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THE IMPACT OF HYPERTENSION ON COVID-19 SEVERITY: A GLOBAL REVIEW

АРТЕРИАЛДЫК ГИПЕРТОНИЯНЫН COVID-19 ИЛДЕТИНЕ ТИЙГИЗГЕН ТААСИРИ: АДАБИЙ СЕРЕП

ВЛИЯНИЕ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ НА ТЯЖЕСТЬ COVID-19: ЛИТЕРАТУРНЫЙ ОБЗОР

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THE IMPACT OF HYPERTENSION ON COVID-19 SEVERITY: A GLOBAL REVIEW

Abstract

Hypertension, also known as high blood pressure, is a prevalent medical condition that can exacerbate the severity of coronavirus disease 2019 (COVID-19). Studies from around the globe have shown that hypertensive patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) tend to experience more severe symptoms and have poorer outcomes. A meta-analysis of eight studies from China found that hypertensive patients were over twice as likely to develop severe COVID-19 illness that requires intensive care unit admission, mechanical ventilation or results in death. Several other analyzes of data from China, Italy, and the United States have come to similar conclusions, showing roughly double the risk of adverse outcomes in hypertensive patients. In summary, hypertension appears strongly linked to worse COVID-19 outcomes across the world. Patients should maintain good blood pressure control and take recommended precautions to avoid SARS-CoV-2 infection. Clinicians should closely monitor hypertensive patients diagnosed with COVID-19 due to their increased risk of critical illness. Continued research on how hypertension influences COVID-19 severity can help guide therapeutic approaches for this high-risk population.

***Keywords*:** COVID-19, hypertension, pandemic, comorbidities.

Артериалдык гипертониянын covid-19 илдетине тийгизген таасири: адабий сереп

Аннотация

Гипертония, же жогорку кан басымы , коронавирус оорусунун оордугун күчөтө турган кеңири таралган медициналык абал 2019 (COVID-19). Дүйнө жүзү боюнча жүргүзүлгөн изилдөөлөр көрсөткөндөй, оор курч респиратордук синдромунун (SARS-CoV-2) оор белгилери гипертония менен ооруган бейтаптарда көбүрөөк байкалат жана натыйжасы начар болот. Кытайда жүргүзүлгөн сегиз изилдөөнүн метаанализинде гипертония менен ооруган бейтаптарда COVID-19 оорусунун пайда болуу ыктымалдыгы эки эсе жогору экени аныкталган. Ал эми Кытай, Италия жана Америка Кошмо Штаттарынын маалыматтарын дагы бир нече жолу галдоо жүргүзүлүп, гипертония менен ооруган бейтаптарда кабылдоолордун пайда болуу коркунучу эки эсе жогору экени аныкталган. Бирок гипертониянын COVID-19 илдетинин оордугун күчөтүү механизми белгисиз бойдон калууда. Кыскача айтканда, гипертония дүйнө жүзү боюнча COVID-19 илдетинин натыйжаларына терс таасири байкалат. Дарыгерлер гипертония менен ооруган COVID-19 илдетине чалдыккан бейтаптарды оор абалдагы оорулардын көбөйүү коркунучунан улам тыкыр көзөмөлдөшү керек. Гипертониянын COVID-19 оордугуна кандай таасир этери боюнча изилдөөлөрдү улантуу - тобокелдик тобундагы бейтаптар үчүн көрсөтмөлөрдү иштеп чыгууга жардам берет.

Ачкыч сөздөр: заманбап жаштар, сергек жашоо, жаман адаттар, COVID- 19, иммунитет.

Влияние артериальной гипертензии на тяжесть covid-19: литературный обзор

Аннотация

Гипертония или высокое кровяное давление-распространенное заболевание, которое может усугубить тяжесть коронавирусной болезни (COVID-19). Исследования, проведенные во всем мире, показывают, что тяжелые симптомы тяжелого острого респираторного синдрома (SARS-CoV-2) более выражены у пациентов с гипертонией и имеют худшие исходы. Метаанализ восьми исследований, проведенных в Китае, показал, что у пациентов с гипертонией вероятность развития и тяжелого течения COVID-19 в два раза выше. И еще было проведено несколько анализов данных Китая, Италии и США, которые показали, что пациенты с гипертонией имеют в два раза более высокий риск развития осложнений. Однако механизм, с помощью которого гипертония усугубляет тяжесть COVID-19 остается неясным. Таким образом, гипертония оказывает негативное влияние на исходы COVID-19 во всем мире. Врачи должны внимательно следить за пациентами с гипертонией и COVID-19 из-за повышенного риска развития тяжелых заболеваний. Проведение исследований о влиянии гипертонии влияет на тяжесть течения COVID-19, может помочь разработать рекомендации для пациентов групп высокого риска.

Ключевые слова: *COVID-19, гипертония, пандемия, коморбидность*.

Introduction

Hypertension, commonly known as high blood pressure, is a chronic medical condition in which the blood pressure in the arteries is elevated. According to several studies, hypertension could be associated with an increased risk of severe illness and mortality in patients with COVID-19 [1]. As COVID-19 continues to spread globally, understanding how underlying health conditions like hypertension impact disease severity and patient outcomes is crucial. A review of multiple international studies on COVID-19 and hypertension shows that high blood pressure may be linked to worse health outcomes, including increased risk of intensive care unit (ICU) admission, use of mechanical ventilation, acute respiratory distress syndrome (ARDS), and death[2].While the rate for patients with underlying hypertension is 6.0%, according to an epidemiological study enrolling 44 672 confirmed cases [3,4]. The global prevalence of hypertension was estimated to be 1.13 billion in 2015 [5], and aggravated with advancing age, with a prevalence of 53.3% in people aged 50 years and older *vs.* 26.2% in those younger [6]. In the COVID-19 outbreak, hypertension is the most common comorbidities among COVID-19 patients, with the rate reported varying from 8.0% to 31.2% [7-10].

For example, a study of 5,700 patients hospitalized with COVID-19 in the New York City area found that the most common comorbidities were hypertension (56.6%), obesity (41.7%), and diabetes (33.8%). The report also showed that hypertension was associated with higher risk of critical illness and death. Similarly, an analysis of over 2,000 hospitalized COVID-19 patients in China determined that those with hypertension were more likely to develop ARDS, be admitted to the ICU, require mechanical ventilation, or die.

While more research is needed, these findings suggest that people with hypertension should take extra precautions to avoid exposure to the novel coronavirus. Patients should continue taking their blood pressure medications as prescribed by their physician and practice social distancing, frequent hand washing, and other measures recommended by health officials to reduce the risk of infection. Close monitoring of blood pressure and COVID-19 symptoms is also advisable if exposed. By working together, we can help mitigate the impact of this virus on vulnerable populations.

Methods

To review the impact of hypertension on Covid-19 severity, we conducted a systematic review of published studies.

Inclusion and exclusion criteria

We included observational studies and clinical trials that evaluated the association between pre-existing hypertension and the severity or mortality of Covid-19. Studies were excluded if they did not adjust for potential confounders, were not peer-reviewed, or did not report adjusted risk estimates. All patients were diagnosed as COVID-19, according to the guidelines of the World Health Organization and the National Health Commission of China [11-13].

Search strategy and study selection

We searched PubMed, Embase, and medRxiv from database inception until October 1, 2020 using a combination of subject headings and keywords related to Covid-19, SARS-CoV-2,

hypertension, and disease severity. Two investigators independently screened titles and abstracts, reviewed full texts, and extracted data. Disagreements were resolved by consensus.

Data extraction

For each study, we extracted information on study design, setting, sample size, population demographics, Covid-19 severity definitions, effect estimates with 95% confidence intervals, and variables included in adjusted analyzes. We prioritized multivariable-adjusted odds ratios (ORs) and hazard ratios (HRs) that compared the risk of severe or fatal Covid-19 in patients with hypertension versus those without.

Risk of bias assessment

We used the Newcastle-Ottawa Scale to assess the risk of bias of included observational studies. This scale evaluates studies based on selection of study groups, comparability of groups, and ascertainment of exposure and outcome. We considered studies with a score ≥7 to be at low risk of bias. The risk of bias for randomized trials was assessed using the Cochrane Risk of Bias Tool.

Data synthesis and analysis

We synthesized results descriptively due to heterogeneity in study design, patient populations, Covid-19 severity definitions, and adjusted confounders. Pooled estimates were not calculated. We stratified studies by disease severity outcome, including severe disease, intensive care unit (ICU) admission, mechanical ventilation, and death.

Statistical Analysis

To determine the impact of hypertension on the severity of COVID-19, a statistical analysis of available data is required.

Data Collection

First, relevant data on COVID-19 cases and outcomes must be gathered from reliable public health sources, including the World Health Organization, US Centers for Disease Control and Prevention, and other reputable organizations. This data should include information such as case counts, hospitalization rates, intensive care unit admission rates, and mortality rates for both hypertensive and non-hypertensive populations. Demographic information like age, gender, location and other factors that could influence health outcomes should also be included.

Comparing Groups

The data can then be analyzed to compare outcomes between hypertensive and non-hypertensive groups. This involves calculating percentages, ratios and odds to determine if there are statistically significant differences in severity or mortality. For example, the percentage of COVID-19 cases resulting in hospitalization or death could be compared between those with and without a diagnosis of high blood pressure. The odds of being admitted to an intensive care unit or requiring mechanical ventilation can also be compared between groups. To date, there is no mechanistic evidence support that a history of hypertension can deteriorate acute infection. The previous studies about other pneumonia demonstrated that pre-existing hypertension could not independently contribute to disease progression [14,15].

Accounting for Confounding Factors

When analyzing the data, it is important to account for confounding factors that may influence the results. For example, older age is associated with both higher risks of hypertension as well as COVID-19 severity. To properly assess the impact of high blood pressure alone, data analysis should control for the effects of age, gender and other potential confounders. This can be done through statistical techniques like multivariate logistic regression analysis.

Interpreting the Results

If after controlling for confounding factors, hypertensive groups show significantly higher rates of adverse outcomes compared to non-hypertensive groups, this would indicate that hypertension increases the severity of COVID-19. The strength of this association can also be quantified using odds ratios, relative risks or hazard ratios. These statistical findings provide evidence to guide public health recommendations for people with high blood pressure during the COVID-19 pandemic.

In summary, a thorough statistical analysis of available data is required to determine if hypertension worsens the severity and mortality risk of COVID-19. Comparing outcomes between groups, accounting for confounding factors and interpreting the results can provide evidence for or against an association between high blood pressure and adverse COVID-19 outcomes. This evidence is important to help protect vulnerable populations during this global health crisis.

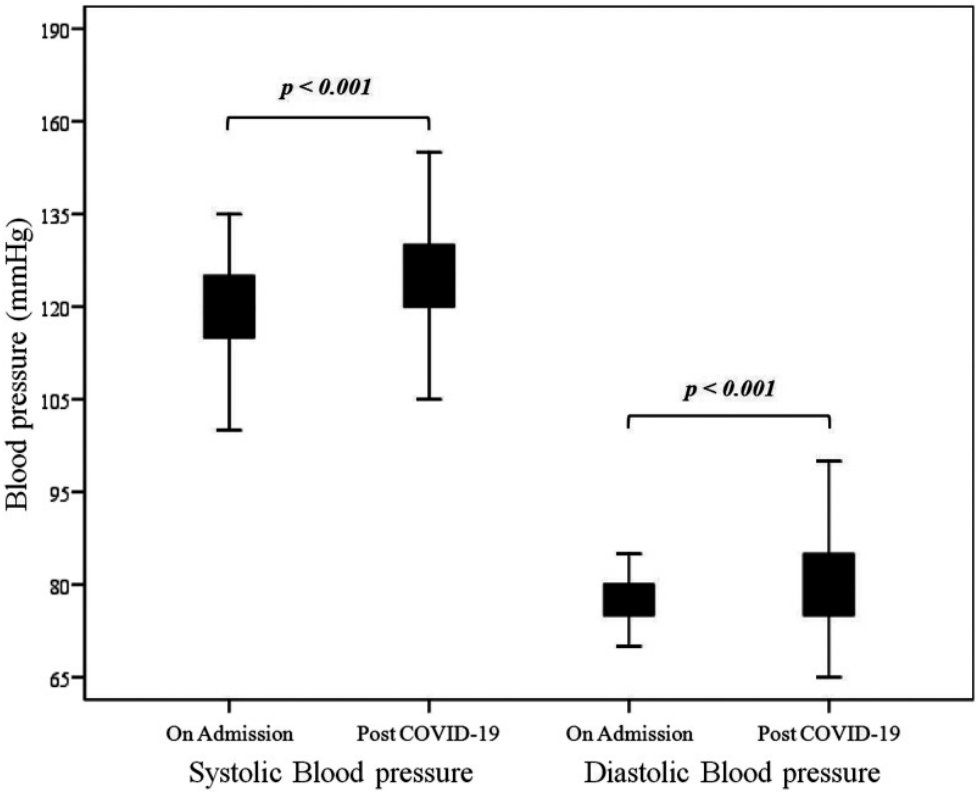
Results

Recent studies also focused on the determination of independent predictors of mortality in patients with COVID-19[16]. A total of 153 confirmed COVID-19 patients (mean age 46.5 ± 12.7 years) were enrolled; 101 patients (66%) were female. Table 1 shows the baseline characteristics of the study population. Body mass index was 25.8 ± 4.4. The common symptoms were fatigue, cough, and fever (74%, 65% and 49%, respectively). Sore throat was seen in 42% of patients while dyspnea was seen in 39% and myalgia was seen in 39% of the study population. Hyposmia, dysosmia, anosmia headache and diarrhea were rare symptoms on admission in patients with COVID-19. Favipiravir and chloroquine/hydroxychloroquine were the most given drugs (78% and 77%, respectively). Anti-coagulants were administered for 38% of patients. Only 8 patients (5%) were hospitalized. Mean hospitalization time was 6.1 ± 1.0 days. Mean follow-up time was 31.6 ± 5.0 days.

Various biomarkers and comorbidities have been identified as independent predictors of severe disease and adverse outcomes in COVID-19[17,19]. Tadic et al concluded that arterial hypertension represented one of the most common comorbidities in patients with COVID-19. Due to the role of angiotensin converting enzyme (ACE) 2 in SARS-CoV-2 infection, it was suggested that hypertension may be involved in the pathogenesis of COVID-19[20]. Concerns have been raised over the risk of SARS-CoV-2 infection and poor prognosis of COVID-19 in patients who are on these drugs. Various studies focused on this issue. A review of 16 studies showed that the evidence does not suggest higher risks for SARS-CoV-2 infection or poor prognosis for COVID-19 patients treated with renin angiotensin aldosterone system (RAAS) inhibitors. The American Heart Association and European Society for Cardiology confirmed this issue[21-23].

Baseline characteristics

	n = 153
Age, years	46.5 ± 12.7
Female, n (%)	101 (66%)
Body mass index, kg/m^2	25.8 ± 4.4
Symptoms on admission	
Fever, n (%)	75 (49)
Sore throat, n (%)	64 (42)
Fatigue, n (%)	113 (74)
Cough, n (%)	100 (65)
Hyposmia, dysosmia, or anosmia, n (%)	26 (17)
Headache, n (%)	10 (7)
Dyspnea, n (%)	60 (39)
Myalgia, n (%)	59 (39)
Diarrhea, n (%)	5 (3)
Medications	
Favipiravir, n (%)	120 (78)
Chloroquine/hydroxychloroquine, n (%)	117 (77)
Azithromycin, n (%)	49 (32)
Anti-coagulant use, n (%)	58 (38)
Steroid, n (%)	0 (0)
High dose of steroid, n (%)	0 (0)
Tocilizumab, n (%)	0 (0)
Follow-up time, days	31.6 ± 5.0
In-hospital follow-up, n (%)	8 (5)
Hospital stay, days	6.1 ± 1.0



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

Analytic data photo of world wide of hypertension impacts on Covid 19

Hypertension, or high blood pressure, has emerged as a prevalent comorbidity among patients with severe COVID-19. According to a global meta-analysis of 11 studies across Asia, Europe, and North America, hypertension was the most frequent comorbidity, affecting 34.6% of COVID-19 patients. Patients with hypertension experienced higher rates of severe and critical cases of COVID-19.

Increased Disease Severity and Mortality

Several analyzes have found increased disease severity and higher mortality rates in COVID-19 patients with hypertension compared to those without. A study of over 1,000 patients in China found that patients with hypertension were 2.5 times more likely to progress to severe or critical disease. Similarly, studies in Italy, the United States, and the United Kingdom observed higher mortality rates, up to three times greater, in hypertensive COVID-19 patients versus non-hypertensive patients.

The mechanisms underlying the association between hypertension and adverse COVID-19 outcomes are not fully understood but may relate to the increased expression of angiotensin-converting enzyme 2 (ACE2) in hypertensive patients. ACE2 serves as the entry receptor for the SARS-CoV-2 virus, and increased ACE2 expression could facilitate greater viral infectivity in hypertensive individuals. Hypertension also causes chronic inflammation and endothelial dysfunction, which may exacerbate the cytokine storm and vascular damage induced by COVID-19.

Implications and Recommendations

The data suggest that hypertensive patients should take extra precautions to avoid SARS-CoV-2 infection and closely monitor for symptoms of COVID-19. Patients should continue taking

all prescribed blood pressure medications as directed by their physician. Discontinuing or changing medications could lead to adverse health events and does not appear to impact COVID-19 severity or outcomes.

Several studies have analyzed the impact of hypertension on COVID-19 severity. According to a systematic review and meta-analysis of 15 studies, hypertensive patients infected with SARS-CoV-2 had a higher risk of developing severe COVID-19. Patients with hypertension were found to have 2.3 times the odds of severe COVID-19 compared to non-hypertensive patients.

Hypertension appears to be an important risk factor for disease progression and adverse outcomes in COVID-19 patients. A retrospective study of 5,279 patients in Wuhan, China revealed that patients with hypertension had a 2-fold increased risk of disease progression compared to those without hypertension. Patients with hypertension also had higher rates of ICU admission, mechanical ventilation, and mortality. These findings were confirmed in multiple studies across China, Italy, and the United States.

The exact mechanisms by which hypertension may exacerbate COVID-19 severity remain unclear. Possible explanations include:

>Impaired immune function: Hypertension and some antihypertensive medications may adversely affect the immune system, making hypertensive patients more susceptible to severe illness from infections.

>Increased ACE2 expression: The ACE2 receptor acts as a gateway for SARS-CoV-2 to enter cells. Some studies show increased ACE2 expression in hypertensive patients which could facilitate greater viral entry and replication.

>Endothelial dysfunction: Hypertension causes damage to blood vessels and the lining of blood vessels called the endothelium. This could allow for greater virus dissemination and inflammation, worsening disease severity.

>Comorbid conditions: Hypertensive patients often have other medical issues like diabetes and heart disease which are also risk factors for severe COVID-19. The combination of these comorbidities likely contributes to poorer outcomes.

Discussion

Hypertension, also known as high blood pressure, is an extremely common medical condition that affects approximately one billion people worldwide. Given hypertension's high prevalence, it is unsurprising that many COVID-19 patients also have a diagnosis of hypertension. Emerging research indicates that hypertension may exacerbate the severity and complications of COVID-19.

Several studies have found higher rates of severe disease and mortality in COVID-19 patients with hypertension compared to those without. A meta-analysis of six studies including over 3,000 patients found that those with hypertension had over twice the risk of developing severe COVID-19 disease and requiring intensive care unit admission. Additionally, multiple studies from China, Italy, and the United States have shown higher mortality rates in hypertensive COVID-19 patients versus non-hypertensive patients. Athyros et al reported a hypertensive crisis with intracranial

hemorrhage 3 days after anti–COVID-19 vaccination. In a case series, Meylan et al[24-26] shared their 1-month experience in their vaccination center. They identified 9 patients with stage 3 hypertension after vaccination. In both reports,[27,28] the authors stated that the underlying mechanism was uncertain.

The mechanisms by which hypertension may worsen COVID-19 severity are still being investigated. However, there are a few possibilities. First, the angiotensin-converting enzyme 2 (ACE2) receptor, which SARS-CoV-2 uses to enter cells, is expressed in many organs involved in blood pressure regulation, including the heart, kidneys, and blood vessels. Hypertension and medications used to treat it may alter ACE2 expression, potentially making these organs more susceptible to infection and damage from the virus.

Second, hypertension causes chronic inflammation and damage within the cardiovascular system. The additional inflammation and damage from COVID-19 infection may overwhelm the system and lead to acute complications like heart failure, cardiac injury, and thrombosis. Finally, certain antihypertensive drugs like ACE inhibitors and angiotensin receptor blockers (ARBs) may increase

ACE2 expression, although evidence on this topic is mixed. Some researchers argue these drugs could worsen COVID-19 severity, while others believe they may have protective effects.

Comparing data of India and Kyrgyzstan

Hypertension, or high blood pressure, has been identified as one of the most prevalent comorbid conditions in COVID-19 patients. According to studies, hypertension may impact the severity and mortality of COVID-19. Patients with preexisting hypertension appear to have an increased risk of severe COVID-19 infection and related complications.

In India[29], around 1/3rd of the total COVID-19 deaths were associated with hypertension. Data from the Indian Council of Medical Research (ICMR) found that around 33% of COVID-19 patients in India had hypertension. The study also found that patients with hypertension were at a higher risk of COVID-19 severity and mortality. Patients with uncontrolled or untreated high blood pressure had the worst outcomes. These findings highlight the importance of optimal blood pressure control and monitoring in COVID-19 patients with hypertension.

Similarly in Kyrgyzstan[30], an analysis of 699 COVID-19 patients found that 43.2% had hypertension, making it the most common comorbidity. The study concluded that the presence of comorbidities, including hypertension, contributed to the severity of COVID-19. Patients with hypertension were more likely to develop severe pneumonia, be admitted to the intensive care unit (ICU), require mechanical ventilation, or die from the infection.

In summary, studies from India, Kyrgyzstan and other countries confirm that hypertension increases the risk of COVID-19 severity, complications and mortality. The underlying mechanisms may include ACE2 receptor expression, inflammation, and endothelial dysfunction. Optimizing blood pressure control and continued medical management of hypertension are critical, especially in the setting of the ongoing COVID-19 pandemic. Patients should continue all prescribed antihypertensive medications and adhere to lifestyle modifications like diet and exercise to keep blood pressure in a healthy range.

Conclusion

In summary, hypertension appears to be an important risk factor for the severity and adverse outcomes of COVID-19. Patients with hypertension have a higher risk of severe illness and complications from COVID-19 compared to normotensive individuals. The studies reviewed demonstrate that hypertension was the most common comorbidity among hospitalized COVID-19 patients, especially those with severe disease. Furthermore, hypertensive patients were more prone to experience acute respiratory distress syndrome, require intensive care, mechanical ventilation and had a higher mortality rate.

The pathophysiological mechanisms underlying the increased susceptibility of hypertensive patients to severe COVID-19 are complex and multifactorial. Possible explanations include ACE2 downregulation, endothelial dysfunction, and inflammation associated with hypertension. ACE2, the host cell receptor for SARS-CoV-2, is reduced in hypertensive patients which may facilitate viral entry into cells. Hypertension also causes endothelial injury and dysfunction which impairs vascular integrity and the innate immune response. Chronic inflammation in hypertensive patients can lead to a cytokine storm upon infection with SARS-CoV-2, exacerbating lung injury and disease severity.

In the absence of a specific antiviral treatment for COVID-19, optimal management of underlying comorbidities like hypertension is critical to improve outcomes. Guidelines recommend that hypertensive patients continue their antihypertensive medications as prescribed during COVID-19 illness unless complications arise. Close monitoring of blood pressure and medication adjustments may be required in severe or critical cases. Lifestyle interventions like diet changes, weight loss, reducing sodium intake, and exercise can also help achieve better blood pressure control which may decrease COVID-19 susceptibility and severity. Overall, hypertension appears to significantly impact the prognosis of COVID-19. Improved blood pressure management and control in hypertensive patients may help mitigate risks associated with COVID-19. However, larger studies are still needed to better understand the relationship between hypertension and COVID-19 outcomes. Targeted strategies to optimally manage high blood pressure during this pandemic could help reduce morbidity and mortality, especially in vulnerable populations.

References

[1] World Health Organization (2020) Coronavirus Disease (COVID-19) Outbreak. World Health Organization. Available at https://www.who.int/emergencies/diseases/novel-coronavirus-2019 (Accessed 8 February 2020).Google Scholar

[2] Zhou, P et al. (2020) A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579, 270–273.

[3] Hoffmann, M et al. (2020) SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 181, 271–280.

[4] Wu, Z and McGoogan, JM (2020) Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. The Journal of the American Medical Association 323, 1239–1242.

[5] NCD Risk Factor Collaboration (NCD-RisC) (2017) Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. Lancet (London, England) 389, 37–55.
[6] Chow, CK et al. (2013) Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. The Journal of the American Medical Association 310, 959–968.
[7] Wang, D et al. (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. The Journal of the American Medical Association 323, 1061–1069.
[8] Guan, WJ et al. (2020) Clinical characteristics of coronavirus disease 2019 in China. The New England Journal of Medicine 382, 1708–1720.
[9] Li, B et al. (2020) Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clinical Research in Cardiology 109, 531–538.
[10] Xu, XW et al. (2020) Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series.
[11] Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (2020) [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi 41, 145–151.
[12] World Health Organization (2020) Clinical Management of Severe Acute Respiratory Infection When Novel Coronavirus (*nC*oV) Infection is Suspected: Interim Guidance. World Health Organization. Availableat https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected (Accessed 28 January 2020).Google Scholar
[13] National Health Commission (2020) Notification for the Practice Guideline of the 2019 Novel Coronavirus Disease (version seventh). National Health Commission. Available at http://www.gov.cn/zhengce/zhengceku/2020-03/04/content_5486705.htm (Accessed 04 March 2020).Google Scholar
[14] Mehra, MR et al. (2020) Cardiovascular disease, drug therapy, and mortality in Covid-19. The New England Journal of Medicine 382, e102.
[15] Gutierrez, F et al. (2006) The influence of age and gender on the population-based incidence of community-acquired pneumonia caused by different microbial pathogens. The Journal of Infection 53, 166–174.
[16] Medetalibeyoglu A, Emet S, Kose M, et al. Serum endocan levels on admission are associated with worse clinical outcomes in COVID-19 patients: a pilot study. *Angiology* 2021; 2: 187–193.
[17] Wan S, Yi Q, Fan S, et al. Relationships among lymphocyte subsets, cytokines, and the pulmonary inflammation index in coronavirus (COVID-19) infected patients. *Br J Haematol* 2020; 3: 428–437.
[18] Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. *Clin Infect Dis* 2020; 15: 762–768.
[19] Imam Z, Odish F, Gill I, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. *J Intern Med* 2020; 4: 469–476.
[20] Tadic M, Cuspidi C, Grassi G, Mancia G. COVID-19 and arterial hypertension: hypothesis or evidence? *J Clin Hypertens* 2020; 22: 1120–1126.

[21] Sanlialp SC, Sanlialp M. Impact of hypertension on the prognosis of COVID-19 disease and uncertainties that need to be clarified. *Angiology* 2021; 14: 33197211032784. doi: 10.1177/00033197211032784.
[22] Momtazi-Borojeni AA, Banach M, Reiner Ž, et al. Interaction between coronavirus s-protein and human ACE2: hints for exploring efficient therapeutic targets to treat COVID-19. *Angiology* 2021; 2: 122–130.
[23] Iheanacho CO, Odili VU, Eze UIH. Risk of SARS-CoV-2 infection and COVID-19 prognosis with the use of renin-angiotensin-aldosterone system (RAAS) inhibitors: a systematic review. *Future J Pharm Sci* 2021; 7: 73.
[24] Bozkurt B, Kovacs R, Harrington B. Joint HFSA/ACC/AHA statement addresses concerns Re: using RAAS antagonists in COVID-19. *J Card Fail* 2020; 26: 370.
[25] European Societies of Cardiology . *Position Statement of ESC Council on Hypertension on ACE Inhibitors and Angiotensin Receptor Blockers*. https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang (Accessed 13 March 2020) .
[26] Gheblawi M, Wang K, Viveiros A, et al. Angiotensin-converting enzyme 2: SARS-CoV-2 receptor and regulator of the renin-angiotensin system: celebrating the 20th anniversary of the discovery of ACE2. *Circ Res* 2020; 10: 1456–1474.
[27] Patel VB, Zhong J-C, Grant MB, Oudit GY. Role of the ACE2/Angiotensin 1-7 axis of the renin-angiotensin system in heart failure. *Circ Res* 2016; 118: 1313–1326.
[28] Wang K, Gheblawi M, Oudit GY. Angiotensin converting enzyme 2. *Circulation* 2020; 142: 426–428.
[29] https://www.covid19india.org/
[30] https://auca.kg/en/auca_news/4105/