2021 CMBEC44
Virtual Conference
CMBES/SCGB May 11-13, 2021

Modelling Capillary O_2 Transport Consequences in COVID-19 Induced Sepsis

K. C. Afas[1,3] and D. Goldman[1,2,3]

[1] Department of Medical Biophysics, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON N6A 5C1
[2] Department of Applied Mathematics, Faculty of Science, University of Western Ontario, London, ON N6A 5C1
[3] School of Biomedical Engineering, University of Western Ontario, London, ON N6A 5C1

I. COVID PANDEMIC AND THE ENDOTHELIUM

The outbreak of Coronavirus (SARS-CoV-2) in December 2019, termed COVID-19, is one of the most recent examples of the damage a novel disease surrounded by a low volume of research can inflict on the healthcare system, patients, and globe alike. To date, according to the World Health Organization, there have been just under two million fatalities globally as a result of COVID-19, while cases reported on a weekly basis show little sign of a significant decrease [1]. Much research coming to light is quick to highlight clinical manifestations in the cardiovascular and respiratory systems [2]; another of COVID-19's consequences is the induction of sepsis as a result of a "cytokine storm" due to immune response. The virus has a special affinity to endothelial receptors placing endothelium at an increased risk, and the resulting cytokines are known to cause endothelial injury along microcirculatory vessels [3], which are the site of primary blood flow distribution and O_2 transport. Despite the prominence of endothelial involvement in the progression of COVID-induced sepsis, there are not many studies targeted at the virus' microcirculatory manifestation, including perspectives on the feasibility of microcirculatory monitoring.

II. NOVEL CONTINUOUS MICROCIRCULATORY O_2 TRANSPORT MODEL

One of the obstacles in such a task is a lack of methods suitable for monitoring relevant metrics. The partial pressure of O_2 (PO_2), is a prime candidate to assess; PO_2 decreases below a threshold within the microcirculation, often herald a functional decline in skeletal muscle, corneal tissue, and other regions where the microcirculation is present in high density. Additionally, non-invasive clinical [4] and even experimental (IVVM) microcirculatory techniques allowing for blood velocity and capillary saturation (SO_2) measurements, are unable to directly assess tissue PO_2. Instead, IVVM-based microcirculatory tissue O_2 analysis relies on biophysical models to assess tissue PO_2 distributions. Recently, for such a purpose, a continuous coupled partial differential equation (PDE) model of **two** layers of skeletal muscle tissue coupled via diffusion at their boundaries was developed, accounting for tissue O_2 diffusion and consumption, capillary O_2 convection, and capillary-tissue O_2 transfer. This model was validated against a dataset accessible from an IVVM protocol involving a controlled exposure of skeletal muscle using an O_2 exchange chamber, and allows for speculation on the regulation of macro-scale arrangements of tissue-capillary modules [5]. The IVVM dataset used for validation indicates hemodynamic parameters *near* to the O_2 chamber exhibit substantial variations. The prevailing theory is capillary perfusion limits the depth of penetration of the chamber O_2, and local hemodynamic parameter responses serve to regulate capillary SO_2 in skeletal muscle towards homogeneity with neighboring capillary modules. The model allows the implementation of this hypothesis by the a-priori fixing of hemodynamics to an established baseline in the layer far from the O_2 chamber and determining the corresponding parameters in the near layer that homogenize capillary PO_2. These compensatory values are expected to be altered in COVID-induced sepsis. To investigate this, both capillary density, and tissue consumption in the model will be adapted to represent observed COVID-19 values in patients receiving extra-corporeal membrane oxygenation [4], and quantitative decreases in the regulatory capacity of capillary velocities and inlet saturations will be observed. This observation should help shed light on the burden of COVID-19 on the body's microcirculation.

REFERENCES

1. Organization World Health. Coronavirus disease (COVID-19) pandemic 2021.
2. Varga Zsuzsanna, Flammer Andreas J, Steiger Peter, et al. Endothelial cell infection and endotheliitis in COVID-19 *The Lancet.* 2020;395:1417–1418.
3. Ye Qing, Wang Bili, Mao Jianhua. The pathogenesis and treatment of the `Cytokine Storm' in COVID-19 *Journal of Infection.* 2020;80:607–613.
4. Carsetti Andrea, Damiani Elisa, Casarotta Erika, et al. Sublingual microcirculation in patients with SARS-CoV-2 undergoing veno-venous extracorporeal membrane oxygenation *Microvascular Research.* 2020;132:104064.
5. Afas Keith Christian, Vijay Raashi, Goldman Daniel. A Two-Compartment Model of Oxygen Transport in Skeletal Muscle using Continuously Distributed Capillaries *Journal of Mathematical Biosciences.* 2021;(In press).