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1. Title:

The Covid-19 Critical Care Consortium Observational Study and New frontiers in Acute Respiratory Distress Syndrome from Translational Pre-clinical Studies

2. Scientific abstract:

Clinical Study

The Covid-19 pandemic is an unprecedented global situation. The WHO calculates that between 60-80% of the world population will be infected. This will place an overwhelming burden on hospitals, but specifically on intensive care resources. Never before have we have seen this disease, nor its magnitude. We have no data on how best to care for our patients – specifically elderly people, patients with important comorbidities or the sickest patients who require intensive care. The study will provide essential information on the clinical course of COVID-19 during the intensive care unit stay, and will help in the management of these patients. In particular, since January 2020, we have worked tirelessly to create a network of research institutions and hospitals that currently comprises more than 360 intensive care units worldwide, including prominent institutions such as John Hopkins, Massachusetts General Hospital/Harvard University, University of California, University of Milan, University of Barcelona, University of Hong Kong and many others in 54 countries and across six continents (JA*MA. 2020; 323(22):2233-2234. doi: 10.1001/jama.2020.8341)*. The Consortium was rapidly aligned with the established International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) and the Short PeRiod IncideNce sTudy of Severe Acute Respiratory Infection (SPRINT-SARI) networks. Of note, several repositories exist of hospitalized COVID-19 patients. Yet, major strengths of the COVID-19-Critical Care Consortium database are 1) specific focus on critically ill patients, 2) inclusion of international patients managed differently, due to heterogeneous country-specific recommendations. During a pandemic, it is essential to collect data that may reflect changes in practice and management across countries, in order to provide well established international recommendations to assist policy makers. To the best of our knowledge, the COVID-19 Critical Care Consortium is currently the only international network of intensive care units aimed to characterize critically-ill COVID-19 patients.

Laboratory study

This project focuses on the pulmonary inflammatory biofluids that ensues in Acute Respiratory Distress Syndrome (ARDS), a syndrome with a current mortality up to 45%. Despite five decades of research, physicians still lack effective therapies against this lethal syndrome. In addition, ARDS caused by COVID-19

has caused a tremendous burden to healthcare systems worldwide and has further complicated management of those patients. One of the potential hurdles is that ARDS caused by COVID-19 and other etiologies is primarily an uncontrolled pulmonary inflammation, but lacks methods to characterize and monitor such inflammation. In our proposed study, we will describe a new pathogenic mechanism in the development and progression of the syndrome, namely inflammatory biofluids-induced lung injury (BILI). Indeed, ARDS patients produce a conspicuous amount of inflammatory biofluids, but the dynamics of their displacement and the resulting pulmonary injury are still elusive, due to unavailable methods to promptly characterize and image these fluids. This research endeavor will develop a new imaging technique based on electrical impedance tomography to estimate the amount of fluids produced during ARDS and to study, for the first time, dislodgement of these fluids during various interventions applied routinely in ARDS patients. The inclusive characterization of the harmful effects of these noxious biofluids will open a new field of investigation to control the intrapulmonary widespread of inflammation and to limit pulmonary injury which consistently results in worse outcomes for ARDS patients. The cutting-edge technology will be likely applied in many other lines of investigations, including patients with chronic mucus retention. In conclusion, the development of this new technology not only will benefit ARDS critically-ill patients, but potentially all patients with chronic respiratory diseases.

3. *Keywords:* COVID-19, SARS-CoV-2, ARDS, Mechanical Ventilation, Electrical Impedance Tomography