Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Prevention of endothelial dysfunction and thrombotic events in COVID-19 patients with familial hypercholesterolemia

The importance of dyslipidemia medications in patients with coronavirus disease 2019 (COVID-19) is currently not sufficiently recognized in the prevention of thrombotic events.[1] This is especially true for COVID-19 patients with familial hypercholesterolemia (FH), a genetically determined form of hypercholesterolemia.

FH is the most common genetic cause of cardiovascular disease, with an estimated worldwide prevalence of 1 in 250. The lifelong highly elevated serum LDL cholesterol (LDL-C) concentration leads to a strongly increased risk of a premature atherosclerotic cardiovascular disease (ASCVD) event.[2] The persistent high level of LDL-C also causes endothelial dysfunction already in young children, and there is a positive correlation between serum LDL-C and severity of endothelial dysfunction in children with FH.[3,4] Moreover, Charakida et al.[4] found that plasminogen activator inhibitor 1 levels were higher in children with FH and were associated with the concentrations of both total cholesterol and lipoprotein(a) [Lp(a)], the latter of which, besides carrying cholesterol into atherosclerotic lesions, also possesses direct proinflammatory and atherothrombotic features.[5] Thus, in patients with FH, throughout their lives, the vascular endothelium is exposed to metabolic abnormalities, notably high plasma LDL-C and Lp(a) levels, which are associated with endothelial dysfunction.[3]

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects humans via angiotensin-converting enzyme 2 receptors, which are expressed primarily in endothelial cells. Analysis of in-hospital deaths among COVID-19 patients has confirmed that previous ASCVD associates with increased mortality.[6] Of note, SARS-CoV-2 causes endotheliitis (ie, inflammation particularly of the microvascular endothelium), which may be related to systemic impairment of microcirculatory function and lead to activation of the coagulation cascade.[7] Indeed, COVID-19 patients suffer from the formation of microthrombi, which is potentially even more prevalent in FH patients with pre-existing endothelial dysfunction caused by the lifelong elevated serum LDL-C and Lp(a) levels.

FH patients with diagnosed ASCVD usually need a combination of a statin and a PCSK9 inhibitor to achieve very low LDL-C target levels. Regarding FH patients with COVID-19, it is noteworthy that statins decrease serum D-dimer levels by about 15%,[8] and PCSK9 inhibitors decrease the level of the atherothrombogenic Lp(a) by about 30%.[9,10] Accordingly, statin-PCSK9 inhibitor dual therapy has the potential to decrease two factors underlying the increased risk of thrombotic complications in COVID-19, and FH patients suffering from COVID-19 should receive maximal cholesterol-lowering therapy also for this reason. In particular, the unique feature of statins as mild anticoagulants[11] and the demonstrated favorable prognosis in hospitalized COVID-19 patients on statin therapy[6] favor such conclusion.

Conflict of interest

AV has no conflict of interest. PTK has received lecture honoraria and/or travel fees from Amgen, Novartis, Raisio Group, and Sanofi.

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