Letter to the Editor

Would ACEIs/ARBs be beneficial for COVID-19 patients without hypertension?

Ever since angiotensin converting enzyme 2 (ACE2) was reported as a receptor of SARS-CoV-2, which is the pathogen causing novel coronavirus disease 2019 (COVID-19), there was an intense discussion about whether to abandon ACE inhibitors (ACEIs)/ angiotensin receptor blockers (ARBs) in hypertension patients with COVID-19. For now, thanks to increasing excellent retrospective studies from different countries [1], it became more and more convincing that COVID-19 patients with hypertension or other cardiovascular diseases who used to take ACEIs/ARBs should continue ACEIs/ ARBs therapy.

However, a more aggressive opinion was reported by Juan M Saavedra and colleagues that ARBs can be included as additional therapy for COVID-19 patients without hypertension. Theoretically, the decrease of ACE2, caused by SARS-CoV-2 infection, would break the balance between ACE and ACE2. As a result, Renin-Angiotensin-Aldosterone system (RAAS) was positively regulated and angiotensin II type 1 receptor was over stimulated, which may further cause inflammation activation, endothelial injury, mitochondrial dysfunction and pulmonary capillary permeability increasing, followed by edema and acute lung failure. Besides, ARBs were reported to restore ACE2/Ang1−7/Mas axis, which bring RAAS back to balance. All these potential benefits make ARBs hopeful agents to prevent the progress of COVID-19, in the authors' opinion [2].

Even this hypothesis makes sense to some degree and the alternation of RAAS was also detected (Seen in Fig. 1), we do not approve of attaching too much importance to ACEIs/ARBs in fighting COVID-19 so far. There still lack clear and comprehensive detections of RAAS in COVID-19 patients. According to our unpublished data, RAAS was quite normal when the antibody has appeared (Seen in Table1). Another research in our country showed that during rehabilitation, ACE2 continued to increase while the level of AngIIdecreased to normal [3].

Besides, when we went through the data from published research, it seems ACEIs/ARBs couldn't benefit COVID-19 patients. Reynolds et al. conducted a study based on data from the electronic health records of 12,594 patients in the New York University Langone Health system who were tested for Covid-19 between March 1 and April 15, 2020. Among positive COVID-19 patients, there is no significant difference of severity rate between those with ACEIs/ARBs and without [275/1110 vs 274/1101, 95 %CI (−3.7 to 3.5)]. The conclusion stands still if we only focused on hypertension patients [252/1019 vs 249/986, 95 %CI (−4.3–3.2)] [4]. Another study in Italy, a conditional logistic-regression multivariate analysis was applied in 6272 patients and 30,759 matched control. Using of ARBs or ACEIs did not show any association with Covid-19 (adjusted odds ratio, 0.95 [95 % CI, 0.86–1.05] for ARBs and 0.96 [95 % CI, 0.87–1.07] for ACE inhibitors) [5].

Taken together, we speculate that the change of RAS is just a concomitant symptom of COVID-19, instead of an important factor that facilitating infection. More clinic reports as well as meta-analyze and basic research are still in need before applying ACEIs/ ARBs in COVID-19 treatment.
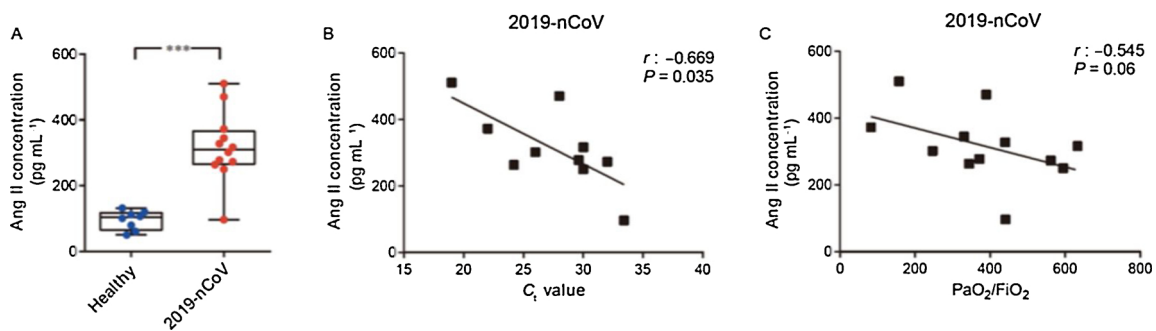

Fig. 1. From Liu Yingxia et al. In COVID-19, AngII was upregulated and seemed to be related to pulmonary function.

Table 1
RAS indicates tested when antibody appeared.

	Value (Mean ± SD, pg/mL)	Reference Value (pg/mL)
Renin	11.88 ± 4.99	4.00 − 38.00
AngII	83.39 ± 26.78	49.00 − 252.00
Aldosterone	105.04 ± 22.75	40.00 − 310.00

Declaration of Competing Interest

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

Acknowledgement

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