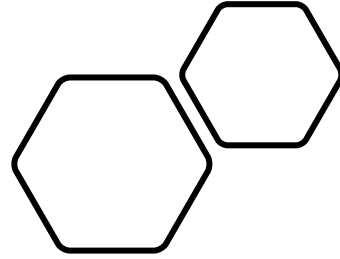


Hypertension and COVID-19 infection



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Objectives

Does COVID-19 cause new hypertension?

Does hypertension is an important risk factor for severe disease or increasing mortality?

Does ACEI has a role in increasing diseases severity?

Does ACEI or ARBs are superior to other antihypertensives?

Does anti hypertensive therapy affect the coarse of illness?

Does COVID-19 vaccine has an effect on hypertension?

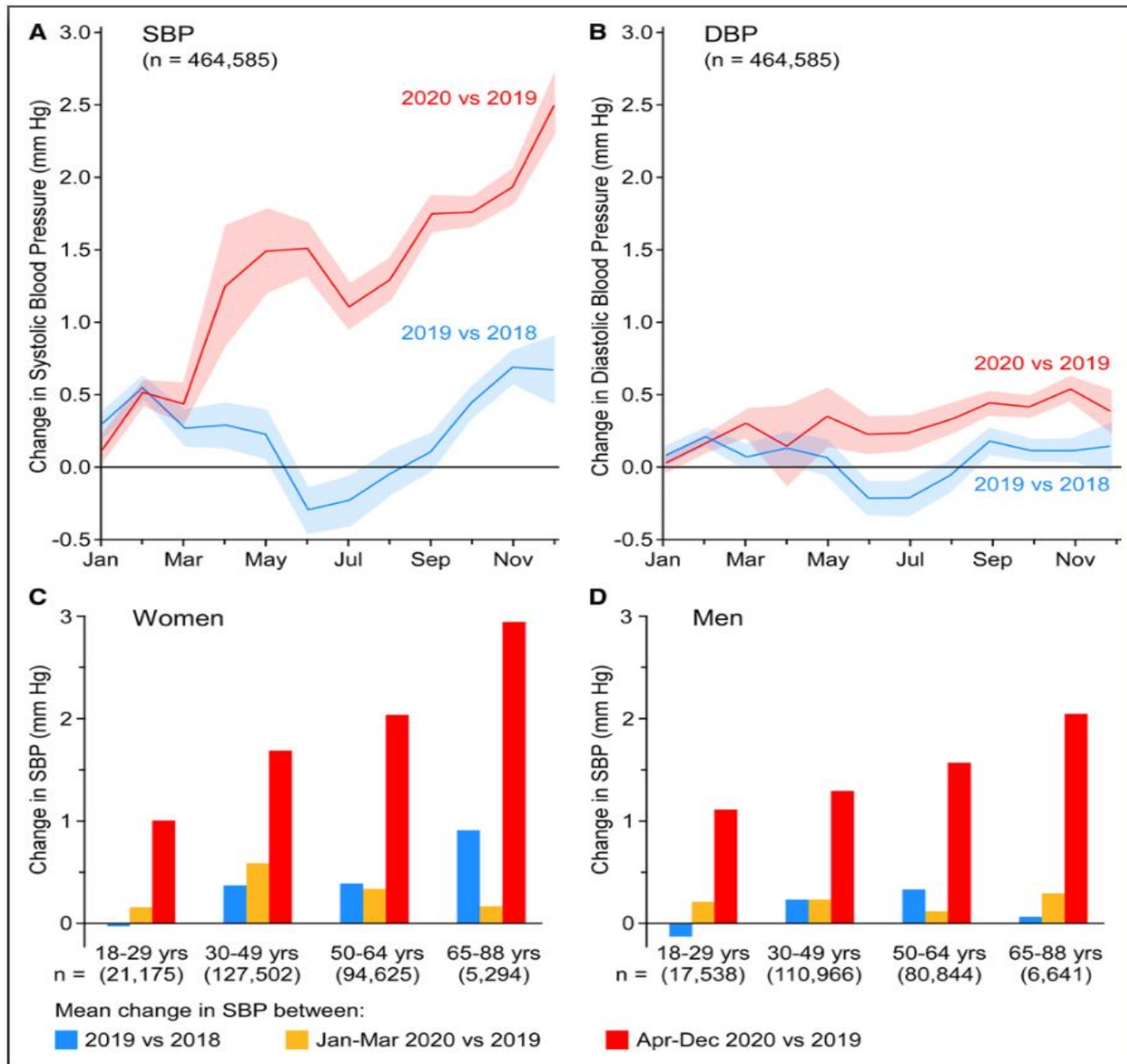


RESEARCH LETTER

Rise in Blood Pressure Observed Among US Adults During the COVID-19 Pandemic

Luke J. Laffin, MD *, Harvey W. Kaufman, MD*, Zhen Chen, MS, Justin K. Niles, MA, Andre R. Arellano, BS, Lance A. Bare, PhD, and Stanley L. Hazen, MD, PhD

Changes from the preceding year in both systolic and diastolic BP showed no differences between 2019 and January to March 2020 ($P=0.8$ for systolic and $P=0.3$ for diastolic BP; [Figure](#)). In contrast, annual BP increase was significantly higher in April to December 2020 than 2019 ($P<0.0001$ for systolic and diastolic BP). During the pandemic period, mean changes each month, compared with the previous year, ranged from 1.10 to 2.50 mmHg for systolic BP and 0.14 to 0.53 mmHg for diastolic BP; systolic and diastolic BP increases held true for men and women and across age groups; larger increases were seen in women for both systolic and diastolic BP, in older participants for systolic BP, and in younger participants for diastolic BP (all $P<0.0001$).



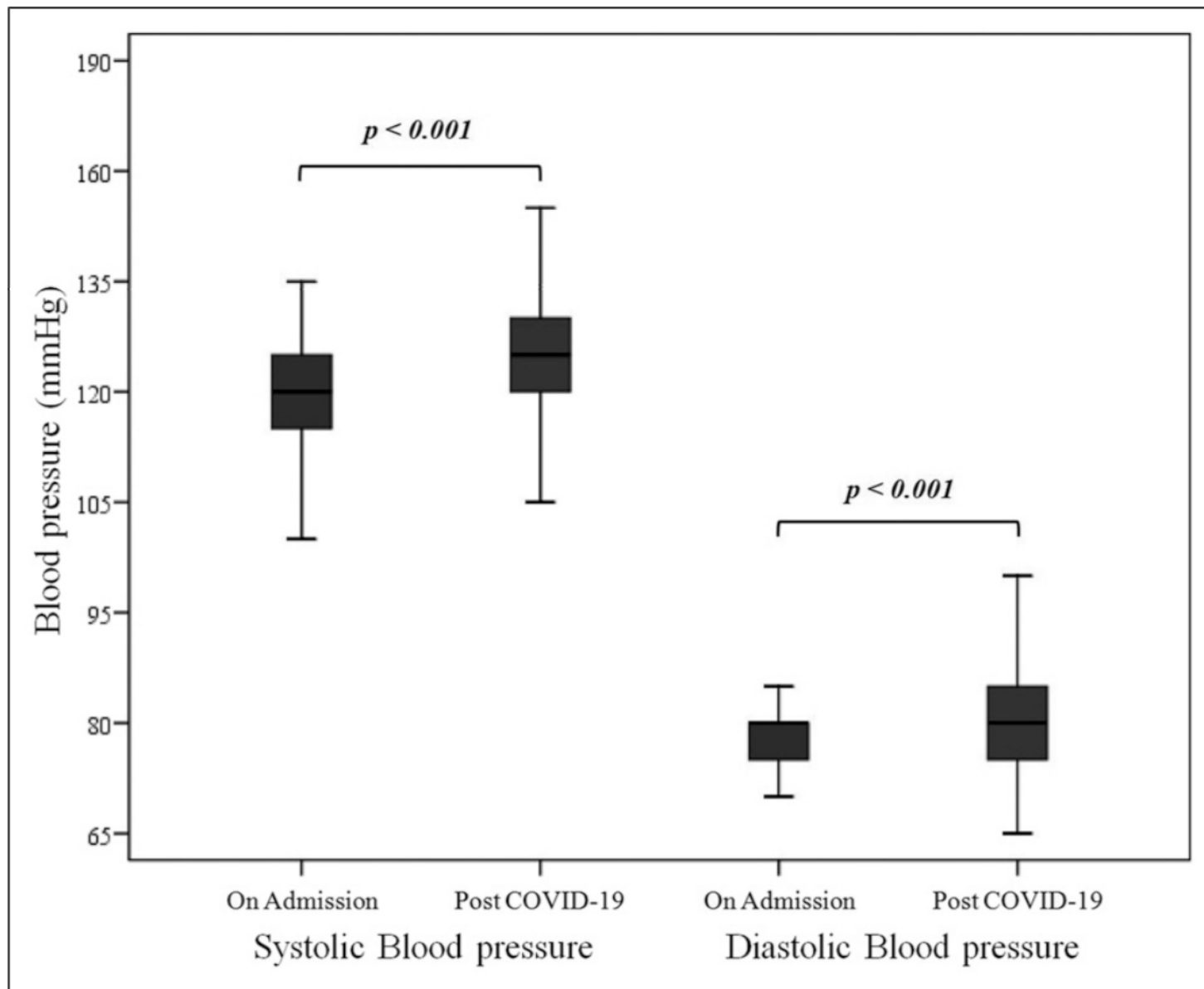


Figure 2. Systolic and diastolic blood pressure on admission and post COVID-19 period.

ORIGINAL ARTICLES

Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis

Giuseppe Lippi¹, Johnny Wong², Brandon M. Henry³

DOI: [10.20452/pamw.15272](https://doi.org/10.20452/pamw.15272)

Published online: March 31, 2020

Article contents



WHAT'S NEW?

Hypertension has been widely reported to increase in severity in patients with coronavirus disease 2019 (COVID-19) and is related to higher mortality in this population. However, early studies on COVID-19 showed mixed findings with respect to hypertension. We aimed to assess the relationship between COVID-19 and

hypertension in a pooled analysis of early reports on COVID-19. We found that hypertension is associated with an approximately 2.5-fold higher risk of both increased severity and mortality. In a meta-regression analysis, we observed that this effect was mainly seen in patients over the age of 60 years. As more data are needed in this field,

we encourage medical professionals to adhere to more stringent public health precautions when treating patients with hypertension. Hypertension should be considered a clinical predictor of disease severity in older patients with COVID-19.

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Position Statement of the ESC Council on Hypertension on ACE-Inhibitors and Angiotensin Receptor Blockers

13 Mar 2020

Based on initial reports from China, and subsequent evidence that arterial hypertension may be associated with increased risk of mortality in hospitalized COVID-19 infected subjects, hypotheses have been put forward to suggest a potential adverse effects of angiotensin converting enzyme inhibitors (ACE-i) or Angiotensin Receptor Blockers (ARBs). It has been suggested, especially on social media sites, that these commonly used drugs may increase both the risk of infection and the severity of SARS-CoV2. The concern arises from the observation that, similar to the coronavirus causing SARS, the COVID-19 virus binds to a specific enzyme called ACE2 to infect cells, and ACE2 levels are increased following treatment with ACE-i and ARBs.

Because of the social media-related amplification, patients taking these drugs for their high blood pressure and their doctors have become increasingly concerned, and, in some cases, have stopped taking their ACE-I or ARB medications.

This speculation about the safety of ACE-i or ARB treatment in relation to COVID-19 does not have a sound scientific basis or evidence to support it. Indeed, there is evidence from studies in animals suggesting that these medications might be rather protective against serious lung complications in patients with COVID-19 infection, but to date there is no data in humans.

The Council on Hypertension strongly recommend that physicians and patients should continue treatment with their usual anti-hypertensive therapy because there is no clinical or scientific evidence to suggest that treatment with ACEi or ARBs should be discontinued because of the Covid-19 infection.


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Original research

Hypertension as an independent risk factor for severity and mortality in patients with COVID-19: a retrospective study

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 [Jiankun Chen](#)^{1, 2}, [Yuntao Liu](#)^{1, 2}, [Jinying Qin](#)¹, [Chunyan Ruan](#)¹, [Xianghui Zeng](#)¹, [Aiting Xu](#)³, [Rongyuan Yang](#)^{1, 2}, [Jiqiang Li](#)^{1, 2}, [Huayang Cai](#)¹, [Zhongde Zhang](#)¹

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Results A total of 220 (29.9%) patients were hypertensive, and 516 (70.1%) patients were not hypertensive. PSM eliminated demographic and comorbidity differences between the two groups. Of all participants, 32 patients died (4.3% mortality), including 17 out of 220 in the hypertension group (7.7%) and 15 out of 516 in the non-hypertension group (2.9%). The incidence of intensive care unit (ICU) stay in the hypertension group (12.8%) was higher than in the non-hypertension group (5.3%) ($p < 0.05$). Logistic regression analysis showed that hypertension was an independent risk factor for death, not other comorbidities. Kaplan-Meier analysis showed that mortality was higher in the hypertension group than in the non-hypertension group before and after PSM ($p < 0.05$). There was no statistically significant difference in ICU therapy, mortality and hospitalisation time between hypertensive patients with or without ARBs/ACE inhibitors ($p > 0.05$).

Conclusion Hypertension was an independent risk factor for the severity and mortality of patients with COVID-19. ARBs/ACE inhibitors should not be discontinued in hypertensive patients with COVID-19.

COVID-19 and arterial hypertension: Hypothesis or evidence?

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Abstract

Investigations reported that hypertension, diabetes, and cardiovascular diseases were the most prevalent comorbidities among the patients with coronavirus disease 2019 (COVID-19). Hypertension appeared consistently as the most prevalent risk factors in COVID-19 patients. Some investigations speculated about the association between renin-angiotensin-aldosterone system (RAAS) and susceptibility to COVID-19, as well as the relationship between RAAS inhibitors and increased mortality in these patients. This raised concern about the potential association between hypertension (and its treatment) and propensity for COVID-19. There are only a few follow-up studies that investigated the impact of comorbidities on outcome in these patients with conflicting findings. Hypertension has been proven to be more prevalent in patients with an adverse outcome (admission in intensive care unit, use of mechanical ventilation, or death). So far, there is no study that demonstrated independent predictive value of hypertension on mortality in COVID-19 patients. There are many speculations about this coronavirus and its relation with different risk factors and underlying diseases. The aim of this review was to summarize the current knowledge about the relationship between hypertension and COVID-19 and the role of hypertension on outcome in these patients.

6 | CONCLUSIONS

Recent findings reported that arterial hypertension represented one of the most common comorbidities in patients with COVID-19. This prevalence ranged between 10% and 34%. The impact of hypertension on outcome and particularly on mortality in COVID-19 patients is not clear due to lack of data. Studies did not provide evidence that RAAS inhibitors should be avoided or switched in these patients.

Large studies that will consider all potential sources of bias and confounding factors, as well as longer follow-up, are necessary. The public pressure to find all answers is very high, but physicians' duty is to stay rational and has scientific approach to available and upcoming data.

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Risk of SARS-CoV-2 infection and COVID-19 prognosis with the use of renin–angiotensin–aldosterone system (RAAS) inhibitors: a systematic review

[Chinonyerem O. Iheanacho](#) , [Valentine U. Odili](#) & [Uchenna I. H. Eze](#)

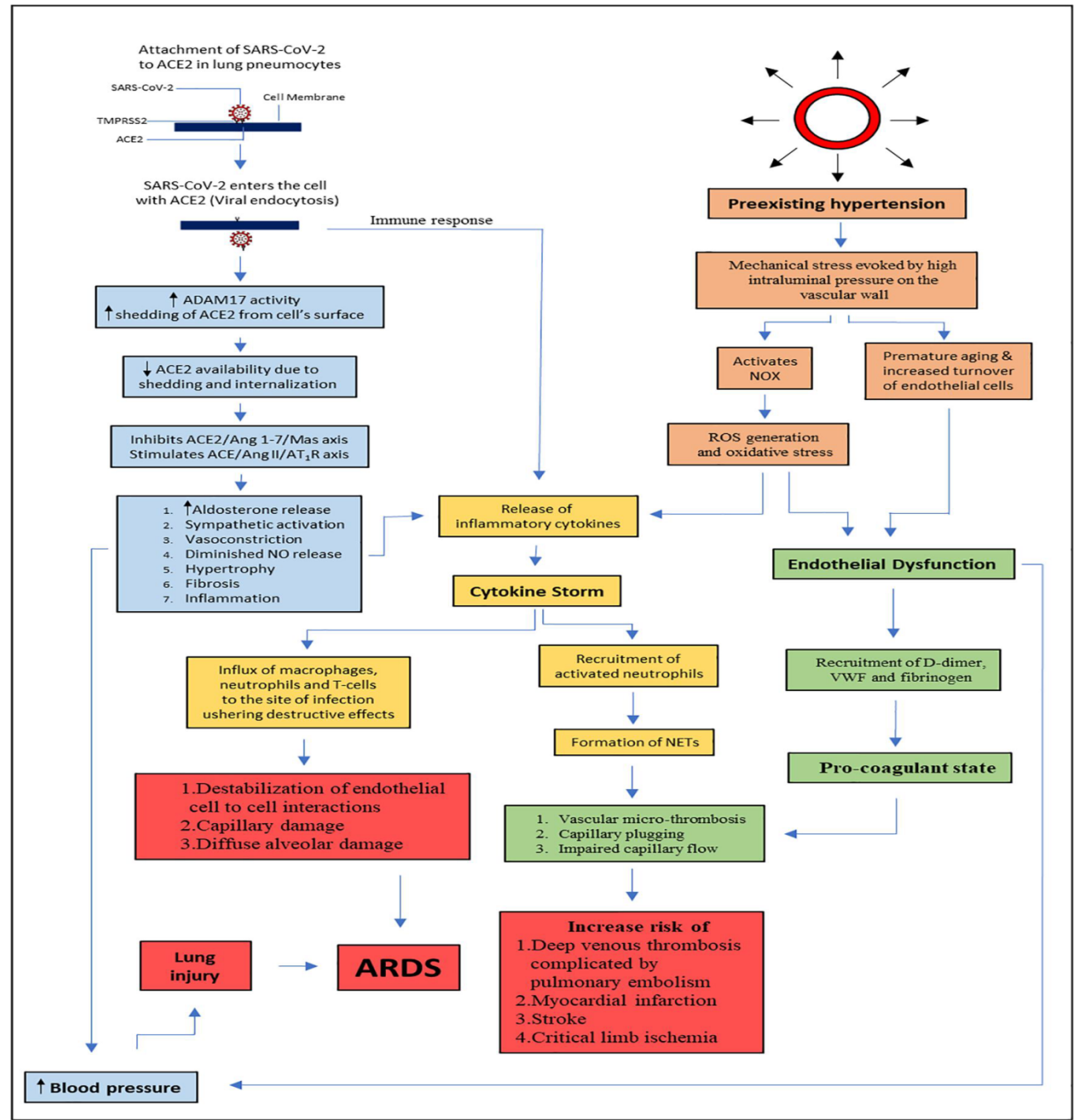
[Future Journal of Pharmaceutical Sciences](#) **7**, Article number: 73 (2021) | [Cite this article](#)

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Conclusion

Despite potential enhanced expression of ACE2 during therapy with RAAS inhibitors, available evidence shows no significant associations between exposure to RAAS inhibitors and susceptibility to COVID-19, as well as poor disease prognosis. The results show that RAAS therapy may not be associated with higher risks for contracting COVID-19, higher risks of disease severity and mortality from COVID-19. Associations that relate to improved clinical outcomes were rather seen, suggesting beneficial effects of its continued use among patients with clinical needs, regardless of COVID-19.

This finding therefore supports the position statements of the American Heart Association and the European Societies of Cardiology on the continued use of RAAS inhibitors in COVID-19 patients and persons in high-risk communities, except medically recommended otherwise.





COVID-19 and Hypertension: The What, the Why, and the How



Shah-Abas Muhamad¹, Azizah Ugusman^{1*}, Jaya Kumar¹, Dominik Skiba², Adila A. Hamid¹ and Amilia Aminuddin¹^{*}

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HYPERTENSION AS A RISK FACTOR FOR SEVERE COVID-19 OUTCOME

Hypertension has gained popularity among researchers owing to its over-representation among COVID-19 patients (Schiffrin et al., 2020). The observational and retrospective studies conducted near Wuhan area have reported that hypertension is the most common co-morbidity observed in patients affected by COVID-19, ranging from 15 to 30% (Wang et al., 2020a; Zhang et al., 2020c; Zhou et al., 2020). In one of the largest studies conducted between December 11, 2019 and January 29, 2020 in Wuhan with data encompassing on 1,099 COVID-19 patients, 165 patients (~15%) had high blood pressure. The same study also reported a total of 23.7% of hypertensive patients had higher disease severity compared to 13.4% of normotensive subjects. Whereas, 35.8% of hypertensive patients reached the composite endpoint of intensive care unit (ICU) admission, mechanical ventilation, and death compared to just 13.7% of normotensive patients (Guan et al., 2020b).

A separate study in China investigating 138 laboratory-confirmed COVID-19 patients reported similar high prevalence (31.2%) of hypertension among the patients. The researchers also found that 58.3% of hypertensive patients with COVID-19 infection were admitted to ICU compared to 21.6% of patients with normal blood pressure (Wang et al., 2020a). In a cohort of 1,590 patients from 575 hospitals, preexisting hypertension was independently associated with severe COVID-19 (hazard ratio 1.575, 95% CI: 1.07–2.32) (Guan et al., 2020a). Altogether, the findings indicate that hypertensive patients have a higher risk of developing severe outcome from COVID-19.

CONCLUSION AND FUTURE DIRECTIONS



Hypertensive patients are more vulnerable to develop serious complications of COVID-19. **Figure 3** summarizes the link between hypertension and COVID-19 that involves endothelial dysfunction and RAS dysregulation. SARS-Cov-2 entry to the host cell involves ACE2, which is an important enzyme in blood pressure homeostasis. Therefore, modification of RAS may affect the development and progression of COVID-19. Early hypothesis describing exacerbation of the disease following the use of antihypertensive medications such as ACEi and ARBs was not clinically proven. To date, there are no clinical data to implicate ACEi or ARBs in either improvement or worsening of COVID-19 cases, or as a risk factor for COVID-19 infection. There is also no substantial evidence to support discontinuation of ACEi or ARBs or alternate pharmacotherapy to manage hypertension in patients with COVID-19. Large studies that consider all potential sources of biasness and confounding factors are warranted in near future to affirm the link between preexisting hypertension and COVID-19 severity and to devise better pharmacological management of COVID-19 patients with hypertension.

ORIGINAL ARTICLE

Impact of Arterial Hypertension and Use of Antihypertensive Pharmacotherapy on Mortality in Patients Hospitalized due to COVID-19: The CRACoV-HHS Study

Wiktoria Wojciechowska , Michał Terlecki , Marek Klocek , Agnieszka Pac , Agnieszka Olszanecka , Katarzyna Stolarz-Skrzypek, Marek Jastrzębski , Piotr Jankowski , Aleksandra Ostrowska, Tomasz Drożdż , Aleksander Prejbisz , Piotr Dobrowolski , Andrzej Januszewicz, Marcin Krzanowski , Maciej T. Małecki, Tomasz Grodzicki, Reinhold Kreutz, Marek Rajzer , and CRACoV-HHS Investigators†

CONCLUSIONS: Although the diagnosis of preexisting hypertension per se had no significant impact on in-hospital mortality among patients with COVID-19, treatment with any first-line blood pressure–lowering drug had a profound beneficial effect on survival in patients with hypertension. These data support the need for antihypertensive pharmacological treatment during the COVID-19 pandemic.

DISCUSSION

Hypertension was the most common clinical condition in the group of patients hospitalized due to COVID-19 in this study. This prevalence of about 60% was similar to the prevalence observed among subjects in the general population over 50 years of age in epidemiological studies from Poland.²⁵ Overall, patients with hypertension in our cohort were older and had more coexisting comorbidities with a potential impact on clinical outcome than patients without hypertension. Therefore, in-hospital mortality in patients with preexisting hypertension was higher in crude

analysis than in patients without hypertension. However, the preexisting diagnosis of hypertension per se was not an independent predictor of in-hospital death. In contrast, significant predictors of death, besides older age and male sex were higher hsCRP levels, heart failure, and chronic kidney disease. The 2 latter conditions are widely recognized as a consequence of long-lasting hypertension.^{22,24} Preexisting hypertension was an independent predictor of in-hospital death during COVID-19 only in patients free of cardiovascular diseases.

This can be explained also as these patients had not been used to get medical treatment. Of interest, the treatment with first-line BP-lowering drugs had a significant impact on mortality in patients with hypertension, that is, the use of any class of first-line antihypertensive medications as recommended in guidelines^{22,24} increased the probability of surviving COVID-19 hospitalization.

COVID-19.⁵ Moreover, in the analyses of 13 early studies, which included a total of 3822 patients, there was a significant association of hypertension with mortality due to COVID-19.²⁸ However, in the study of Sun et al,¹² hypertension was a predictor of death but only in combination with diabetes (odds ratio, 3.02 [95% CI, 1.48–6.15]). Other recently published data did not confirm the previous observation about the negative influence of hypertension on prognosis in patients with COVID-19.⁶ In a meta-analysis of 18 studies (14 558 individuals), the estimated pooled relative risk of mortality among patients with COVID-19 was significantly increased for comorbidities, including cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, and cancer, but not for hypertension or diabetes.⁶

In a study by the Italian Society of Hypertension of 1591 patients hospitalized due to COVID-19 in multivariable analyses, only older age, diabetes, chronic obstructive pulmonary disease, and chronic kidney disease but not hypertension predicted increased mortality.¹⁰ In a different group of Italian patients hospitalized with COVID-19 and admitted to intensive care units, hypertension was also not an independent predictor of in-hospital mortality.²⁹ Similarly, in our results, we did not identify preexisting hypertension as an independent predictor of in-hospital death when analyzed along with other comorbidities and other risk factors. Among those comorbidities, only a history of heart failure or chronic kidney disease—well-known consequences of hypertension—were associated with in-hospital death.

It is of interest that some studies indicated that treatment with ACE inhibitors or ARB may even protect against infection and reduce mortality in COVID-19.^{12,15,18}

In the study by the Italian Society of Hypertension, there was no interference of antihypertensive therapy with COVID-19 mortality.¹⁰ In the study of Ran et al,³⁹ ARBs did not increase the risk of adverse events in patients with hypertension; moreover, poor BP control was independently associated with higher risks of adverse outcomes of COVID-19, including heart failure, which in our study was a main determinant of in-hospital mortality. With respect to medical treatment, Bauer et al. found that therapy with any first-line antihypertensive drug does not worsen

COVID-19 severity.¹⁴ Another large observational study suggests a lower risk of worse COVID-19 outcome (hospitalization and death or intubation) in patients with hypertension treated over a long period with ACE inhibitors or ARBs compared to those treated with calcium channel blockers.⁴⁰ However, some limitations of the

evidence on the role of antihypertensive treatment in patients with COVID-19 presented to date should also be taken into consideration. A high proportion of studies was based on small sample sizes, and many studies failed to include adequate adjustments for confounding variables.

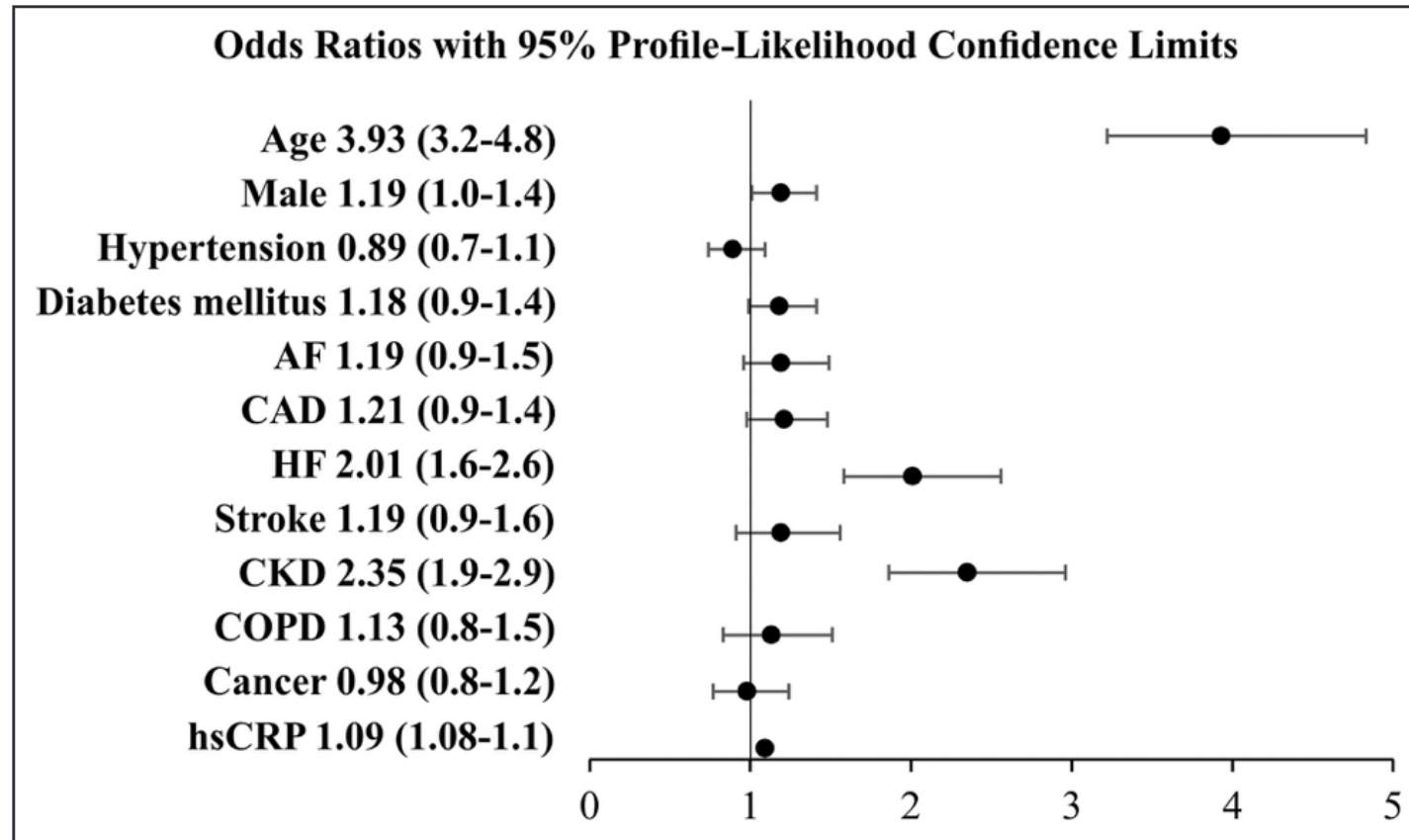


Figure 1. Independent predictors of in-hospital death in multivariable logistic regression analysis in whole study group N= 5191 (171 patients excluded due to missing data. Age: indicates patients at age equal or above median for study group; AF - atrial fibrillation, CAD - coronary artery disease, HF - heart failure, Stroke; CKD - chronic kidney disease, COPD - chronic obstructive pulmonary disease; CRP (C-reactive protein) units - indicates increase in 10 mg/L of hsCRP (high-sensitivity C-reactive protein).

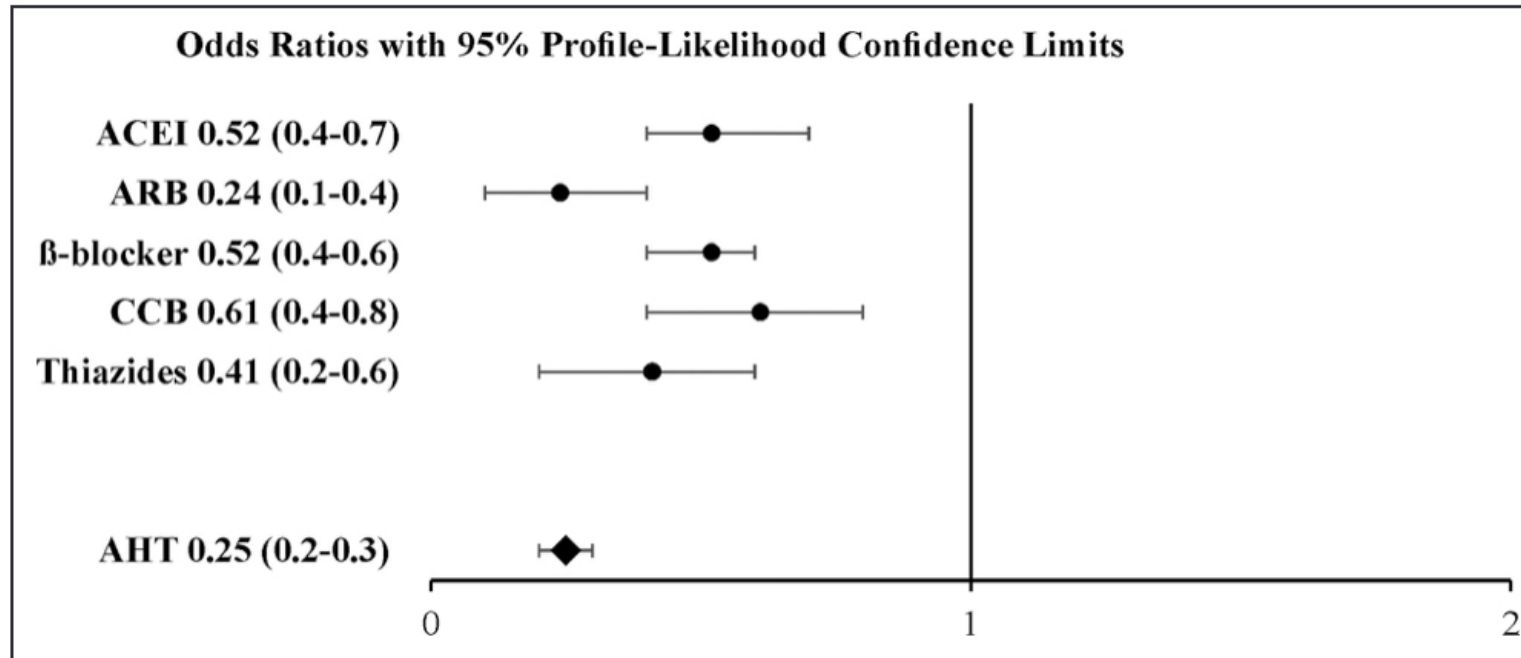
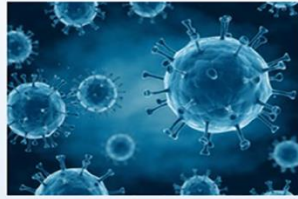


Figure 2. Independent predictors of in-hospital death in multivariable logistic regression analysis in patients with hypertension N=3028 (59 patients excluded due to missing data). The models include age, sex, diabetes, atrial fibrillation, coronary artery disease, heart failure, stroke, chronic kidney disease, chronic obstructive pulmonary disease, cancer, and highly sensitive C-reactive protein level increase (the whole models are presented in [Figure S2](#)). ACE inhibitor indicates angiotensin-converting enzyme inhibitor; AHT, treatment with any class of main antihypertensive drugs; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; and Thiazides, thiazide diuretics or thiazides like diuretics.



SARS-CoV-2 Infection



Hospitalization due to COVID-19



Age > 65 years
Diabetes mellitus
Coronary artery disease
Heart failure
Chronic kidney disease
Atrial fibrillation
Increased hsCRP

Prognosis



Age < 65 years
Treatment with blood pressure lowering drugs

Hypertension – no impact on in-hospital death



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High blood pressure may double the risk of severe COVID, even after full vaccination

Hypertension Journal Report



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Blood Pressure Categories



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 - 129	and	LESS THAN 80
BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 - 139	or	80 - 89
BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Blood Pressure Chart

Blood Pressure Categories Infographic describing the corresponding blood pressure readings between normal and hypertensive crisis.

Research Highlights:

- In a study of more than 900 adults in Los Angeles who had been fully vaccinated and received one booster dose of the COVID-19 vaccines, individuals who had high blood pressure were more than 2.5 times likely than those who did not have high blood pressure to require hospitalization for a severe COVID-19 illness during a surge of the Omicron variant, December 2021 through April 2022.
- High blood pressure presented a greater risk for developing severe COVID-19 than other chronic health conditions, including kidney disease, type 2 diabetes, chronic obstructive pulmonary disease (COPD) or heart failure.

Hypertensive Crisis Following COVID-19 Vaccination

Elnaz Khani, PharmD¹ and Taher Entezari-Maleki, PharmD, PhD^{1,2}

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Clinical Pharmacology.
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Recently, hypertensive crisis, mainly following messenger RNA (mRNA)-based vaccines, has raised concerns. Meylan et al¹ reported 9 cases with stage III hypertension just a few minutes following administration of mRNA-based coronavirus disease 2019 (COVID-19) vaccines, mainly with the Pfizer/BioNTech (BNT162b2) vaccine. Accordingly, Athyros and Doumas² reported a case of hypertensive crisis with blood pressure (BP) of 210/110 mm Hg and an intracranial hemorrhage 3 days after the Moderna (mRNA-1273) COVID-19 vaccine in a 71-year-old woman, who died after 9 days. However, the potential link between COVID-19 vaccines and the BP rise remains unclear. It is

Conclusions

1-THERE MAY BE AN ASSOCIATION BETWEEN NEW COVID INFECTION AND INCREASES IN BLOOD PRESSURE.

2-THERE IS A GREAT CONFLICT REGARDING ASSOCIATION BETWEEN HYPERTENSION AND SEVERE COVID INFECTION.

3-ACEIs USE HAS NO ROLE IN INCREASING SEVERITY OF COVID BUT MAY BE ASSOCIATED WITH BETTER OUTCOME IF USED TO TREAT HYPERTENSIVE COVID CASES.

4-TREATMENT OF HYPERTENSION WITH ANY ANTIHYPERTENSIVE DRUGS IS ASSOCIATED WITH BETTER OUTCOME IN CASES TREATED FOR SEVERE COVID INFECTION.

5-COVID VACCINATION MAY HAVE AN ASSOCIATION WITH SURGE IN BLOOD PRESSURE.

THANKS

