Association of early myocardial injury with major adverse outcomes in patients with COVID-19

AHA Rapid Response Grant COVID-19 and Its Cardiovascular Impact

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I. INTRODUCTION

Our understanding of diagnosis, treatment and outcomes of coronavirus disease 2019 (COVID-19) is rapidly evolving. First reports from China clearly indicate that older patients with underlying cardiovascular disease and/or cardiac risk factors demonstrate higher mortality rates (1,2). Most recent reports provided novel insights into the incidence of myocardial injury in COVID-19 patients and its association with adverse outcomes (3,4). In both studies, patients with myocardial injury manifested by elevated high-sensitivity troponin I (TnI) levels had significantly higher in-hospital mortality rates compared with those without myocardial injury, (59.6 and 8.9% (3) and 51 vs 4.5 % (4)). Among patients with myocardial injury, higher levels of TnI were associated with higher mortality rates. While the highest mortality rates were observed in patients with elevated TnI and underlying cardiovascular disease (CVD), mortality rates were also considerable in patients with elevated TnI and without prior CVD. In contrast, patients with known cardiovascular disease without TnI elevation had more favorable outcomes. Cardiac injury was independently associated with an increased risk of mortality in patients with COVID-19 (4). The arming reports clearly indicate that the data from larger populations from multiple centers are needed to further characterize and better understand the association between myocardial injury and adverse outcomes in COVID-19 patients.

II. STUDY AIM *(What specific question is being addressed?)*

The aim of the proposed study is to analyze the incidence, clinical outcomes and predictors of myocardial injury in a large patient population with COVID-19 treated in Mount Sinai Hospital

(MSH) system. In addition, we will explore the association between TnI levels and clinical characteristics, biomarkers, cardiac tests data and treatment approaches to uncover the potential mechanisms responsible for COVID-19 induced myocardial injury.

III. STUDY POPULATION *(What population(s) is being studied?)*

By October 2020, there had been 4,695 COVID-19 positive patients treated in the Mount Sinai Hospital (MSH). All consecutive patients admitted to the MSH system from February 2020 to October 2020 with laboratory-confirmed COVID-19 will be included in the retrospective study.

IV. STUDY DESIGN AND PROCEDURES

Medical history, demographic characteristics, clinical data (symptoms, treatment, complications and outcomes), laboratory findings and cardiac biomarkers on admission and during hospitalization will be collected retrospectively using electronic medical records by trained research personnel and reviewed by physicians. In addition, we will collect available electrocardiography, echocardiography and radiography (chest radiography or computed tomography) data. Patients will be categorized according to the presence or absence of cardiac injury defined as blood levels of high sensitivity troponin (hsTn) above the 99th-percentile upper reference limit. The primary end point will be death; secondary end points will include the rate of pulmonary embolism, acute kidney injury and admission to the intensive care. The study population will be stratified into categories according to the presence and type of myocardial injury according to the Fourth Universal Definition of Myocardial infarction. The cumulative incidence of all-cause mortality will be assessed using the Kaplan-Meier method and compared across the study groups with the log-rank test. Multivariate regression models will be used to determine the independent risk factors for death. Statistical analyses will be performed by an independent statistical center not involved in the data collection

VI. OUTCOMES *(What is the anticipated actionable outcome?)*

The study will provide novel insights into the incidence and consequences of COVID-19 associated myocardial injury in US population and its impact in early and late outcomes after the infection. We plan to develop a statistical model to predict the risks for myocardial injury induced death in COVID-19 patients and identify responses to different treatment strategies. This information will be pivotal for other centers who have yet had the surge of COVID cases. We

plan on fast track publication. Furthermore, electrocardiography, echocardiography and radiology data analyses will be used to uncover the potential mechanisms responsible for the link between myocardial injury and mortality. The findings will provide invaluable insights into the clinical outcomes and mechanisms underlying the collision between the acute COVID-19 epidemic and ongoing epidemic of cardiovascular disease.

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