Hypertension and COVID-19

Scientific brief 17 June 2021



Introduction

Chronic noncommunicable diseases have been identified as risk factors for SARS CoV-2 infection and as prognostic for severe COVID-19 and other unfavourable outcomes (e.g. admission to intensive care units or mortality). Hypertension is a noncommunicable disease affecting millions of people around the world. Whether hypertension increases the risk of acquiring SARS CoV-2 infection, or the risk of severe COVID-19, remains unclear. As the basis for this scientific brief, a rapid systematic review was commissioned to examine whether hypertension increases the risk of SARS CoV-2 infection and the risk of severe COVID-19. The brief summarizes the role of hypertension as a risk and prognostic factor in COVID-19, while itemizing research and knowledge gaps.

Related WHO recommendations

Previously, WHO has acknowledged that hypertension – along with other cardiovascular diseases – increased the risk of severe COVID-19 and mortality from COVID-19.(1) Similarly, a WHO Information Note reported that people with pre-existing noncommunicable diseases, including hypertension, appeared to be more vulnerable to developing a severe form of COVID-19.(2)

Methods

A protocol for the rapid review was documented in advance of evidence retrieval and data analysis. A systematic review was carried out using Medline, Embase and Global Health through Ovid; the search was conducted on 11th January 2021 without language restrictions. Systematic reviews with meta-analyses of association or risk estimates were only included if they reported evidence on hypertension (either self-reported or diagnosed) as the exposure and COVID-19 or severe COVID-19 as the outcomes. SARS-COV-2 diagnosis could have been based on any laboratory test (e.g. rt-PCR), imaging or clinical diagnosis. Standard systematic review methods were followed. The AMSTAR-2 tool was used to assess the quality of the systematic reviews included in this brief synthesis. Results are presented narratively. Finally, starting from the last search date of the selected systematic reviews, primary studies retrieved through our literature search were screened and relevant reports (providing adjusted association/risk estimates) were narratively summarized herein.

Review of the evidence

There were 53 peer-reviewed systematic reviews and meta-analyses studying hypertension as the exposure and severe COVID-19 as the outcome, (3-55) where severity could have been defined as admission to intensive care units, mechanical ventilation, disease progression, clinically-defined severity or a combination of these (i.e., composite outcome) or mortality. Most studies followed a retrospective or prospective design, based on registries or cohorts of patients. Almost all systematic reviews and meta-analyses revealed that hypertension was strongly associated with severe COVID-19. Nonetheless, it was unclear whether the pooled estimates were crude or adjusted (e.g. related to other co-morbidities). There were no systematic reviews and meta-analyses examining whether hypertension increased the risk of acquiring SARS CoV-2 infection. Nine primary studies were selected (56-64), all of which reported adjusted association/risk estimates. The variables included in the regression models were age, sex, signs, symptoms and comorbidities. The outcomes were

severe disease and mortality. These nine reports suggested that hypertension was associated with higher risk of unfavourable outcomes in COVID-19.

Limitations

There were three key limitations to drawing definite conclusions. First, systematic reviews and meta-analyses did not clearly report whether the association or risk estimates they pooled were based on crude or adjusted results. Second, literature searches were conducted between February and August 2020. Although there were already several original reports at that time, these included limited samples and, in many cases, reported unadjusted association or risk estimates. Third, many of the systematic reviews summarized herein did not conduct a risk of bias assessment, and when they did, it is possible that they did not use the most appropriate tool for studies of prognostic factors (such as QUIPS).

Knowledge gaps

The available evidence is consistent overall in suggesting that hypertension increases the risk of COVID-19, admission to intensive care units, severe disease and mortality. Whether these increased risks were independent of other risk factors, however, has not been fully elucidated. Future original studies, systematic reviews and meta-analyses, including individual-level meta-analyses, could complement the current evidence. Hypertension as a risk factor for acquiring SARS CoV-2 infection has not been studied by systematic reviews and meta-analyses. Future systematic reviews, meta-analyses and original studies should also clearly explain how the presence of hypertension was ascertained (e.g. self-reported, extracted from past medical records or drugs claims or actively measured as part of the study).

Conclusions

Almost all available evidence suggests that hypertension increases the risk of severe COVID-19, defined as, admission to intensive care, clinically-defined severity or a combination of these; or mortality. It was sometimes unclear, however, whether this prognostic profile was independent of other risk factors. There were no systematic reviews or meta-analysis studying whether people with hypertension, in comparison to otherwise healthy individuals, were at higher risk of being infected by SARS CoV-2.

Plans for updating

WHO continues to monitor the situation closely for any changes that may affect the information in this scientific brief. Should any factors change, WHO will issue a further update. Otherwise, the validity of this brief will be reviewed one year after the date of publication.

References

- 1. World Health Organization and the United Nations Development Programme, 2020. COVID-19 and NCD risk factors. https://www.who.int/docs/default-source/ncds/un-interagency-task-force-on-ncds/uniatf-policy-brief-ncds-and-covid-030920-poster.pdf?ua=1.
- 2. World Health Organization, 2020. Information note on COVID-19 and NCDs. URL: https://www.who.int/publications/m/item/covid-19-and-ncds.
- 3. Awortwe C, Cascorbi I. Meta-analysis on outcome-worsening comorbidities of COVID-19 and related potential drug-drug interactions. Pharmacological research. 2020;161:105250.
- 4. Bae S, Kim SR, Kim M-N, Shim WJ, Park S-M. Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis. Heart (British Cardiac Society). 2020.
- 5. Bajgain KT, Badal S, Bajgain BB, Santana MJ. Prevalence of comorbidities among individuals with COVID-19: A rapid review of current literature. American journal of infection control. 2020.

- 6. Barek MA, Aziz MA, Islam MS. Impact of age, sex, comorbidities and clinical symptoms on the severity of COVID-19 cases: A meta-analysis with 55 studies and 10014 cases. Heliyon. 2020;6(12):e05684.
- 7. 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. Journal of the Endocrine Society. 2020;4(9):bvaa102.
- 8. Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of Sex, Age, and Comorbidities with Mortality in COVID-19 Patients: A Systematic Review and Meta-Analysis. Intervirology. 2020:1-12
- 9. Chidambaram V, Tun NL, Haque WZ, Majella MG, Sivakumar RK, Kumar A, et al. Factors associated with disease severity and mortality among patients with COVID-19: A systematic review and meta-analysis. PloS one. 2020;15(11):e0241541.
- 10. 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. Diabetology & metabolic syndrome. 2020;12:75.
- 11. Del Sole F, Farcomeni A, Loffredo L, Carnevale R, Menichelli D, Vicario T, et al. Features of severe COVID-19: A systematic review and meta-analysis. European journal of clinical investigation. 2020;50(10):e13378.
- 12. Dorjee K, Kim H, Bonomo E, Dolma R. Prevalence and predictors of death and severe disease in patients hospitalized due to COVID-19: A comprehensive systematic review and meta-analysis of 77 studies and 38,000 patients. PloS one. 2020;15(12):e0243191.
- 13. Figliozzi S, Masci PG, Ahmadi N, Tondi L, Koutli E, Aimo A, et al. Predictors of adverse prognosis in COVID-19: A systematic review and meta-analysis. European journal of clinical investigation. 2020;50(10):e13362.
- 14. Hessami A, Shamshirian A, Heydari K, Pourali F, Alizadeh-Navaei R, Moosazadeh M, et al. Cardiovascular diseases burden in COVID-19: Systematic review and meta-analysis. The American journal of emergency medicine. 2020.
- 15. Hu J, Wang Y. The Clinical Characteristics and Risk Factors of Severe COVID-19. Gerontology. 2021:1-12.
- 16. Izcovich A, Ragusa MA, Tortosa F, Lavena Marzio MA, Agnoletti C, Bengolea A, et al. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. PloS one. 2020;15(11):e0241955.
- 17. Jain V, Yuan J-M. Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: a systematic review and meta-analysis. International journal of public health. 2020;65(5):533-46.
- 18. Khan MMA, Khan MN, Mustagir MG, Rana J, Islam MS, Kabir MI. Effects of underlying morbidities on the occurrence of deaths in COVID-19 patients: A systematic review and meta-analysis. Journal of global health. 2020;10(2):020503.
- 19. Li J, He X, Yuan Y, Zhang W, Li X, Zhang Y, et al. Meta-analysis investigating the relationship between clinical features, outcomes, and severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia. American journal of infection control. 2021;49(1):82-9.
- 20. Li X, Guan B, Su T, Liu W, Chen M, Bin Waleed K, et al. Impact of cardiovascular disease and cardiac injury on in-hospital mortality in patients with COVID-19: a systematic review and meta-analysis. Heart (British Cardiac Society). 2020;106(15):1142-7.
- 21. Lippi G, Wong J, Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis. Polish archives of internal medicine. 2020;130(4):304-9.
- 22. Liu H, Chen S, Liu M, Nie H, Lu H. Comorbid Chronic Diseases are Strongly Correlated with Disease Severity among COVID-19 Patients: A Systematic Review and Meta-Analysis. Aging and disease. 2020;11(3):668-78.

- 23. Lu L, Zhong W, Bian Z, Li Z, Zhang K, Liang B, et al. A comparison of mortality-related risk factors of COVID-19, SARS, and MERS: A systematic review and meta-analysis. The Journal of infection. 2020;81(4):e18-e25.
- 24. Luo L, Fu M, Li Y, Hu S, Luo J, Chen Z, et al. The potential association between common comorbidities and severity and mortality of coronavirus disease 2019: A pooled analysis. Clinical cardiology. 2020;43(12):1478-93.
- 25. Matsushita K, Ding N, Kou M, Hu X, Chen M, Gao Y, et al. The Relationship of COVID-19 Severity with Cardiovascular Disease and Its Traditional Risk Factors: A Systematic Review and Meta-Analysis. Global heart. 2020;15(1):64.
- 26. 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. European journal of integrative medicine. 2020;40:101226.
- 27. Meng M, Zhao Q, Kumar R, Bai C, Deng Y, Wan B. Impact of cardiovascular and metabolic diseases on the severity of COVID-19: a systematic review and meta-analysis. Aging. 2020;12(22):23409-21.
- 28. Mesas AE, Cavero-Redondo I, Alvarez-Bueno C, Sarria Cabrera MA, Maffei de Andrade S, Sequi-Dominguez I, et al. Predictors of in-hospital COVID-19 mortality: A comprehensive systematic review and meta-analysis exploring differences by age, sex and health conditions. PloS one. 2020;15(11):e0241742.
- 29. Momtazmanesh S, Shobeiri P, Hanaei S, Mahmoud-Elsayed H, Dalvi B, Malakan Rad E. Cardiovascular disease in COVID-19: a systematic review and meta-analysis of 10,898 patients and proposal of a triage risk stratification tool. The Egyptian heart journal: (EHJ): official bulletin of the Egyptian Society of Cardiology. 2020;72(1):41.
- 30. Moula AI, Micali LR, Matteucci F, Luca F, Rao CM, Parise O, et al. Quantification of Death Risk in Relation to Sex, Pre-Existing Cardiovascular Diseases and Risk Factors in COVID-19 Patients: Let's Take Stock and See Where We Are. Journal of clinical medicine. 2020;9(9).
- 31. Mudatsir M, Fajar JK, Wulandari L, Soegiarto G, Ilmawan M, Purnamasari Y, et al. Predictors of COVID-19 severity: a systematic review and meta-analysis. F1000Research. 2020;9:1107.
- 32. Nandy K, Salunke A, Pathak SK, Pandey A, Doctor C, Puj K, et al. Coronavirus disease (COVID-19): A systematic review and meta-analysis to evaluate the impact of various comorbidities on serious events. Diabetes & metabolic syndrome. 2020;14(5):1017-25.
- 33. Noor FM, Islam MM. Prevalence and Associated Risk Factors of Mortality Among COVID-19 Patients: A Meta-Analysis. Journal of community health. 2020;45(6):1270-82.
- 34. Parohan M, Yaghoubi S, Seraji A, Javanbakht MH, Sarraf P, Djalali M. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. The aging male: the official journal of the International Society for the Study of the Aging Male. 2020:1-9.
- 35. Parveen R, Sehar N, Bajpai R, Agarwal NB. Association of diabetes and hypertension with disease severity in covid-19 patients: A systematic literature review and exploratory meta-analysis. Diabetes research and clinical practice. 2020;166:108295.
- 36. Patel U, Malik P, Usman MS, Mehta D, Sharma A, Malik FA, et al. Age-Adjusted Risk Factors Associated with Mortality and Mechanical Ventilation Utilization Amongst COVID-19 Hospitalizations-a Systematic Review and Meta-Analysis. SN comprehensive clinical medicine. 2020:1-10.
- 37. Pranata R, Lim MA, Huang I, Raharjo SB, Lukito AA. Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: A systematic review, meta-analysis and meta-regression. Journal of the renin-angiotensin-aldosterone system: JRAAS. 2020;21(2):1470320320926899.
- 38. Radwan NM, Mahmoud NE, Alfaifi AH, Alabdulkareem KI. Comorbidities and severity of coronavirus disease 2019 patients. Saudi medical journal. 2020;41(11):1165-74.

- 39. Rahman A, Sathi NJ. Risk factors of the severity of COVID-19: A meta-analysis. International journal of clinical practice. 2020:e13916.
- 40. Sepandi M, Taghdir M, Alimohamadi Y, Afrashteh S, Hosamirudsari H. Factors Associated with Mortality in COVID-19 Patients: A Systematic Review and Meta-Analysis. Iranian journal of public health. 2020;49(7):1211-21.
- 41. Shoar S, Hosseini F, Naderan M, Mehta JL. Meta-analysis of Cardiovascular Events and Related Biomarkers Comparing Survivors Versus Non-survivors in Patients With COVID-19. The American journal of cardiology. 2020;135:50-61.
- 42. Singh AK, Gillies CL, Singh R, Singh A, Chudasama Y, Coles B, et al. Prevalence of co-morbidities and their association with mortality in patients with COVID-19: A systematic review and meta-analysis. Diabetes, obesity & metabolism. 2020;22(10):1915-24.
- 43. Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: A systematic review and meta-analysis. PloS one. 2020;15(8):e0238215.
- 44. Tian W, Jiang W, Yao J, Nicholson CJ, Li RH, Sigurslid HH, et al. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. Journal of medical virology. 2020;92(10):1875-83.
- 45. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. Aging. 2020;12(7):6049-57.
- 46. Wang X, Fang X, Cai Z, Wu X, Gao X, Min J, et al. Comorbid Chronic Diseases and Acute Organ Injuries Are Strongly Correlated with Disease Severity and Mortality among COVID-19 Patients: A Systemic Review and Meta-Analysis. Research (Washington, DC). 2020;2020:2402961.
- 47. 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(48):e23327.
- 48. Wu T, Zuo Z, Kang S, Jiang L, Luo X, Xia Z, et al. Multi-organ Dysfunction in Patients with COVID-19: A Systematic Review and Meta-analysis. Aging and disease. 2020;11(4):874-94.
- 49. Xu L, Mao Y, Chen G. Risk factors for 2019 novel coronavirus disease (COVID-19) patients progressing to critical illness: a systematic review and meta-analysis. Aging. 2020;12(12):12410-21.
- 50. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases. 2020;94:91-5.
- 51. 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. Epidemiology and infection. 2020;148:e106.
- 52. Zhao J, Li X, Gao Y, Huang W. Risk factors for the exacerbation of patients with 2019 Novel Coronavirus: A meta-analysis. International journal of medical sciences. 2020;17(12):1744-50.
- 53. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. The Journal of infection. 2020;81(2):e16-e25.
- 54. Zhou Y, Yang Q, Chi J, Dong B, Lv W, Shen L, et al. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis. International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases. 2020;99:47-56.
- 55. Zuin M, Rigatelli G, Zuliani G, Rigatelli A, Mazza A, Roncon L. Arterial hypertension and risk of death in patients with COVID-19 infection: Systematic review and meta-analysis. The Journal of infection. 2020;81(1):e84-e6.
- 56. Al Kuwari HM, Abdul Rahim HF, Abu-Raddad LJ, Abou-Samra AB, Al Kanaani Z, Al Khal A, et al. Epidemiological investigation of the first 5685 cases of SARS-CoV-2 infection in Qatar, 28 February-18 April 2020. BMJ open. 2020;10(10):e040428. Epub 2020/10/10.

- 57. Cen Y, Chen X, Shen Y, Zhang XH, Lei Y, Xu C, et al. Risk factors for disease progression in patients with mild to moderate coronavirus disease 2019-a multi-centre observational study. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2020;26(9):1242-7. Epub 2020/06/12.
- 58. Cheng X, Cai G, Wen X, Gao L, Jiang D, Sun M, et al. Clinical characteristics and fatal outcomes of hypertension in patients with severe COVID-19. Aging (Albany NY). 2020;12(23):23436-49. Epub 2020/11/17.
- 59. de Souza CD, de Arruda Magalhães AJ, Lima AJ, Nunes DN, de Fátima Machado Soares É, de Castro Silva L, et al. Clinical manifestations and factors associated with mortality from COVID-19 in older adults: Retrospective population-based study with 9807 older Brazilian COVID-19 patients. Geriatrics & gerontology international. 2020;20(12):1177-81. Epub 2020/10/29.
- 60. Mejia F, Medina C, Cornejo E, Morello E, Vasquez S, Alave J, et al. Oxygen saturation as a predictor of mortality in hospitalized adult patients with COVID-19 in a public hospital in Lima, Peru. PloS one. 2020;15(12):e0244171.
- 61. Park BE, Lee JH, Park HK, Kim HN, Jang SY, Bae MH, et al. Impact of Cardiovascular Risk Factors and Cardiovascular Diseases on Outcomes in Patients Hospitalized with COVID-19 in Daegu Metropolitan City. Journal of Korean medical science. 2021;36(2):e15. Epub 2021/01/12.
- 62. Parra-Bracamonte GM, Lopez-Villalobos N, Parra-Bracamonte FE. Clinical characteristics and risk factors for mortality of patients with COVID-19 in a large data set from Mexico. Annals of epidemiology. 2020;52:93-8.e2. Epub 2020/08/18.
- 63. Wei ZY, Qiao R, Chen J, Huang J, Wu H, Wang WJ, et al. The influence of pre-existing hypertension on coronavirus disease 2019 patients. Epidemiol Infect. 2021;149:e4. Epub 2021/01/06.
- 64. Xiong TY, Huang FY, Liu Q, Peng Y, Xu YN, Wei JF, et al. Hypertension is a risk factor for adverse outcomes in patients with coronavirus disease 2019: a cohort study. Annals of medicine. 2020;52(7):361-6. Epub 2020/07/28.

WHO continues to monitor the situation closely for any changes that may affect this scientific brief. Should any factors change, WHO will issue a further update. Otherwise, this scientific brief document will expire two years after the date of publication.

© World Health Organization 2021. Some rights reserved. This work is available under the <u>CC BY-NC-SA 3.0 IGO</u> licence.

WHO reference number: WHO/2019-nCoV/Sci Brief/Hypertension/2021.1