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Hyperinflammation as underlying mechanism predisposing patients with cardiovascular diseases for severe COVID-19

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It was already realized early in the COVID-19 pandemic that patients with cardiovascular disease, such as arterial hypertension, have a higher risk for an adverse course of COVID-19, raising the question of the underlying mechanisms.[1] Furthermore, when it was described that the viral spike (S) glycoprotein mediates viral entry via binding to the angiotensin-converting enzyme 2 (ACE2),[2,3] the question was raised

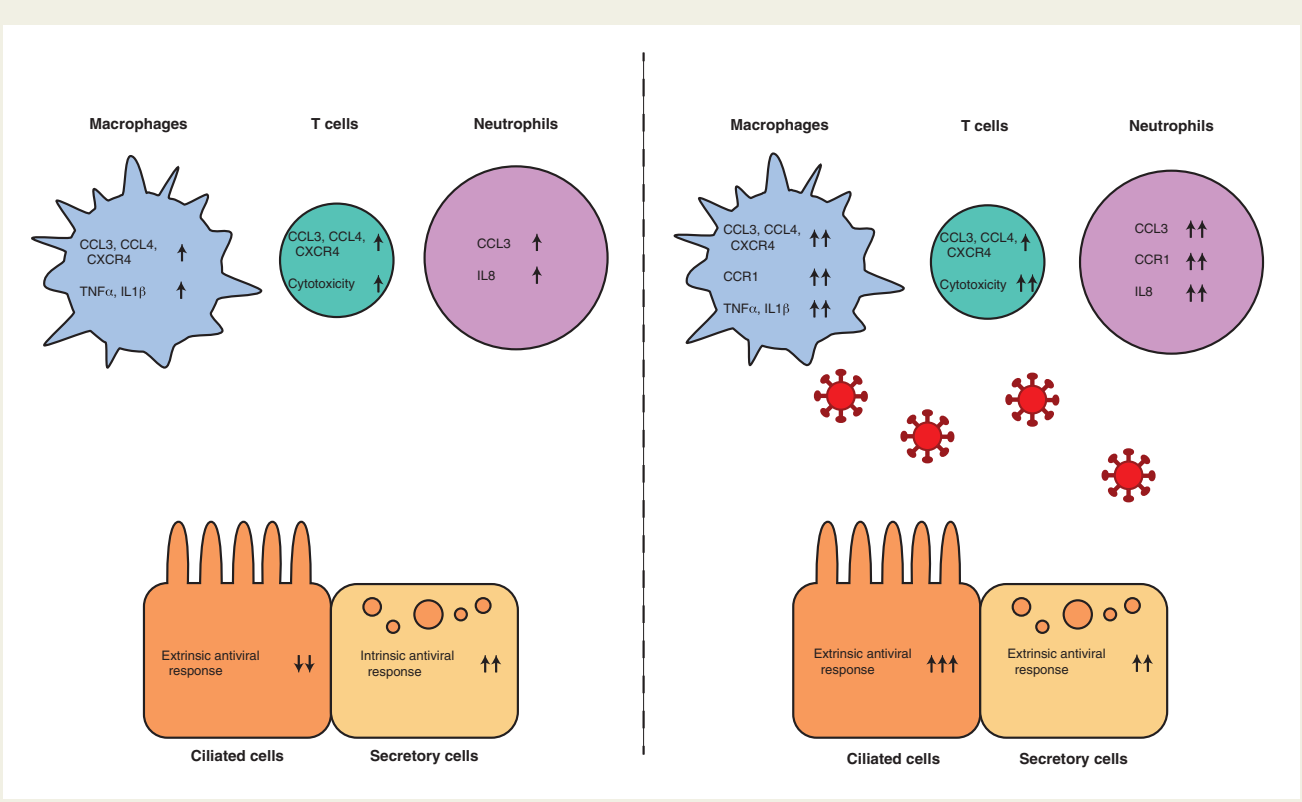

Figure 1 Altered expression of genes in immune and epithelial cells in hypertensive as compared to non-hypertensive patients. The analyses suggest a distinct inflammatory predisposition in patients with hypertension that are SARS-CoV-2-negative (left side), and an augmented immune response in hypertensive SARS-CoV-2-positive COVID-19 patients (right side). Arrows indicate the direction of regulation, with numbers and weight of the arrows giving the strength of differential regulation.

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whether therapies acting on the renin-angiotensin system, such as ACE inhibitors (ACEI) or angiotensin receptor blockers (ARBs), could affect the risk of infection or the clinical course of COVID-19. In a recent study, both aspects have been approached by using in-depth single-cell sequencing data of airway samples.[4]

Predisposition for immune activation in patients with hypertension

Notably, a distinct inflammatory predisposition of different immune cell subtypes relevant to COVID-19 was observed in patients with hypertension that correlated with critical disease progression but was already present before SARS-CoV-2 infection, i.e. in SARS-CoV-2-negative patients with hypertension (*Figure 1*).[4] Moreover, immune activation in hypertensive patients was largely augmented under COVID-19 providing a novel potential explanation for the adverse course of the disease related to a hyperinflammatory response in these patients with cardiovascular disease.[4] Notably, in the RECOVERY trial treatment with dexamethasone reduced mortality among patients with COVID-19 who were receiving either oxygen alone or invasive mechanical ventilation,[5] supporting the concept that immune dysregulation contributes to the critical clinical course of the disease.

No increase of airway SARS-CoV-2 entry receptor ACE2 expression in hypertension or cardiovascular disease

In the single-cell sequencing study of airway samples, no difference in ACE2 expression and initial viral concentration was observed among patients with hypertension or cardiovascular disease.[4] Furthermore, ACE2 expression was not altered in patients receiving ACEI/ARB treatment in both, SARS-CoV-2-positive and -negative patients.[4] These data are in line with observational studies that did not support an increased risk of infection with ACEI/ARB treatmen[6] and further support the ESC recommendation not to interrupt ACEI/ARB treatment in the COVID-19 pandemic. The impact of ACE inhibition or ARB treatment on the clinical course of COVID-19 is currently further examined in several randomized clinical studies.

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