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Letter to the Editor

Statins and other drugs: Facing COVID-19 as a vascular disease



It has been extensively reported that acute respiratory distress syndrome (ARDS) in coronavirus disease 2019 (COVID-19) is characterized by a strong pro-inflammatory condition, so-called cytokine storm, and by downregulation of angiotensin-converting enzyme 2 (ACE2) levels. The possibility that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may directly infect vascular endothelium and myocardium is becoming increasingly evident. Severe endothelial injury associated with the presence of intracellular virus and disrupted cell membranes, as well as thrombosis with microangiopathy and alveolar-capillary microthrombi in COVID-19 patients, has been reported [1]. Endothelial cells infected with SARS-CoV-2 and diffuse endothelial inflammation have also been observed in COVID-19 patients [2]. Since ACE2 receptors are extensively expressed in endothelial cells of many organs, SARS-CoV-2 infection may be followed by massive endothelial dysfunction and apoptosis, fostering endotheliitis. Endothelial dysfunction is also associated with increased cardiac troponins [3], and the values of these biomarkers were found to be significantly increased in COVID-19 patients with severe illness [4].

Bifulco and Gazerro claimed potential clinical benefits of statins in patients with viral pathologies, including COVID-19, and encouraged for experimental and clinical studies [5]. In this regard, De Spiegeleer et al. [6] have recently reported that statins users presented less symptoms during COVID-19 than non-users, which also remained significant after adjusting for age, sex, functional status and hypertension. Moreover, other outcomes such as long-stay hospitalization or death were better among statins users, although the differences were not statistically significant. It is widely known that statins exert some pleiotropic functions, including anti-inflammatory effects, which may contribute to lower the immune response against viral infection, and their administration is associated with ACE2 upregulation. The favorable effects of statins are also mediated by a wide range of mechanisms, encompassing decrease of angiotensin II (Ang II) type I receptor (AT1R) expression, Ang II-dependent intracellular signaling inhibition, mitigation of oxidative stress and inflammation, inhibition of Ang II and aldosterone synthesis, increase of Ang-(1–7) levels, as well as activation of p-ERK pathway. Although all these mechanisms would need to be confirmed in the setting of COVID-19, statins may represent a potentially promising strategy in COVID-19 therapy, at least as a potential coadjutant drug.

Since COVID-19 is hence characterized by a severe vascular involvement, especially in the advanced stages, medications such as statins or ACE inhibitors should not be discontinued in patients who were already taking them but even consideration shall be given to initiating

their administration as a coadjutant of other COVID-19 treatments such as other drugs targeted to improve endothelial function (e.g., anti-inflammatory, anti-cytokine drugs and ACE inhibitors), and anticoagulants.

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.

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