

Antihypertensive medication and outcome in patients with COVID-19 compared to non-COVID respiratory infections

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Background: Recent reports suggested no adverse effects of antihypertensive medication including inhibitors of the renin-angiotensin system on outcome of patients with coronavirus disease 19 (COVID-19). However, most of these studies lack adequate control groups, and regional and socio-economic differences may additionally affect clinical course and outcome of COVID-19.

Methods: In the prospective observational cohort COReNA Virus survival (COVIVA) study at our university hospital, we consecutively enrolled patients presenting to the emergency department with symptoms suggestive of COVID-19 between March and June 2020. Patients tested positive for COVID-19 (cases) were compared with patients tested negative, who had a respiratory infection (respiratory control). Primary outcome measure was the composite of ICU admission, 3'-day mortality or rehospitalization for respiratory symptoms.

Results: The final analysis consisted of 191 patients with COVID-19 and

323 respiratory controls. Sixty cases (31.4%) and 87 (26.9%) respiratory control patients were on ACE inhibitors (ACE-I) or angiotensin II receptor blockers (ARB). In unadjusted models the hazard ratio [95% CI] for the composite outcome for patients on ACE-I/ARBs was 2.36 [1.34; 4.16], $p=0.003$ and 2.05 [1.03; 4.09], $p=0.04$ among patients with COVID-19 and respiratory controls, respectively. The corresponding multivariable adjusted HRs were 1.32 [0.68; 2.55], $p=0.41$ and 1.20 [0.58; 2.48], $p=0.62$. Furthermore, we did not observe an increased risk for the outcome when assessing ACE-I and ARBs separately or other antihypertensive agents, both in COVID-19 patients and respiratory controls (Table).

Conclusions: In a Swiss cohort of patients with COVID-19 or non-COVID respiratory controls treatment with ACE-I/ARBs or other antihypertensive medication was not associated with adverse events after accounting for comorbidities and risk factors.

Table: Association between baseline antihypertensive medication and outcome

	Outcome: ICU admission, 30-day mortality or rehospitalization for respiratory symptoms			
	HR (95% CI) unadjusted	p-value	HR (95% CI) adjusted*	p-value
COVID-19 n=191				
Any antihypertensive drug	2.72 [1.50; 4.91]	<0.001	1.54 [0.76; 3.13]	0.23
ACE inhibitor or ARB	2.36 [1.34; 4.16]	0.003	1.32 [0.68; 2.55]	0.41
ACE inhibitor	2.40 [1.22; 4.71]	0.01	1.29 [0.59; 2.79]	0.41
ARB	1.61 [0.85; 3.04]	0.14	1.11 [0.56; 2.19]	0.76
Beta-blockers	2.54 [1.32; 4.89]	0.005	1.11 [0.49; 2.51]	0.81
Diuretics	1.87 [1.00; 3.48]	0.05	0.90 [0.44; 1.84]	0.77
Calcium-channel blockers	1.35 [0.61; 3.01]	0.46	0.80 [0.35; 1.84]	0.60
Respiratory controls n=323				
Any antihypertensive drug	3.62 [1.72; 7.61]	<0.001	1.71 [0.67; 4.36]	0.26
ACE inhibitor or ARB	2.05 [1.03; 4.09]	0.04	1.20 [0.58; 2.48]	0.62
ACE inhibitor	2.76 [1.24; 6.11]	0.01	1.55 [0.68; 3.54]	0.30
ARB	1.16 [0.48; 2.82]	0.74	0.84 [0.34; 2.05]	0.70
Beta-blockers	4.55 [2.30; 9.02]	<0.001	2.29 [1.00; 5.24]	0.05
Diuretics	2.75 [1.38; 5.49]	0.004	1.07 [0.46; 2.49]	0.88
Calcium-channel blockers	2.39 [1.11; 5.13]	0.03	1.51 [0.66; 3.45]	0.32

COVID-19 = corona virus disease 19; ARB= Angiotensin II receptor blocker; ACE-I=angiotensin converting enzyme inhibitor; HR=hazard ratio; ICU=intensive care unit; *adjusted for age, history of renal failure, history of cardiac disease