LETTER TO THE EDITOR



Re: Is there a difference in the effect between the angiotensin-converting enzyme inhibitor and angiotensin-receptor blocker on the COVID-19?

To the Editor

We thank Dr Chen et al. for their insightful comments on our metaanalysis and appreciate the opportunity to address their concerns. Dr Chen et al. suggested that a difference might exist between the effects of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) on the COVID-19. However, the limited studies precluded us from performing a subgroup analysis stratified by renin-angiotensin-aldosterone system inhibitors or blockers as described in our study limitations. Recently, several new articles were published, so we re-searched the databases (Pubmed, Embase, medRxiv) and added three articles¹⁻³ (combining with our pervious meta-analysis⁴) for providing the specific results for a ACEIs or ARBs. As shown in Figure 1, there is no significant difference between ACEIs or ARB in the effect on positive COVID-19, severity and death (P for positive COVID-19 = .76, P for severe COVID-19 = .63, P for death = .47) (Figure 1). Secondly, inflammation certainly plays a crucial role in COVID-19. Another meta-analysis also found that interleukin-6 levels were reduced in the ACEI group COVID-19 from positive patients vs non-ACEIs.⁵ However, an open-label study did not find a significant improvement of sarilumab (an interleukin-6 blocker) in clinical improvement and mortality in patients with severe COVID-19 compared with the standard of care group.⁶ Therefore, more trials were needed to clarify its mechanism of ACEIs/ARBs on immune response in COVID-19.

CONFLICT OF INTEREST

The author declares no potential conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors

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(A) Postive COVID-19

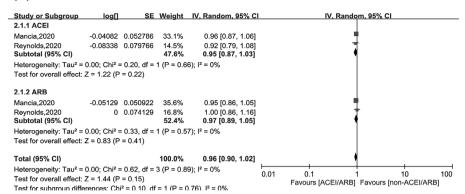
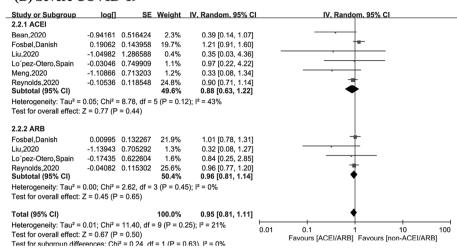


FIGURE 1 Summary of the associations between use of ACEI/ARB and clinical outcomes among patients with COVID-19 stratified by ACEI and ARB: A, risk of COVID-19 infection; B, risk of severe COVID-19 infection; C, mortality. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers

(B) Severe COVID-19



(C) Mortality

Study or Subgroup	log[]	SE	Weight	IV, Random, 95% C	CI IV, Random, 95% CI
2.3.1 ACEI					
Fosbøl,Danish	-0.0202	0.163927	7.3%	0.98 [0.71, 1.35]	5]
Lo'pez-Otero,Spain	-1.96611	1.289859	0.1%	0.14 [0.01, 1.75]	5]
Mehra,2020	-1.10866	0.551868	0.8%	0.33 [0.11, 0.97]	7]
Meng,2020	-0.75502	1.64044	0.1%	0.47 [0.02, 11.71]	1]
Trifrò,ltaly Subtotal (95% CI)	0.09531	0.032511	38.5% 46.8%	1.10 [1.03, 1.17] 0.92 [0.67, 1.28]	
Heterogeneity: Tau ² = 0.05; Chi ² = 7.98, df = 4 (P = 0.09); l ² = 50%					
Test for overall effect: 2	Z = 0.49 (P	= 0.63)			
2.3.2 ARB					
Fosbøl,Danish	-0.22314	0.152297	8.3%	0.80 [0.59, 1.08]	B]
Lo'pez-Otero,Spain	0.431782	0.660326	0.5%	1.54 [0.42, 5.62]	2]
Mehra,2020	0.207014	0.176823	6.4%	1.23 [0.87, 1.74]	4] •
Trifrò, Italy	0.113329	0.034064	37.9%	1.12 [1.05, 1.20]	D]
Subtotal (95% CI)			53.2%	1.06 [0.88, 1.28]	₹
Heterogeneity: Tau ² = 0.02; Chi ² = 5.27, df = 3 (P = 0.15); l ² = 43%					
Test for overall effect: 2	Z = 0.61 (P	= 0.54)			
Total (95% CI)			100.0%	1.07 [0.97, 1.17]	n 🕨
Heterogeneity: Tau ² = 0.01; Chi ² = 13.38, df = 8 (P = 0.10); l ² = 40%					
Test for overall effect: Z = 1.31 (P = 0.19)					0.01
Test for overall effect. 2 = 1.31 (P = 0.19) Favours [ACEI/ARB] Favours [non-ACEI/ARB] Test for subgroup differences: Chi² = 0.53, df = 1 (P = 0.47), l² = 0%					