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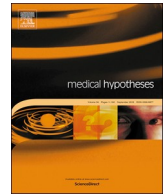
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## COVID-19, myocardial edema and dexamethasone

### ABSTRACT

Severe acute respiratory syndrome corona virus 2(SARS-CoV-2), the cause of coronavirus disease- 2019 (COVID-19) after emerging in china in late 2019 is spreading rapidly across the world.

The most common cause of death in patient with COVID-19 is the rapid progression of acute respiratory distress syndrome (ARDS) shortly after the beginning of dyspnea and hypoxemia. Patients with severe COVID-19 may also develop acute cardiac, kidney and liver injury that are associated with poor prognosis and can lead to high mortality rate.

Numerous randomized trials are ongoing to find an effective, safe and widely available treatment. Remdisivir is the only FDA -approved antiviral agent for treatment of severe COVID-19. Glucocorticoids (GCs) have been used for treatment of cytokine storm syndrome and respiratory failure in hospitalized patient with severe covid-19. One of the therapeutic effects of GCs is stability of vascular endothelial barrier and decreasing tissue edema.

In our opinion, the decreasing vascular permeability effect of glucocorticoids in the injured myocardium might has an important additional factor in reducing mortality in severe, hospitalized COVID-19 patients.

### Introduction

From the beginning of the coronavirus disease 2019 outbreak in December 2019, in Wuhan China, the COVID-19 rapidly spread across the world [1] with an actual international public health emergency.

### Myocardial Injury in COVID-19

Acute myocardial injury, mainly defined by elevated cardiac biomarkers is not uncommon in COVID-19 patients with an incidence ranging from 7.2% to 12% and considered as a risk factor for in-hospital mortality among severe COVID-19 patients [2].

A recent study from china documented that 15.8% of all admitted patients have had myocardial injury based on high blood level of troponin I (cTnI) and also patients who died had suffered more often from myocardial injury during hospitalization compared with survivors 75.8% vs. 9.7% [3].

Although the exact pathophysiologic mechanism of myocardial injury in COVID-19 remains under investigation, there are multiple possible etiologies, including acute viral myocarditis, acute ischemic injury due to coronary artery obstruction, and inflammatory myocardial edema due to the systemic immune response [4].

Mounting evidence indicates that vascular leakage and tissue edema play a main role in the pathogenesis of acute lung injury (ARDS) and myocardial injury in patients with severe COVID-19 [5]. Several mechanisms may contribute in the pathogenesis of myocardial edema: First, there is invasion of endothelial cells (EC) by SARS-CoV-2. The resultant endotheliitis is characterized by EC dysfunction, cell lysis and a subsequent necrotic response. Second, there is a downregulation of the angiotensin-converting enzyme 2(ACE2). SARS-CoV-2 enters cells via binding to the cellular membrane receptor ACE2 [6], which in turn reduces ACE2 availability, leading to and increase of angiotensin 2 and an activation of the kallikrein–bradykinin pathway and eventually to an increased vascular permeability. As a third mechanism, the surge of inflammatory cytokines and vasoactive molecules leads to augmented

EC contractility and loosening of inter-endothelial junctions [7].

Cardiac magnetic resonance (CMR) has recently emerged as the most sensitive noninvasive imaging modality for confirming myocardial injury. In a recently published autopsy series in patients with COVID-19, no significant diffuse lymphocytic inflammatory infiltration in the heart muscle or large areas of myocardial necrosis were observed [8]. There is a significant correlation between published CMR case reports and autopsy-based finding in showing absence of late gadolinium enhancement which indicates lack of myocyte necrosis and scar formation in most of COVID-19 related- cardiac injury. However, CMR consistently demonstrates diffuse myocardial edema by transitional increasing left ventricular wall thickness and high signal intensity on water-sensitive T2 -weighted images (T2 mapping and T2 -STIR) [9–12].

Prolonged episodes of myocardial edema not only affect systolic and diastolic function with reduced ventricular compliance, but also may lead to the formation of diffuse myocardial fibrosis [13]. The latter may be irreversible and have therefore longstanding consequences for ventricular functional capacity.

### Dexamethasone

Preliminary report of the RECOVERY trial has shown reduced death rates of more than 20% in hospitalized COVID-19 patients who received dexamethasone [14,15].

Glucocorticoids (GCs) are steroid hormones that have inflammatory and immunosuppressive effects on a different cells group and lead to many different physiological and pathological effects.

One of the systemic effects of GCs is diminishing edema formation by altering endothelial cell barrier function. Decreasing brain edema especially after pathologic events like acute ischemic stroke, post surgery and radiotherapy has been recognized for many years [16].

Several published studies have shown that dexamethasone has a positive effect on myocardial vascular permeability and helps maintain the barrier function of endothelial cells during ischemic stress [17,18].

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## Conclusion

We think that dexamethasone may play a pivotal role in decreasing deaths in COVID-19 patients by helping maintain vascular permeability. Such a therapeutic effect not only resolve edema and inflammation in the lung but also on the myocardial tissue will likely lead to a decrease of myocardial edema and thereby improves systolic and diastolic ventricular function. Furthermore, it may prevent the formation of global fibrosis as a chronic, potentially irreversible complication of COVID-19.

This hypothesis should be tested using CMR in patients with COVID-19-related acute cardiac injury before and after dexamethasone treatment.

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## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110307>.

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