data from 3,562 patients with ARDS enrolled in previous trials (5). Additionally, Amato *et al.* demonstrated that increases in PEEP or decreases in tidal volume dictated by randomization were only beneficial if there was an associated decrease in driving pressure. The concordance of these two studies concerning driving pressure is compelling. The finding of increased survival with lower driving pressure supports Amato *et al.*'s post hoc analysis and should lead to further investigation through randomized control trials aimed at decreasing driving pressure via ventilator management.

Mechanical ventilation strategies using lower end-

inspiratory (plateau) airway pressures, lower tidal volumes, and higher PEEP, i.e., lung-protective strategies, have been previously associated with increased survival in randomized clinical trials (6,7). This study again demonstrated that lower plateau pressures, and higher PEEP were associated with survival in concordance with prior studies (8). However, risk of hospital mortality was similar in patients with lower tidal volume ( $<8$  cmH<sub>2</sub>O mL/kg predicted body weight) compared to those with higher tidal volume. This is likely secondary to widespread adoption of low tidal volume ventilation and should not negate the impact of low tidal volume ventilation on survival.

A lower respiratory rate (20.3 *vs.* 21.6 breaths/min,  $P \leq 0.001$ ) was also associated with improved survival (1). This is a novel finding which would benefit from further study.

ARDS remains under-recognized and the rate of implementation of evidence-based ventilatory strategies is under-utilized by treating physicians. We strongly feel that continued investigation of targeting driving pressure and lower respiratory rate are indicated based on the findings of Laffey *et al.*

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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