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ACE2 down-regulation may contribute to the increased thrombotic risk in COVID-19

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This commentary refers to 'Reduction in ACE2may mediate the prothrombotic phenotype in COVID-19', by Y.X. Gue and D.A. Gorog, doi:10.1093/eurheartj/ehaa534.

Coronavirus disease 2019 (COVID-19) has spread rapidly worldwide, with high morbidity and mortality. Thrombotic events are highly prevalent in patients admitted for COVID-19.[1] However, the specific molecular mechanisms underlying coagulation abnormalities in patients affected by severe COVID-19 are not well known. Gue and Gorog speculate that the reduction in angiotensin-converting enzyme 2 (ACE2) activity that occurs in COVID-19 may lead to an increase in vascular permeability, tissue factor expression, and extrinsic coagulation pathway activation, as well as to an increase in plasminogen activator inhibitor 1 and reduced fibrinolysis.[2] Notably, an association between the ACE2 pathway and thrombosis had already been observed. In rats with an induced thrombosis of the inferior vena cava, the inhibition of ACE2 activity was associated with a significant increase in the thrombus weight, while the administration of an ACE2 activator caused reduction in the platelet adhesion to the endothelium and in the thrombus size, and a prolongation of the time of thrombus formation.[3]

The role of ACE2 as a pathophysiological pathway leading to thrombosis in COVID-19 is interesting and plausible, in addition to other mechanisms, such as the excessive inflammatory response.[4] Moreover, antiviral treatment and potential drug–drug interactions affecting the coagulation system may contribute to hypercoagulability.

ACE2 may be activated in patients with concomitant cardiovascular disease, whereas it does not seem to be affected by ACE inhibitor (ACEI) and angiotensin receptor blocker (ARB) therapies.[4] However, no data are available regarding the interaction between these drugs and COVID-19 thrombotic complications. Accordingly, it is not recommended to interrupt ACEIs/ARBs in patients on chronic treatment with these medications, such as those with heart failure.[5] In our cohort, no significant differences were noted in the incidence of venous and arterial thrombosis among patient receiving ACEI/ARB therapy compared with the others (20% vs. 14%; $P = 0.544$). However, the low rate of events (9 vs. 6) and the role of comorbidities make it impossible to draw any conclusion. Treatment with ACEIs/ARBs had no relationship to outcomes on multivariable analysis.[1] Further investigations are needed to better elucidate the role of ACE2 and ACEI/ARB therapy on the occurrence of thrombotic events in COVID-19 patients.

Conflict of interest: none declared.

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