Abstract: 150P

The cardiovascular effects of mechanical ventilation

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Mechanical ventilation (MV) is a life-saving intervention used for a variety of conditions, ranging from infants born prematurely, patients suffering from systemic sepsis through to the development of acute respiratory distress syndrome (ARDS) as a result of the COVID-19 pandemic. It has been well documented that MV can cause injury to the lungs as a result of three key processes; volutrauma (occurring when the lungs are ventilated above their optimal tidal volume), atelectrauma (decruitment of alveoli in under-ventilated areas of the lungs) and biotrauma (a culmination of inflammatory mediators released due to mechanical damage. Unfortunately, it has become recognised that the lung biotrauma may 'spill over' into the systemic circulation leading to distal organ damage and increased mortality. While this has been partly characterised in the kidney, the effect on other critical organs is poorly understood.

In this study, we aimed to assess whether the systemic inflammation observed during MV is associated with biochemical and pathological changes within the heart, and whether this response is impacted by volutrauma or atelectrauma. To do this, adult female BALB/c mice were anaesthetised using 150:15mg/kg ketamine:xylazine, tracheostomised and mechanically ventilated for 2 hours (N=16 per group) using one of the following strategies: a) Unventilated controls, b) Low tidal volume (12mL/kg), 2cmH_2O PEEP, c) High tidal volume (20mL/kg), 2cmH_2O PEEP, d) Low tidal volume (12mL/kg), 0cmH_2O PEEP, and e) High tidal volume (20mL/kg), 0cmH_2O PEEP. Following euthanasia using 200mg/kg of pentobarbitone, plasma was collected from each animal alongside cardiac tissue which was collected and divided for gene expression analysis and biochemical/protein analysis. We examined the systemic blood inflammatory response using a multiplex protein assay for 8 markers related to MV and evaluated cardiac inflammation and oxidative stress within the heart tissue using a myeloperoxidase assay and a protein carbonyl assay. We also measured IL-6 levels in the heart tissue using an ELISA.

We found that MV increased systemic plasma IL-6 levels across all ventilation strategies ($P<0.01$) however this was not associated with an increase in IL-6 protein levels in the cardiac tissue ($P=0.78$). Other plasma protein levels including IP-10, KC, MCP-1, MIP-2, VEGF and TNF-α were all unchanged. In contrast, we found that high tidal volume ventilation induced protein carbonyl mediated oxidative stress within the heart ($P=0.007$).

Overall, these results show that MV-induced lung damage leads to systemic release of inflammatory mediators. While this did not translate to increased expression of inflammatory markers in the cardiac tissue, there was some evidence of tissue stress. Whether the oxidative stress we observed is a direct result of systemic inflammation induced by MV, or whether the MV strategy impacts on this response, was unclear from our study. Future work is needed to understand the link between MV and distal organ injury.