SARS-CoV2: should inhibitors of the renin–angiotensin system be withdrawn in patients with COVID-19?

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As previously shown for SARS-CoV, SARS-CoV2 similarly utilizes ACE2 as receptor for viral cell entry. In the RAAS, ACE2 catalyses the conversion of angiotensin II to angiotensin 1–7, which acts as a vasodilator and exerts protective effects in the cardiovascular system. In animal experiments, increased expression and activity of ACE2 in various organs including the heart were found in connection with ACE-I and ARB administration. In addition, more recent data showing increased urinary secretion of ACE2 in hypertensive patients treated with the ARB olmesartan suggest that up-regulation of ACE2 may also occur in humans. These observations have been reiterated in the literature and on the web in recent days and the question arose whether RAAS inhibition may increase the risk of deleterious outcome of COVID-19 through up-regulation of ACE2 and increase of viral load. Despite the possible up-regulation of ACE2 by RAAS inhibition and the theoretically associated risk of a higher susceptibility to infection, there is currently no data proving a causal relationship between ACE2 activity and SARS-CoV2 associated mortality. Furthermore, ACE2 expression may not necessarily correlate with the degree of infection. In the meantime, we are well-advised to stick to what is known. There is abundant and solid evidence of the mortality-lowering effects of RAAS inhibitors in cardiovascular disease. ACE-Is, ARBs, and MRAs are the cornerstone of a prognostically beneficial heart failure therapy with the highest level of evidence with regard to mortality reduction. They all have in common the inhibition of the adverse cardiovascular effects arising from the interaction of angiotensin II with the angiotensin II receptor type 1. Discontinuation of heart failure therapy leads to deterioration of cardiac function and heart failure within days to weeks with a possible respective increase in mortality. Similarly, ACE-Is, ARBs, and MRAs are part of the standard therapy in hypertension and after myocardial infarction. Significant reduction of post-infarct mortality applies to all three substance classes, whereby early initiation of therapy (within days after infarction) is an important factor of success.

In conclusion, based on currently available data and in view of the overwhelming evidence of mortality reduction in cardiovascular disease, ACE-I and ARB therapy should be maintained or initiated in patients with heart failure, hypertension, or myocardial infarction according to current guidelines as tolerated, irrespective of SARSCoV2. Withdrawal of RAAS inhibition or preemptive switch to alternate drugs at this point seems not advisable, since it might even increase cardiovascular mortality in critically ill COVID-19 patients.