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#### Reviewer Questions

This is a well-written review on the use of APRV ventilation mode in the prevention of progression of ARDS and its preemptive use to abort the development of this deleterious condition. However, some points should be addressed - no pathophysiological data are given to understand the potential benefits of ventilating a patient with ARDS or at risk for ARDS (effect on tidal volume and its variability, alveolar recruitment, gas exchange....) - what about clinical studies on the use of APRV in ARDS patients? - figure legends are missing

Thank you for you questions. We did not include strict details on the pathophysiology of APRV in ARDS as the information surrounding this issue is quite voluminous and could stand as a review on its own (which we are currently in the process of writing). Thus, we did not include those specifics in this review. The figure legends are now updated.

1. Please give the shortcomings of conventional tidal volume ventilation on ARDS in detail. 2. The airway pressure release ventilation in the patients with ALI should be added to the text.

Thank you for your questions. Perhaps the greatest shortcoming of conventional mechanical ventilation with regard to ALI/ARDS is that it has done nothing to change ARDS mortality (which has remained static at around 40% for the past two decades). The pulmonary physiology and breath-to-breath mechanics of conventional ventilation that lead to its shortcomings in treating ALI/ARDS are complex and deserve a dedicated review unto themselves (we are currently working on a review that covers this issue along with the breath-to-breath mechanics of APRV). With regard to APRV usage in patients with ALI, we strongly believe that this is the best mode of ventilation to prevent progression of ALI to ARDS, as noted in our animal studies in section 3.1 of the current review. Clinical studies utilizing APRV as a preventative measure to curb ARDS development are few and far between as most clinician researchers use APRV as a "rescue mode" once ARDS is already established. However, Dr. Habashi's retrospective clinical experience that we discuss in section 3.1 of this review appears to demonstrate significant reduction of ARDS incidence when APRV is applied early, even before there is clinical evidence of ALI/ARDS (upon intubation).