The Effects of Mechanical Ventilation on Macrophage Activation: Mathematical Model and Parameter Estimation

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Abstract

Mechanical ventilation is used to provide support to the lungs for patients with severe breathing issues, but as the air is pushed into the alveolar space it can trigger an immune response leading to ventilator-induced lung injury (VILI). A key component of the immune response is recruitment of macrophages, immune cells that differentiate into phenotypes with unique pro- and/or anti-inflammatory roles. An imbalance in pro- and anti-inflammatory responses can have deleterious effects on the individual's health. To develop a greater understanding of the mechanisms of the immune response to VILI and the sensitivity of post-ventilation outcomes, we develop a mathematical model of interactions between the immune system and site of damage, accounting for macrophage polarization. Through Latin Hypercube Sampling and available data, we generate a virtual cohort of patients with biologically feasible dynamics. We use a variety of methods to analyze the results, including a random forest decision tree algorithm and parameter sensitivity with eFAST. Analysis shows that parameters and properties related to epithelial repair and M1 activation and de-activation best predict outcome. We hypothesize interventions and use these treatment strategies to modulate damage in select virtual patients.