



Examining the Association between Hypertension and Outcomes in COVID-19 Patients: A Predictive Analysis

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Abstract: COVID-19 has become a global pandemic resulting in millions of deaths worldwide. Hypertension has been identified as one of the most common pre-existing conditions and risk factors for severe outcomes in COVID-19 patients. Recent research has questioned whether hypertension independently predicts outcomes in COVID-19, apart from other common conditions like diabetes, obesity, cardiovascular disease, kidney disease, liver disease, and lung disease. However, the impact of chronic and new-onset hypertension in COVID-19 has been insufficiently studied. The same applies to the relationship between blood pressure levels and COVID-19 outcomes. It seems the long discussion about whether ACE inhibitors (ACEI) and angiotensin receptor blockers (ARB) affect COVID-19 severity and outcomes is ending, as numerous studies and meta-analyses have disproved initial findings of higher ACEI/ARB use in patients with poor outcomes. Still, controversies remain regarding the links between hypertension and COVID-19. This review aims to provide a clinical overview of currently available evidence on the predictive value of hypertension, the effect of blood pressure levels, the impact of known and new hypertension, and the role of antihypertensives on severity and outcomes in COVID-19 patients.

Keywords: COVID-19, Pandemic, Hypertension, Blood Pressure, Patients.

1. Introduction

COVID-19, caused by SARS-CoV-2, has become a global pandemic responsible for millions of deaths worldwide. Hypertension, diabetes, and cardiovascular disease were soon identified as common conditions in COVID-19 patients [1, 2]. Subsequent studies revealed hypertension as an important risk factor for poor outcomes in COVID-19 [3, 4]. Initial studies reported hypertension as an independent predictor of hospitalization, severe pneumonia, ICU admission, and mortality in these patients [5]. Later research questioned whether hypertension would predict COVID-19 outcomes independently of diabetes, obesity, and other cardiovascular diseases [6]. Furthermore, most studies did not distinguish between patients with chronic versus new-onset hypertension in COVID-19, which could significantly impact results. The relationship between blood pressure level and susceptibility to SARS-CoV-2 or COVID-19 outcomes has been insufficiently studied, and the potential optimal blood pressure target in these patients remains unknown [7].

There was extensive discussion about the impact of antihypertensive therapy, particularly ACE inhibitors (ACEI) and angiotensin receptor blockers (ARB), in COVID-19 patients. After initial reports showing higher prevalence of these medications in COVID-19 patients with cardiac injury and more severe disease course, numerous original studies and meta-analyses found no association with severity or mortality in COVID-19 or even potential benefit of renin-angiotensin-aldosterone system inhibitors in these patients [8].

In the COVID-19 pandemic era, hypertension has received increased attention. COVID-19 complications can be recognized as vascular disorders [9]. Moreover, hypertension-related diseases like cardiovascular disease (CVD) and chronic kidney disease (CKD) are among the most common COVID-19 risk factors [10]. While evidence of hypertension as a potential long COVID risk factor is still insufficient, one study found pre-existing hypertension predicted long COVID. Furthermore, recent evidence suggests hypertension and related conditions may occur as COVID-19 sequelae [11]. Multiple studies reported elevated blood pressure and excess hypertension burden as post-acute COVID-19 sequelae. Given hypertension's systemic nature and links to multiple organs (brain, heart, vessels, kidney, endocrine systems, etc.), whether and how long COVID impacts these organs is an important issue needing attention. As a follow-up to our 2020 report on COVID-19 and hypertension [12], we summarize recent findings on the long COVID-hypertension disorder relationship, and describe possible mechanisms. Hematologic changes also occur - plasma volume and erythrocyte volume increase, but plasma increases more, decreasing hematocrit and causing dilution anemia. Increased venous stasis heightens thromboembolism risk. Maternal immune adaptations provide protection while avoiding detrimental fetal immune response. Although the mechanism is unclear, research supports cooperation between maternal and fetal immunity rather than broad maternal suppression [13].

2. Long COVID and the kidney

Studies show that acute kidney injury is common in patients with COVID-19 during the acute phase of the illness, and this significantly impacts their outcomes. Chronic kidney disease is also an independent risk factor for severe COVID-19, highlighting the close link between COVID-19 and kidney diseases. The kidney injury associated with COVID-19 may be caused by both direct and indirect mechanisms. Directly, SARS-CoV-2 RNA has been found in kidney tissue and the virus can infect kidney cells. Indirectly, factors like acute respiratory distress syndrome, inflammation, endothelial injury, and abnormal blood clotting can worsen kidney function. Overall, COVID-19 can directly damage the kidneys and worsen underlying kidney disease through multiple pathways [14].

3. COVID-19 and blood pressure

Early studies on COVID-19 focused on the prevalence of comorbidities and how risk factors impacted susceptibility, severity, and mortality. Later research found associations between hypertension and more severe disease stages and higher mortality. However, most of these studies did not account for diabetes and obesity in their statistical analyses [15]. A recent study showed that hypertension alone was not an independent predictor of COVID-19 outcomes, but only when combined with diabetes or other risk factors. Some studies found no impact of hypertension or diabetes on COVID-19 outcomes, while others reported both were independently associated with worse outcomes, with or without obesity [16]. One study suggested hypertension only predicted severe COVID-19 in patients under 65 years old, but not in the full study population. Diabetes and congestive heart failure were independent predictors in all age groups. Another large study found hypertension and diabetes separately were predictors of ICU admission and mortality, but not severe COVID-19 overall. Interestingly, having both hypertension and diabetes was not predictive of severe disease [17]. Overall, the impact of hypertension on COVID-19 outcomes remains unclear when accounting for other comorbidities like diabetes and obesity. Larger studies analyzing these factors together are needed. [18].

4. COVID-19 and flu and high blood pressure

New research suggests COVID-19 may increase the risk of developing high blood pressure, even more so than the flu. Researchers analyzed health records from patients in New York City with COVID-19 infections from March 2020 to August 2022. They compared them to records of patients with influenza but not COVID-19 from January 2018 through 2022. All patients had follow-up visits 3-9 months after testing positive [19].

The analysis found patients hospitalized for COVID-19 were over twice as likely to develop persistent hypertension as those hospitalized for influenza. Non-hospitalized COVID-19 patients

were 1.5 times more likely to develop persistent hypertension than non-hospitalized flu patients. Those at higher risk for hypertension after COVID-19 tended to be older, male, Black, or have preexisting conditions like coronary artery disease or chronic kidney disease. Persistent hypertension was also more common in COVID-19 patients treated with corticosteroids [20].

Other factors may have contributed as well, including socioeconomic status, isolation effects, stress, reduced activity, poor diet, and weight gain during the pandemic. Limitations include focusing only on patients who returned to the health system, possibly selecting for more severe COVID-19 cases. Other limitations include possible undiagnosed preexisting hypertension and uncertain COVID-19 vaccination status. Further research should examine whether cardiovascular complications after COVID-19 resolve or lead to long-term effects. But these findings suggest COVID-19 may increase hypertension risk more than influenza [21].

5. COVID-19 infection appears to be able to cause the onset of new high blood pressure, even among those previously normotensive.

An analysis of over 45,000 people infected with SARS-CoV-2 revealed a significant link between the virus and developing persistent high blood pressure, even among those without a prior history of hypertension. Furthermore, individuals with COVID-19 and no previous high blood pressure were far more likely to develop persistent hypertension compared to those infected with influenza. According to the study, certain groups infected with COVID-19 were at an increased risk for developing high blood pressure, including those over 40 years old, men, Black adults, and those with preexisting conditions like COPD, coronary artery disease, or chronic kidney disease. Overall, the findings indicate COVID-19 infection can lead to persistent hypertension, especially among higher risk populations without a history of high blood pressure. The risk appears greater than with influenza infection [22].

6. Conclusions

High blood pressure, or hypertension, is not uncommon among young adults aged 18-39, with about a quarter having the condition. This puts them at risk for severe outcomes like stroke or heart attack. In most cases, high blood pressure has no symptoms, so getting checked by a medical professional is important.

COVID-19 infection appears to be able to cause high blood pressure in previously normotensive individuals. Studies show that SARS-CoV-2 can lead to new onset hypertension, even among people without any prior history of high blood pressure. The data indicates that COVID-19 increases the risk of developing persistent high blood pressure to a greater degree than other viral illnesses like influenza. Individuals infected with COVID-19, especially those in higher risk categories such as older adults, males, and those with preexisting medical conditions, face an elevated likelihood of experiencing new onset hypertension following infection. Additional research is still needed to fully understand the mechanisms linking COVID-19 to incident hypertension, as well as whether the effects are temporary or long-lasting. However, the current evidence clearly demonstrates that COVID-19 can trigger new hypertension diagnoses, presenting an emerging complication of SARS-CoV-2 infection. Careful blood pressure monitoring after COVID-19 illness may help identify newly hypertensive patients. COVID-19 can cause a variety of symptoms, including headaches, though they are less common than fever. In some cases, COVID-19 headaches may actually be due to another condition. Headaches from COVID-19 tend to feel like a throbbing or stabbing pain in the head lasting over 3 days, and are more likely to occur alongside fatigue and loss of smell. COVID-19 headaches may resolve on their own, but over-the-counter pain relievers can help reduce discomfort. Headaches could rarely indicate a blood clot, but this is extremely uncommon. People should contact a doctor for severe post-COVID or post-vaccine symptoms like breathing problems and chest pain. Overall, headaches are an infrequent symptom of COVID-19 that are usually manageable, but medical attention is still warranted for persistent or severe headaches.

A new study suggests COVID-19 may significantly increase the risk of developing high blood pressure. The study found over 1 in 5 patients hospitalized with COVID-19 and over 1 in 10 non-

hospitalized COVID-19 patients were diagnosed with hypertension 6 months later. Compared to those with influenza, people hospitalized for COVID-19 were over twice as likely to later develop high blood pressure. According to the CDC, hypertension raises the risk of heart disease and stroke, the top causes of death in the US. Nearly half of US adults have high blood pressure, which caused nearly 700,000 deaths in 2021. Overall, the study indicates contracting COVID-19, especially severe cases requiring hospitalization, can substantially raise one's risk of developing dangerous high blood pressure compared to other respiratory viruses like the flu.

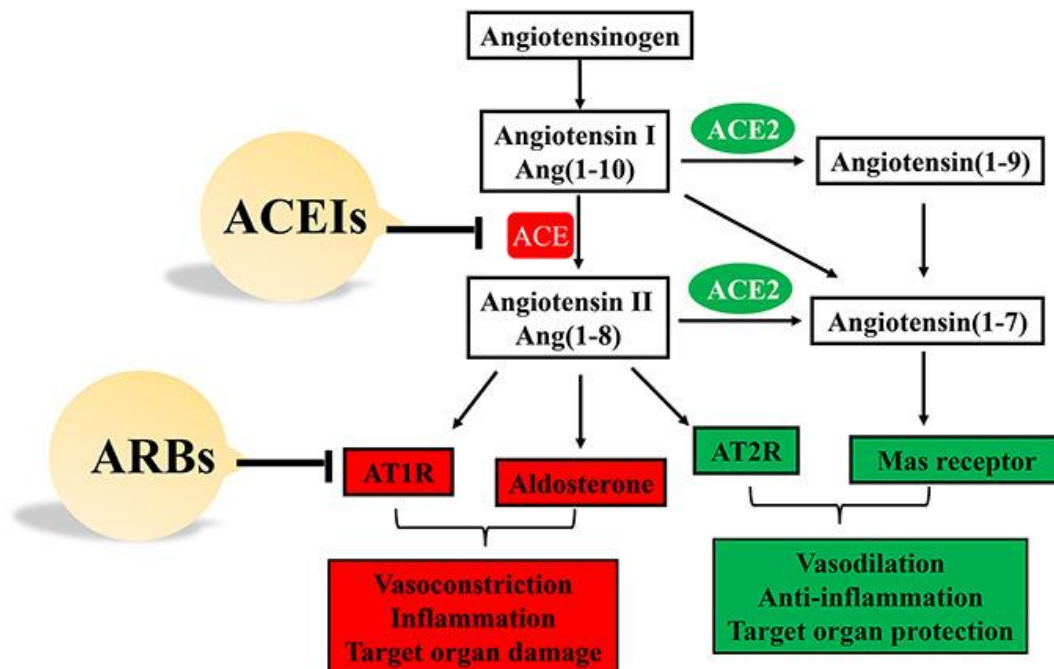


Fig (1) The Role of ACE and ACE2 in the Renin-Angiotensin-Aldosterone System (RAAS). ACE inhibitors and ARB medications target the RAAS system to lower blood pressure and protect organs.

7. References

1. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al.. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* (2020) 382:1708–20.
2. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al.. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019. Pneumonia in Wuhan, China. *JAMA Intern Med.* (2020) 180:934–43.
3. Giannouchos TV, Sussman RA, Mier JM, Poulas K, Farsalinos K. Characteristics and risk factors for COVID-19 diagnosis and adverse outcomes in Mexico: an analysis of 89,756 laboratory-confirmed COVID-19 cases. *Eur Respir J.* (2020) 30:2002144.
4. Wang Z, Deng H, Ou C, Liang J, Wang Y, Jiang M, et al.. Clinical symptoms, comorbidities and complications in severe and non-severe patients with COVID-19: A systematic review and meta-analysis without cases duplication. *Medicine.* (2020) 99:e23327.
5. de Almeida-Pititto B, Dualib PM, Zajdenverg L, Dantas JR, de Souza FD, Rodacki M, et al.. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. *Diabetol Metab Syndr.* (2020) 12:75.
6. Sun Y, Guan X, Jia L, Xing N, Cheng L, Liu B, et al.. Independent and combined effects of hypertension and diabetes on clinical outcomes in patients with COVID-19: a retrospective cohort study of Huoshen mountain hospital and Guanggu Fangcang Shelter Hospital. *J Clin Hypertens.* (2020).
7. Mehraeen E, Karimi A, Barzegary A, Vahedi F, Afsahi AM, Dadras O, et al.. Predictors of mortality in patients with COVID-19-a systematic review. *Eur J Integr Med.* (2020) 40:101226.

8. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al.. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol.* (2020) 5:811–8.
9. Feng Y, Ling Y, Bai T, Xie Y, Huang J, Li J, et al.. COVID-19 with different severities: a multicenter study of clinical features. *Am J Respir Crit Care Med.* (2020) 201:1380–8.
10. Zhang G, Wu Y, Xu R, Du X. Effects of renin-angiotensin-aldosterone system (RAAS) inhibitors on disease severity and mortality in patients with COVID-19: a meta-analysis. *J Med Virol.* (2020).
11. Savarese G, Benson L, Sundström J, Lund LH. Association between renin-angiotensin-aldosterone system inhibitor use and COVID-19 hospitalization and death: A 1,4 million patient nation-wide registry analysis. *Eur J Heart Fail.* (2020).
12. Ssentongo AE, Ssentongo P, Heilbrunn ES, Lekoubou A, Du P, Liao D, et al.. Renin-angiotensin-aldosterone system inhibitors and the risk of mortality in patients with hypertension hospitalised for COVID-19: systematic review and meta-analysis. *Open Heart.* (2020) 7:e001353.
13. Wang Y, Chen B, Li Y, Zhang L, Wang Y, Yang S, et al.. The use of renin-angiotensin-aldosterone system (RAAS) inhibitors is associated with a lower risk of mortality in hypertensive COVID-19 patients: a systematic review and meta-analysis. *J Med Virol.* (2020).
14. Rodilla E, Saura A, Jiménez I, Mendizábal A, Pineda-Cantero A, Lorenzo-Hernández E, et al.. Association of hypertension with all-cause mortality among hospitalized patients with COVID-19. *J Clin Med.* (2020) 9:3136.
15. Zhang J, Wu J, Sun X, Xue H, Shao J, Cai W, et al.. Association of hypertension with the severity and fatality of SARS-CoV-2 infection: a meta-analysis. *Epidemiol Infect.* (2020) 148:e106.
16. Gupta S, Hayek SS, Wang W, Chan L, Mathews KS, Melamed ML, et al.. Factors associated with death in critically ill patients with coronavirus disease 2019 in the US. *JAMA Intern Med.* (2020) 180:1–12.
17. Bauer AZ, Gore R, Sama SR, Rosiello R, Garber L, Sundaresan D, et al.. Hypertension, medications, and risk of severe COVID-19: a Massachusetts community-based observational study. *J Clin Hypertens.* (2020).
18. Barrera FJ, Shekhar S, Wurth R, Moreno-Pena PJ, Ponce OJ, Hajdenberg M, et al.. Prevalence of diabetes and hypertension and their associated risks for poor outcomes in Covid-19 patients. *J Endocr Soc.* (2020) 4:bvaa102.
19. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, et al.. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. *JAMA Intern Med.* (2020) 180:1345–55.
20. Denova-Gutiérrez E, Lopez-Gatell H, Alomia-Zegarra JL, López-Ridaura R, Zaragoza-Jimenez CA, Dyer-Leal DD, et al.. The association of obesity, type 2 diabetes, and hypertension with severe coronavirus disease 2019 on Admission among Mexican patients. *Obesity.* (2020) 28:1826–32.
21. Dennis JM, Mateen BA, Sonabend R, Thomas NJ, Patel KA, Hattersley AT, et al.. Type 2 diabetes and COVID-19-related mortality in the critical care setting: a national cohort study in England, march-july (2020). *Diabetes Care.* (2020) 23:dc201444.
22. Ran J, Song Y, Zhuang Z, Han L, Zhao S, Cao P, et al.. Blood pressure control and adverse outcomes of COVID-19 infection in patients with concomitant hypertension in Wuhan, China. *Hypertens Res.* (2020) 43:1267–76.