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Letter to the Editor

Cardiovascular complications in COVID-19: A systematic review and meta-analysis

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To the Editor

The coronavirus disease 2019 (COVID-19) pandemic poses the most significant modern-day public health challenge since the Spanish flu of 1918, causing substantial morbidity and mortality worldwide.(1) Coronavirus disease 2019 predominantly affects the respiratory system, causing severe pneumonia and respiratory distress syndrome. There is also involvement of multiple organs, and the cardiovascular system has been implicated. In a recent study to investigate characteristics and prognostic factors in 339 elderly patients with COVID-19, Wang and colleagues observed a high proportion of severe and critical cases as well as high fatality rates.(2) The cardiovascular complications recorded were acute cardiac injury (21%), arrhythmia (10.4%) and cardiac insufficiency (17.4%). However, not all cardiovascular manifestations of COVID-19 are clearly defined by published studies and it is also not clear if these conditions are directly caused by COVID-19 or are just unspecific complications.(3) There is a need to understand the interplay between COVID-19 and its cardiovascular manifestations to assist in the optimum management of patients. In this context, we conducted a systematic meta-analysis to attempt to address the following questions: (i) what are the cardiovascular complications associated with COVID-19?; (ii) what is the incidence of these complications?; and (iii) are patients with pre-existing cardiovascular morbidities more susceptible to these cardiovascular complications?

The protocol for this review was registered in the PROSPERO International prospective register of systematic reviews (CRD42020184851). The review was conducted in accordance with PRISMA and MOOSE guidelines (4, 5) (**Supplementary Materials 1-2**). We searched MEDLINE, Embase, and The Cochrane library from 2019 to 27 May 2020 for published studies reporting on cardiovascular outcomes in patients with COVID-19. Details of the search strategy are reported in **Supplementary Material 3**. The prevalence of comorbidities (pre-existing hypertension and cardiovascular disease, CVD) and incidence of cardiovascular complications across studies with their 95% confidence intervals (CIs) were pooled using Freeman-Tukey variance stabilising double arcsine transformation and random-effects models. STATA release MP 16 (StataCorp LP, College Station, TX, USA) was used for all statistical analyses.

Seventeen retrospective cohort studies comprising of 5,815 patients with COVID-19 were included (**Table 1; Supplementary Materials 4-5**). Eleven studies were based in China, four in the USA, one in South Korea and one in the Netherlands. The average age at baseline ranged from 47 to 71 years.

Across 15 studies, the pooled prevalence of pre-existing hypertension (95% CI) in COVID-19 patients was 29.3% (25.5-33.4; I^2 =87%; 95% CI 79, 91%; *p* for heterogeneity<0.01) (**Supplementary Material 6**). The prevalence (95% CI) of pre-existing CVD across 16 studies was 14.6% (11.0-18.4; I^2 =91%; 95% CI 87, 94%; *p* for heterogeneity<0.01) (**Supplementary Material 7**).

Over hospital stays ranging from 2 to 28 days, the pooled incidence was 17.6% (14.2-21.2; I^2 =32%; 95% CI 0, 76%; *p* for heterogeneity=0.20) for heart failure (HF) (n=4 studies); 16.3% (11.8-21.3; I^2 =87%; 95% CI 79, 92%; *p* for heterogeneity<0.01) for myocardial injury (n=11 studies); 9.3% (5.1-14.6; I^2 =78%; 95% CI 52, 90%; *p* for heterogeneity<0.01) for cardiac arrhythmia (n=6 studies); 6.2% (1.8-12.3) for acute coronary syndrome (ACS) (n=2 studies); 5.7% (2.7-9.6) for cardiac arrest (n=2 studies); and 5.6% (3.4-8.3) for disseminated intravascular dissemination (DIC) (n=2 studies) (**Figure 1A**). Subgroup analyses suggested that the incidence of myocardial injury was higher in older age groups and groups with a higher prevalence of pre-existing hypertension; however, the incidence of myocardial injury was similar in groups with high or low prevalence of pre-existing CVD (**Figure 1B**). Over hospital stays ranging from 2 to 28 days following admission, mortality rate ranged from 0.7% to 52.4%, with a pooled rate of 15.3% (10.7-20.5).

The current data based on up-to-date evidence suggests that the most common cardiovascular complications of COVID-19 are HF, myocardial injury and cardiac arrhythmias. Though the mechanisms for cardiovascular complications are still yet to be elucidated, the following multiple pathways have been proposed: (i) direct cardiotoxicity; (ii) systemic inflammation; (iii) myocardial demand-supply mismatch; (iv) plaque rupture and coronary thrombosis; (v) adverse effects of therapies during hospitalization; (vi) sepsis leading to DIC; (vii) increased systemic thrombogenesis; and (viii) electrolyte imbalances.(6, 7) Myocardial injury is reported to mainly result from direct viral involvement of cardiomyocytes and the effects of systemic inflammation.(6) Though venous

thromboembolism incidence was based on a single report, patients with COVID-19 are at increased risk of hypercoagulable states due to prolonged immobilisation, systemic inflammation and risk for DIC.(7)

In addition to pre-existing comorbidities including CVD being associated with worse outcomes in patients with COVID-19,(8, 9) cardiovascular complications such as myocardial injury have also been shown to be associated with increased risk of severe COVID-19 and fatal outcomes.(10) Myocardial injury is commonly defined as substantial elevation of high-sensitivity cardiac troponin levels and it has been reported that elevated troponin levels are associated with greater risk of severe disease and mortality. (10) Monitoring of markers of cardiac damage such as troponin, N-terminal pro B-type natriuretic peptide and creatine kinase during hospitalisation for COVID-19 could help in the identification of patients with possible cardiac manifestations, to enable early and more aggressive intervention.

The inherent limitations included the low sample sizes and methodological design of some of the studies, which was expected given the urgency to report and gain a better understanding of COVID-19; limited number of studies available, hence some of the findings were based on single reports; assays for cardiac injury and their time of assessment during hospitalisation may vary between studies, hence estimates may be biased; and the possibility of patient overlap given that the majority of studies were conducted from China and reports of duplicate publication of study participants in articles.(9)

Aggregate analysis of the literature suggests that the most frequent cardiovascular complications among patients hospitalised with COVID-19 are HF, myocardial injury, cardiac arrhythmias and ACS. Early identification and monitoring of cardiac complications could help in the prediction of more favourable outcomes. The causes of these cardiovascular manifestations warrant further investigation as more data becomes available.

Conflict of interest

None.

Acknowledgements

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References

1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-62. doi:10.1016/S0140-6736(20)30566-3

2. Wang L, He W, Yu X, et al. Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up. J Infect. 2020. doi:10.1016/j.jinf.2020.03.019

3. Ferrari R, Di Pasquale G, Rapezzi C. 2019 CORONAVIRUS: What are the implications for cardiology? Eur J Prev Cardiol. 2020;27(8):793-6. doi:10.1177/2047487320918102

4. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of Observational Studies in Epidemiology. JAMA: The Journal of the American Medical Association. 2000;283(15):2008-12. doi:10.1001/jama.283.15.2008

5. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097

6. Bansal M. Cardiovascular disease and COVID-19. Diabetes & metabolic syndrome. 2020;14(3):247-50. doi:10.1016/j.dsx.2020.03.013

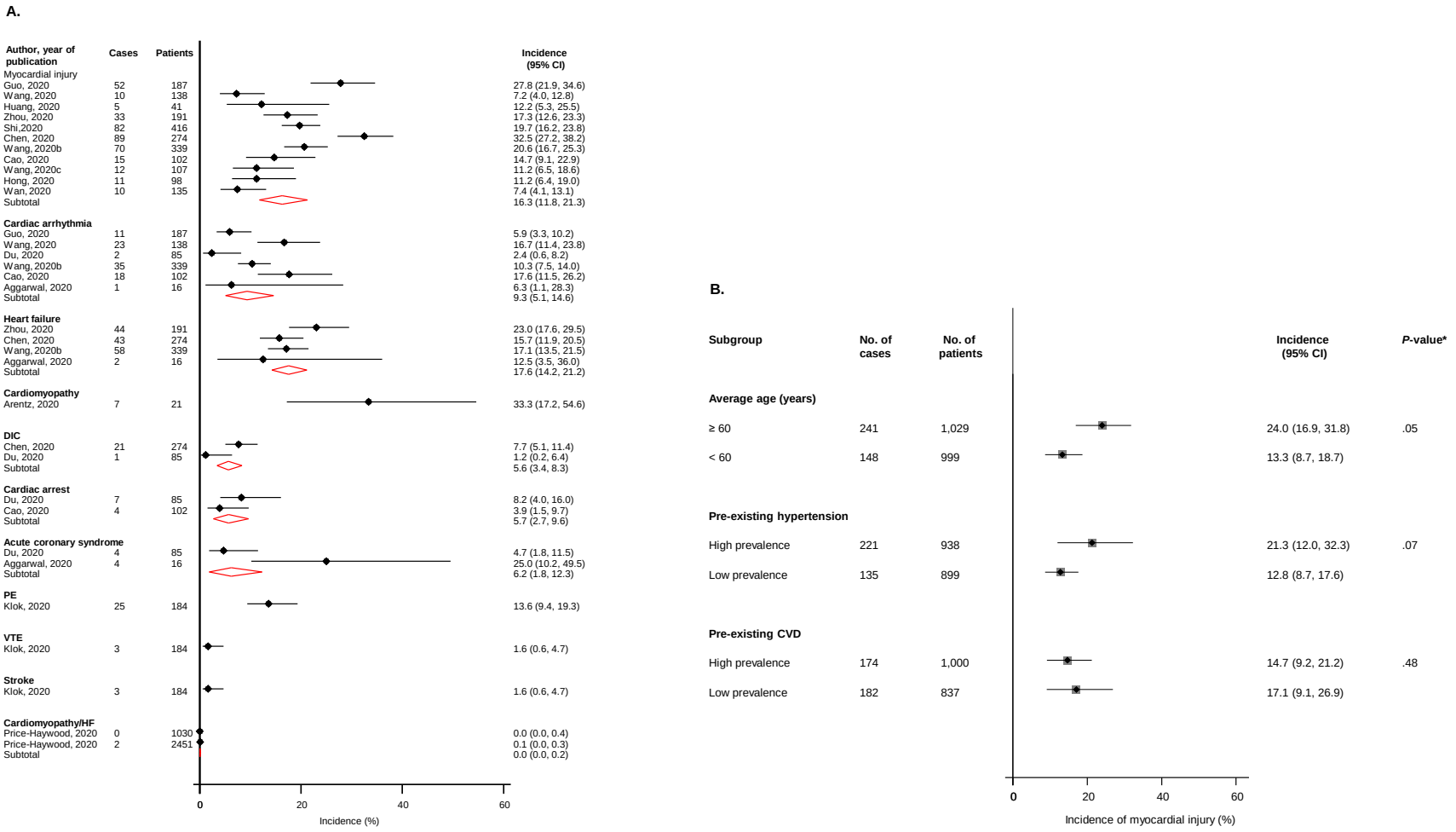
7. Kang Y, Chen T, Mui D, et al. Cardiovascular manifestations and treatment considerations in covid-19. Heart. 2020. doi:10.1136/heartjnl-2020-317056

8. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. Lancet. 2020;395(10229):1014-5. doi:10.1016/S0140-6736(20)30633-4

9. Kunutsor SK, Laukkanen JA. Markers of liver injury and clinical outcomes in COVID-19 patients: A systematic review and meta-analysis. Journal of Infection. 2020 (In Press).

10. Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020. doi:10.1001/jamacardio.2020.1017

Fig. 1 (A) Incidence of cardiovascular complications in COVID-19 patients; (B) Incidence of cardiovascular complications in COVID-19 patients, by clinically relevant characteristics



CI, confidence interval (bars); CVD, cardiovascular disease; DIC, disseminated intravascular coagulation; PE, pulmonary embolism; VTE, venous thromboembolism; *, p-value for meta-regression

Table 1. Characteristics of included studies

Author, year of publication	Source of data	Country	Dates of data collection	Mean/median age (years)	Male %	Hospitalisation (days)	No. of patients	CVD complications	NOS
Guo, 2020	Seventh Hospital of Wuhan City	China	Jan - Feb 2020	58.5	48.7	16.3	187	Myocardial injury; ventricular arrhythmia	5
Wang, 2020	Zhongnan Hospital of Wuhan University	China	Jan, 2020	56.0	54.3	7.0	138	Myocardial injury; cardiac arrhythmia	4
Huang, 2020	Jin Yintan Hospital, Wuhan	China	Dec - Jan 2020	49.0	73.0	7.0	41	Myocardial injury	4
Zhou, 2020	Jinyintan Hospital & Wuhan Pulmonary Hospital	China	Dec - Jan 2020	56.0	62.0	11.0	191	Myocardial injury; HF	5
Shi,2020	Renmin Hospital of Wuhan University	China	Jan - Feb 2020	64.0	49.3	NR	416	Myocardial injury	6
Arentz, 2020	Evergreen Hospital in Kirkland, Washington	USA	Feb - March 2020	70.0	52.0	5.2	21	Cardiomyopathy	4
Chen, 2020	Tongji Hospital in Wuhan	China	Jan - Feb 2020	62.0	62.0	13.0	274	Myocardial injury; HF; DIC	4
Du, 2020	Hannan Hospital and Wuhan Union Hospital	China	Jan - Feb 2020	65.8	72.9	10.1	85	Cardiac arrest; ACS; arrhythmia; DIC	4
Wang, 2020b	Renmin Hospital of Wuhan University	China	Jan - Feb 2020	71.0	49.0	28.0	339	Myocardial injury, arrhythmia HF	4
Cao, 2020	Zhongnan Hospital of Wuhan University	China	Jan - Feb 2020	54.0	52.0	11.0	102	Myocardial injury; arrhythmia; cardiac arrest	4
Klok, 2020	Dutch Univesity Hospitals	Netherlands	March - April 2020	64.0	76.0	7.0	184	PE; VTE; stroke	4
Aggarwal, 2020	UnityPoint Clinic	USA	March - April 2020	67.0	75.0	2.0	16	ACS; cardiac arrhythmia; HF	4
Wang, 2020c	Zhongnan Hospital of Wuhan University and Xishui People's Hospital	China	Up to Feb, 2020	51.0	53.3	11.0	107	Myocardial injury	5
Hong, 2020	Yeungnam University Medical Center	South Korea	Up to March, 2020	55.4	38.8	7.7	98	Myocardial injury	4
Wan, 2020	Northeast Chongqing	China	Jan – Feb 2020	47.0	53.3	5.0	135	Myocardial injury	4
Price-Haywood, 2020	Ochsner Health in Louisiana	Asia	March – April, 2020	55.5	45.7	7.0	1,030	Cardiomyopathy/HF	6
Price-Haywood, 2020	Ochsner Health in Louisiana	Asia	March – April, 2020	53.6	37.7	6.0	2,451	Cardiomyopathy/HF	6

ACS, acute coronary syndrome; DIC, disseminated intravascular coagulation; HF, heart failure; NOS, Newcastle Ottawa Scale; NR, not reported; PE, pulmonary embolism; VTE, venous thromboembolism

SUPPLEMENTARY MATERIAL

Supplementary Material 1	PRISMA checklist
Supplementary Material 2	MOOSE checklist
Supplementary Material 3	MEDLINE literature search strategy
Supplementary Material 4	Selection of studies included in the meta-analysis
Supplementary Material 5	Reference list of included studies
Supplementary Material 6	Prevalence of pre-existing hypertension in COVID-19 patients
Supplementary Material 7	Prevalence of pre-existing cardiovascular disease in COVID-19 patients

Supplementary Material 1: PRISMA checklist

Section/topic	Item No	Checklist item	Reported on page No
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable, background, objectives, data sources, study eligibility criteria, participants, interventions, study appraisal and synthesis methods, results, limitations, conclusions and implications of key findings, systematic review registration number	2
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	Introduction
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)	Introduction
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (such as web address), and, if available, provide registration information including registration number	Methods
Eligibility criteria	6	Specify study characteristics (such as PICOS, length of follow-up) and report characteristics (such as years considered, language, publication status) used as criteria for eligibility, giving rationale	Methods
Information sources	7	Describe all information sources (such as databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	Methods
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	Supplementary material 3
Study selection	9	State the process for selecting studies (that is, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)	Methods
Data collection process	10	Describe method of data extraction from reports (such as piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	Methods
Data items	11	List and define all variables for which data were sought (such as PICOS, funding sources) and any assumptions and simplifications made	Methods
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	Methods
Summary measures	13	State the principal summary measures (such as risk ratio, difference in means).	Methods
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (such as I^2 statistic) for each meta-analysis	Methods
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (such as publication bias, selective reporting within studies)	Methods
Additional analyses	16	Describe methods of additional analyses (such as sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified	Methods
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	Results, Supplementary material 4
Study characteristics	18	For each study, present characteristics for which data were extracted (such as study size, PICOS, follow-up period) and provide the citations	Results, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see item 12).	Results
Results of individual studies	20	For all outcomes considered (benefits or harms), present for each study (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency	Results, Figure 1; Supplementary materials 6-7
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15)	Not applicable
Additional analysis	23	Give results of additional analyses, if done (such as sensitivity or subgroup analyses, meta-regression) (see item 16)	Not applicable
Discussion			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (such as health care providers, users, and policy makers)	Discussion
Limitations	25	Discuss limitations at study and outcome level (such as risk of bias), and at review level (such as incomplete retrieval of identified research, reporting bias)	Discussion
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	Discussion
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (such as supply of data) and role of funders for the systematic review	Page 10

Supplementary Material 2. MOOSE checklist

Cardiovascular complications in COVID-19: A systematic review and meta-analysis

Criteria		Brief description of how the criteria were handled in the review
Reporting of background		
√	Problem definition	Cardiovascular manifestations of COVID-19 are not clearly defined.
√	Hypothesis statement	(i) What are the cardiovascular complications associated with COVID-19? (ii) What is the incidence of these complications? (iii) Are patients with pre-existing cardiovascular morbidities more susceptible to these cardiovascular complications?
√	Description of study outcomes	Cardiovascular complications
√	Type of exposure	Prevalence and incidence estimates
√	Type of study designs used	Observational cohort designs and clinical studies
√	Study population	Adult patients with COVID-19
Reporting of search strategy should include		
√	Qualifications of searchers	Setor K. Kunutsor, PhD
√	Search strategy, including time period included in the synthesis and keywords	Time period: from inception to 27 May 2020 The detailed search strategy can be found in Supplementary material 3
√	Databases and registries searched	MEDLINE, Embase and The Cochrane Library
√	Search software used, name and version, including special features	OvidSP was used to search Embase and MEDLINE EndNote X9 used to manage references
√	Use of hand searching	We searched bibliographies of retrieved papers
√	List of citations located and those excluded, including justifications	Details of the literature search process are outlined in the flow chart. The citation list for excluded studies are available on request.
√	Method of addressing articles published in languages other than English	Not applicable
√	Method of handling abstracts and unpublished studies	Not applicable
√	Description of any contact with authors	None
Reporting of methods should include		
√	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Detailed inclusion and exclusion criteria are described in the Methods section.
√	Rationale for the selection and coding of data	Data extracted from each of the studies were relevant to the population characteristics, study design, exposure, and outcome.
√	Assessment of confounding	We assessed confounding by ranking individual studies on the basis of different adjustment levels and performed sub-group analyses to evaluate differences in the overall estimates according to levels of adjustment.
√	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Study quality was assessed based on the nine-star Newcastle–Ottawa Scale using pre-defined criteria namely: population representativeness, comparability (adjustment of confounders), ascertainment of outcome. Sensitivity analyses by several quality indicators such as study size, duration of follow-up, and adjustment factors.
√	Assessment of heterogeneity	Results
√	Description of statistical methods in sufficient detail to be replicated	Described in methods section
√	Provision of appropriate tables and graphics	Table 1; Figure 1; Supplementary materials 6-7
Reporting of results should include		
√	Graph summarizing individual study estimates and overall estimate	Supplementary materials 6-7
√	Table giving descriptive information for each study included	Table 1
√	Results of sensitivity testing	Not applicable
√	Indication of statistical uncertainty of findings	95% confidence intervals were presented with all summary estimates
Reporting of discussion should include		
√	Quantitative assessment of bias	The systematic review is limited in scope, as it involves studies with limited information.

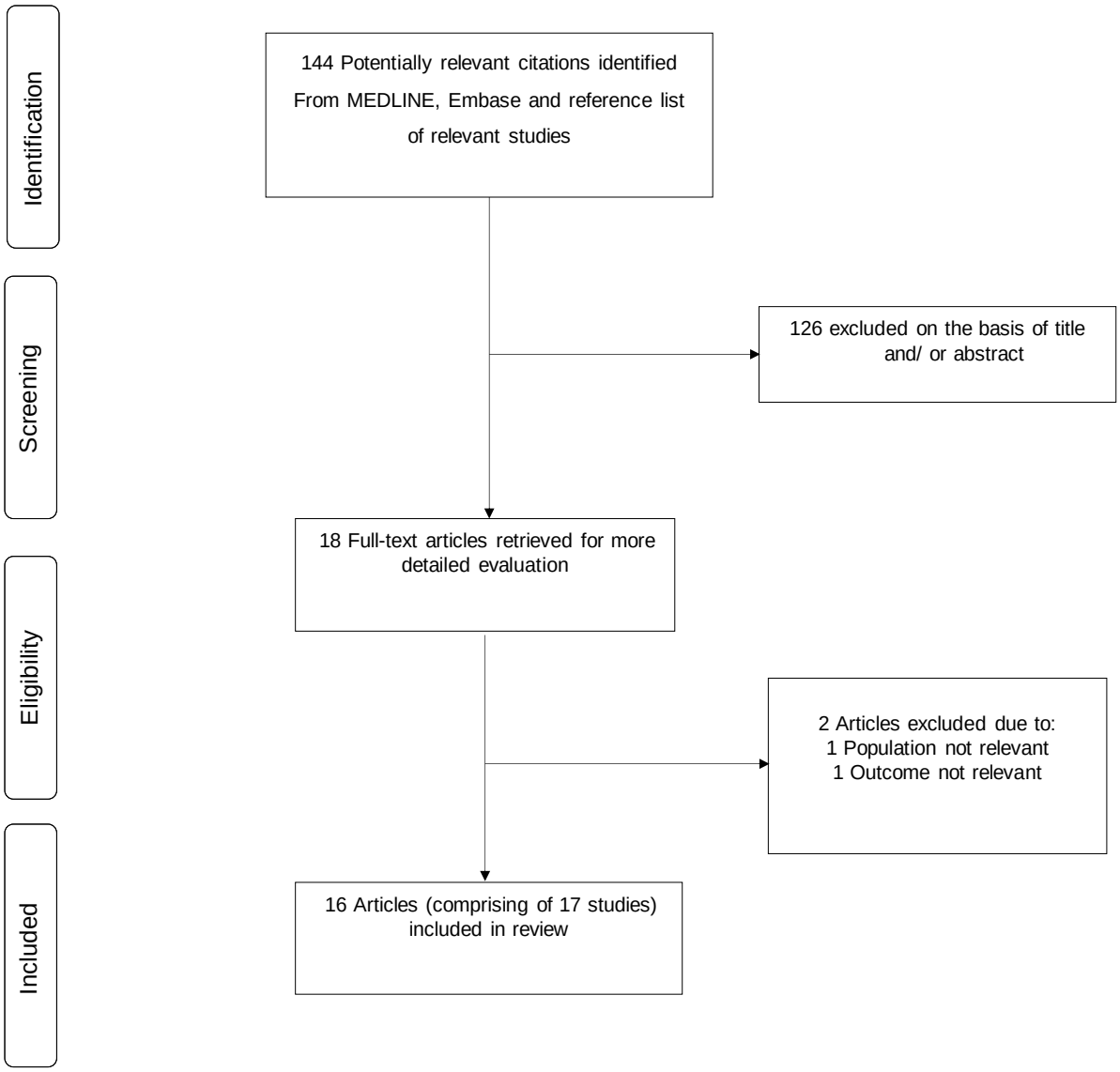
√	Justification for exclusion	All studies were excluded based on the pre-defined inclusion criteria in methods section.
√	Assessment of quality of included studies	Brief discussion included in ‘Methods’ section
Reporting of conclusions should include		
√	Consideration of alternative explanations for observed results	Discussion
√	Generalization of the conclusions	Discussed in the context of the results.
√	Guidelines for future research	We recommend large-scale studies when more data becomes available
√	Disclosure of funding source	In “Acknowledgement” section

Supplementary Material 3: MEDLINE literature search strategy

1 COVID-19.mp. (3926)
2 SARS-CoV-2.mp. (1044)
3 exp Cardiovascular Diseases/ (2362814)
4 exp Arrhythmias, Cardiac/ (207163)
5 exp Atrial Fibrillation/ (54365)
6 exp Ventricular Fibrillation/ (16940)
7 ventricular tachyarrhythmia.mp. (1239)
8 cardiac injury.mp. (3702)
9 myocardial injury.mp. (8353)
10 exp Myocardial Infarction/ (173824)
11 exp Acute Coronary Syndrome/ (15265)
12 exp Acute Coronary Syndrome/ (15265)
13 exp Myocarditis/ (14391)
14 exp Cardiomyopathies/ (93121)
15 exp Heart Failure/ (119900)
16 exp Venous Thromboembolism/ (10498)
17 exp Pulmonary Embolism/ (38540)
18 exp Disseminated Intravascular Coagulation/ (10958)
19 1 or 2 (4030)
20 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (2374706)
21 19 and 20 (105)
22 limit 21 to (english language and humans and yr="2019 -Current") (80)

Each part was specifically translated for searching alternative databases.

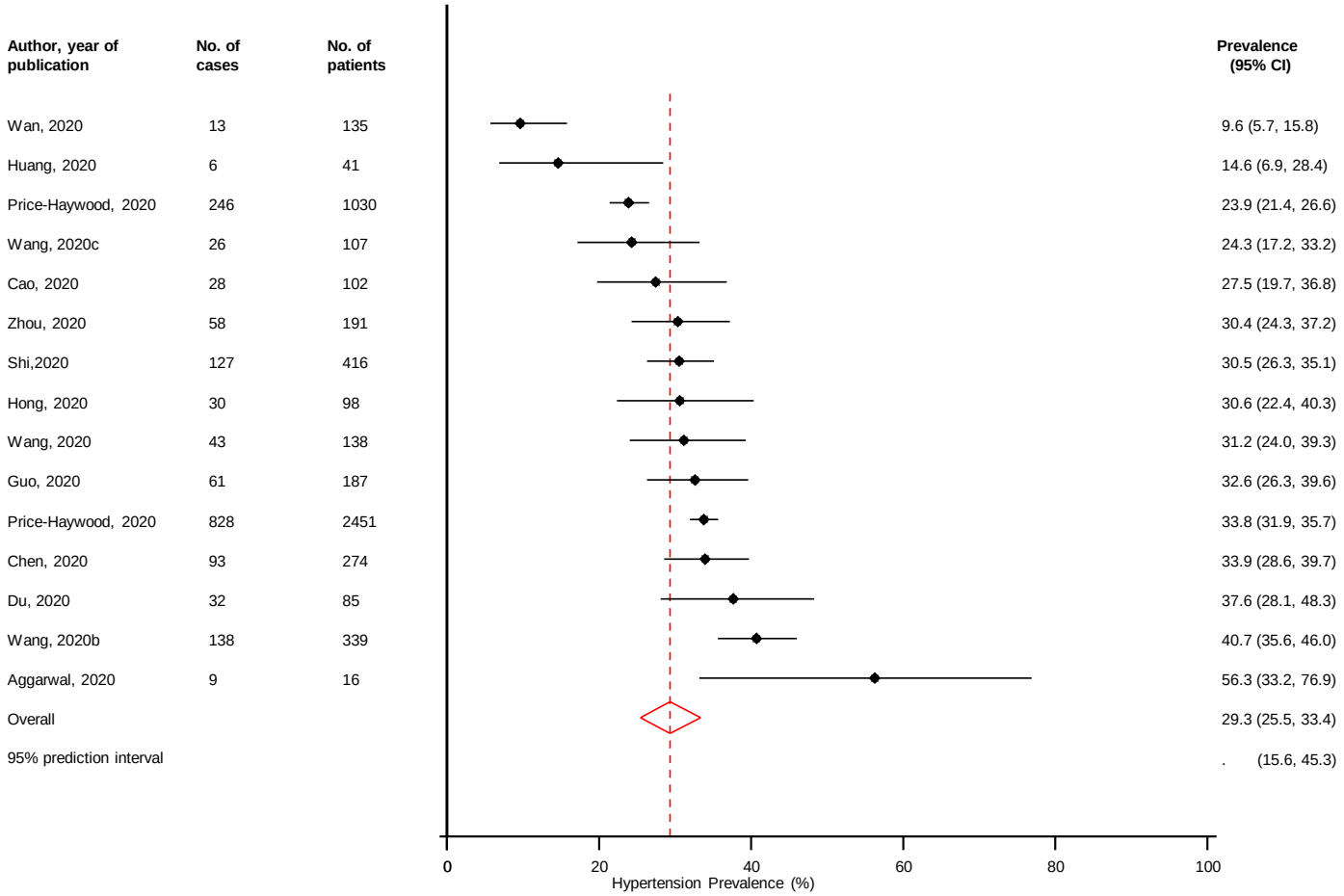
Supplementary Material 4: Selection of studies included in the meta-analysis



Supplementary Material 5: Reference list of included studies

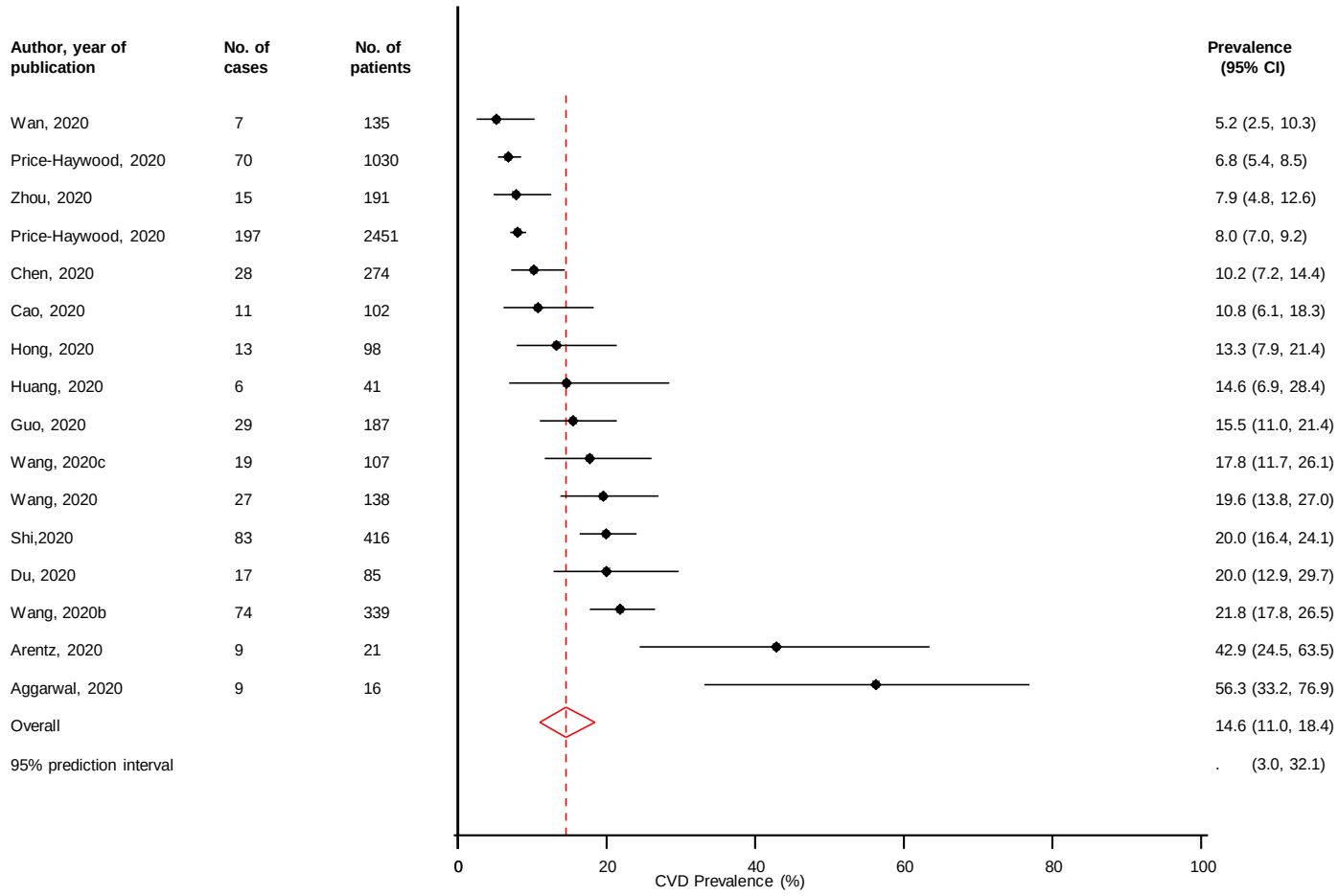
1. Aggarwal S, Garcia-Telles N, Aggarwal G, Lavie C, Lippi G, Henry BM. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): Early report from the United States. Diagnosis (Berl). 2020 May 26;7(2):91-6. PubMed PMID: 32352401. Epub 2020/05/01.
2. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020 Mar 26;368:m1091. PubMed PMID: 32217556. Epub 2020/03/29.
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506. PubMed PMID: 31986264. Pubmed Central PMCID: PMC7159299. Epub 2020/01/28.
4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 Feb 7. PubMed PMID: 32031570. Pubmed Central PMCID: PMC7042881. Epub 2020/02/08.
5. Wang D, Yin Y, Hu C, Liu X, Zhang X, Zhou S, et al. Clinical course and outcome of 107 patients infected with the novel coronavirus, SARS-CoV-2, discharged from two hospitals in Wuhan, China. Crit Care. 2020 Apr 30;24(1):188. PubMed PMID: 32354360. Pubmed Central PMCID: PMC7192564. Epub 2020/05/02.
6. Wang L, He W, Yu X, Hu D, Bao M, Liu H, et al. Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up. J Infect. 2020 Mar 30. PubMed PMID: 32240670. Pubmed Central PMCID: PMC7118526. Epub 2020/04/03.
7. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar 28;395(10229):1054-62. PubMed PMID: 32171076. Epub 2020/03/15.
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 Mar 27. PubMed PMID: 32219356. Pubmed Central PMCID: PMC7101506. Epub 2020/03/29.
9. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol. 2020 Mar 25. PubMed PMID: 32211816. Pubmed Central PMCID: PMC7097841. Epub 2020/03/27.
10. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA. 2020 Mar 19. PubMed PMID: 32191259. Pubmed Central PMCID: PMC7082763. Epub 2020/03/20.
11. Du Y, Tu L, Zhu P, Mu M, Wang R, Yang P, et al. Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan: A Retrospective Observational Study. Am J Respir Crit Care Med. 2020 Apr 3. PubMed PMID: 32242738. Epub 2020/04/04.
12. Cao J, Tu WJ, Cheng W, Yu L, Liu YK, Hu X, et al. Clinical Features and Short-term Outcomes of 102 Patients with Corona Virus Disease 2019 in Wuhan, China. Clin Infect Dis. 2020 Apr 2. PubMed PMID: 32239127. Pubmed Central PMCID: PMC7184479. Epub 2020/04/03.
13. Klok FA, Kruip M, van der Meer NJM, Arbous MS, Gommers D, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020 Apr 10. PubMed PMID: 32291094. Pubmed Central PMCID: PMC7146714. Epub 2020/04/16.
14. Hong KS, Lee KH, Chung JH, Shin KC, Choi EY, Jin HJ, et al. Clinical Features and Outcomes of 98 Patients Hospitalized with SARS-CoV-2 Infection in Daegu, South Korea: A Brief Descriptive Study. Yonsei medical journal. 2020 May;61(5):431-7. PubMed PMID: 32390367. Pubmed Central PMCID: PMC7214108. Epub 2020/05/12.
15. Wan S, Xiang Y, Fang W, Zheng Y, Li B, Hu Y, et al. Clinical features and treatment of COVID-19 patients in northeast Chongqing. J Med Virol. 2020 Mar 21. PubMed PMID: 32198776. Pubmed Central PMCID: PMC7228368. Epub 2020/03/22.
16. Price-Haywood EG, Burton J, Fort D, Seoane L. Hospitalization and Mortality among Black Patients and White Patients with Covid-19. N Engl J Med. 2020 May 27. PubMed PMID: 32459916. Epub 2020/05/28.

Supplementary Material 6: Prevalence of pre-existing hypertension in COVID-19 patients



CI, confidence interval (bars)

Supplementary Material 7: Prevalence of pre-existing cardiovascular disease in COVID-19 patients



CI, confidence interval (bars)