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## Article

# Cardiovascular involvement in patients with COVID-19: a systematic review of prevalence studies

Hamer, Oliver, Phoong, Kar Yen, Harrison, Joanna and Hill, James Edward

Available at <http://clock.uclan.ac.uk/41317/>

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## Commentary on:

Pellicori P, Doolub G, Wong CM, Lee KS, Mangion K, Ahmad M, Berry C, Squire I, Lambiase PD, Lyon A, McConnachie A, Taylor RS, Cleland JGF. COVID-19 and its cardiovascular effects: a systematic review of prevalence studies. *Cochrane Database of Systematic Reviews* 2021, Issue 3. Art. No.: CD013879. DOI: 10.1002/14651858.CD013879.

## Key Points

- Cardiometabolic comorbidities such as hypertension and type 2 diabetes are common in people who are hospitalised with a COVID-19 infection.
- The most common cardiovascular complications in people with COVID-19 are an irregular heartbeat, blood clots in the legs or lungs, and heart failure.
- The rate of cardiovascular complication is higher in people aged over 75 years than in younger people.

## Introduction

The coronavirus disease (COVID-19) caused by the virus Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2) has created a worldwide health crisis affecting over 300 million people (Chung et al., 2021). Due to the high infectivity and transmissibility of the disease, it spread rapidly across the globe (Morens et al., 2020), and the outbreak was declared a pandemic by the World Health Organisation in March 2020 (WHO, 2020). COVID-19 primarily affects the respiratory system, causing widespread inflammation and tissue damage. The common symptoms reported in COVID-19 are fever, dry cough, sore throat, fatigue and tiredness (Alimohamadi et al., 2020). Due to a substantial immune response, it can have a systemic manifestation and have the potential to affect other body systems (Babapoor-Farrokhran et al., 2020).

Multiple studies have found that COVID-19 has a detrimental effect on the cardiovascular system and may produce long-term complications with variable severity (Silva et al., 2021; Manolis et al., 2020). This is likely due to an increase in cardiac physiologic stress, hypoxia, or direct myocardial injury associated with the infection (Long et al., 2020). The severity of cardiac injury has been found to correlate with the severity of COVID-19, mortality, and subsequent prognosis in affected patients (Paterson et al., 2021). In addition, clinical outcomes (e.g., mortality) for patients with previous cardiac diseases and risk factors (e.g., hypertension, diabetes, and obesity) are worse compared to the general population (Chung et al., 2021). Thus, early diagnosis of cardiac involvement via biomarkers is crucial to reduce mortality in patients (Tajbakhsh et al., 2020). The systemic review by Pellicori et al., 2021 aimed to gather evidence of the prevalence, nature, and rate of cardiovascular involvement

(comorbidities and complications) in suspected or confirmed COVID-19 patients. This commentary aims to critically appraise the methods used within the systematic review to discuss the findings in the context of current clinical practice.

## Methods

The Cochrane systematic review employed a comprehensive strategy to search three databases including CENTRAL, Medline (Ovid) and Embase (Ovid) (Pellicori et al., 2021). The Cochrane COVID-19 Study Register and ClinicalTrials.gov were also searched for unpublished or ongoing trials. A range of study designs including randomised controlled trials, cross sectional studies, prospective cohort studies, retrospective cohort studies and case control studies were included. Only studies with 100 or more human participants with suspected or confirmed COVID-19 (of any setting) were eligible for inclusion. Studies were excluded if they were not original peer review articles, case reports describing cardiovascular complications, epidemiological studies with no clinical characteristics, and studies not written in English. Outcomes were restricted to clinical events and cardiovascular complications but were not used as a basis for including or excluding studies.

Comprehensive screening was conducted independently by five review authors in two stages: by title and abstract, then by full text. Excluded records were checked independently by a second review author, resolving discrepancies through discussion with a third author. Data extraction was carried out by four reviewers and checked for accuracy by an independent review author. Risk of bias was assessed independently by four review authors using two tools; the Joanna Briggs Institute (JBI) checklist for prevalence studies; and the JBI checklist for case series (Briggs, 2021). The outcomes of interest included cardiovascular complications, cardiovascular clinical events, mortality, myocarditis, myocardial infarction, stroke, peripheral arterial occlusion, deep venous thrombosis, pulmonary thrombo-embolism, arrhythmias, circulatory failure, raised troponin, raised natriuretic peptides, impaired ventricular systolic function and QT prolongation. Prevalence and incidence rates of these outcomes (in relation to people with COVID-19) were reported using weighted mean prevalence (WMP) or weighted mean incidence (WMI). These were calculated by adding all the prevalence or incidence cases for each study, divided by the total number of the participants included in those cohorts. A narrative synthesis was performed to synthesize the findings of all included studies. A meta-analysis was inappropriate given the variation in study designs and outcomes.

## Results

After removal of duplicates, the database and registry searches identified 5464 studies. Following screening, 220 studies were included in the review. Studies were largely undertaken in middle to high-

income countries with the highest proportion from China (47.7%), the United States of America (20.9%), and Italy (9.5%). Of the 220 studies, 196 (89.5%) were retrospective cohort studies. Mean or median age within the studies ranged from ~ 30 to 78 years with a slightly greater number of male participants. Studies predominantly collected data from participants who had been hospitalised. A total of 102 studies reported on pre-existing cardiovascular comorbidities in people with COVID-19 of which 36.1% (WMP) had hypertension, 22.1% (WMP) had type 2 diabetes, and 10.5% (WMP) had ischaemic heart disease. The prevalence of cardiovascular co-morbidities in people with COVID-19 increased with age, was associated with death, and an increased risk of disease progression.

This review reported on the rate of a wide range of subsequent cardiovascular complications and clinical events in people with suspected or confirmed COVID-19. However, the incidence rates of these complications were unclear because the number of events was not reported by the review authors. In the review, Weighted Mean Incidence (WMI) was used to describe the incidence of cardiovascular complications (as a percentage) from the total population of people suspected or confirmed to have COVID-19. Cardiovascular complications such as arrhythmias (people hospitalised with COVID-19 in 22 studies, WMI: 9.3%), venous thromboembolism (people hospitalised with COVID-19 in 16 studies, WMI: 7.4%), heart failure (20 studies, WMI: 6.8%), deep vein thrombosis (people hospitalised with COVID-19 in 16 studies, WMI: 6.1%), death (number of studies not reported, WMI: 6.1%), and cardiac injury (48 studies, WMI: 4.8%) were common among people with COVID-19. Complications such as pulmonary embolism (people hospitalised with COVID-19 in 16 studies, WMI: 4.3%), Myocarditis (people with severe COVID-19 infection in 3 studies, WMI: 2.6%), myocardial infarction (people hospitalised with COVID-19 in 16 studies, WMI 1.7%), and stroke (20 studies, WMI: 1.2%) were less common among people with COVID-19. The rate of cardiac complications was higher in people aged over 75, and generally lower in people not requiring hospitalisation.

## Commentary

The quality of the review was assessed using the JBI critical appraisal checklist for systematic reviews and evidence synthesis (Aromataris et al., 2015). This review scored 8 out of 11 critical appraisal criteria. The three unfulfilled criteria related to a lack of clarity in how the methods reported incidence rates, a lack of recommendations for policy and/or practice (supported by the reported data), and an absence of any assessment of publication bias.

This review reported the prevalence of co-morbidities and incidence of complications that may allow clinicians to determine the risk of cardiac involvement in COVID-19 patients. From the findings, pre-existing comorbidities such as high blood pressure, diabetes and heart disease are highly prevalent in people hospitalised with COVID-19 and are associated with an increased risk of death. Identification of their presence may help to inform risk stratification and subsequent management of hospitalised

COVID-19 patients. There is also a rationale to recommend higher levels of care and more frequent monitoring for patients hospitalised with COVID-19, as cardiovascular complications are frequent. This could involve frequent measurement of blood pressure, heart rate, and performing blood tests for specific cardiac biomarkers. The synthesis suggests that complications such as heart failure, deep vein thrombosis, and cardiac injury are likely to occur for 1 in 20 patients who present to hospital with COVID-19. A patient with COVID-19 may therefore be best placed or allocated within a unit whereby care is delivered by a clinician with substantial cardiac knowledge. This may be particularly important for COVID-19 patients with cardiac backgrounds who need greater levels of care by healthcare professionals with experience of cardiovascular conditions.

Apart from being cared for in the hospital, it is also crucial to optimise the level of care when patients are being discharged. To further reduce the occurrence of cardiac complications, a recommendation could be made that general practitioners schedule more follow-up appointments to identify early signs of complications and provide prompt treatment. Currently, there is no plan in place for COVID-19 patients after discharge. Therefore, an algorithm would be beneficial and should be produced for post-discharge monitoring. Due to the recent advancement of technologies, digital health monitoring tools may be a useful resource to facilitate the anticipated demand for health monitoring of COVID-19 patients.

Having established that there are substantial rates of cardiovascular complications in patients with COVID-19, further research is needed to establish if they are higher than those reported in similarly ill people with other infections. Research is also needed to identify if cardiovascular complications differ in severity or incidence between the variants of the SARS-CoV2 virus (e.g., Delta and Omicron). Limitations of the included studies reported by this review identified a need for high quality studies to distinguish between pre-existing conditions and new incidence in people hospitalised with COVID-19. These studies could improve the certainty of evidence relating to the incidence of new conditions post diagnosis, improving understanding of disease progression, treatment effects, and adverse events.

### **CPD reflective questions**

- Before applying these findings to your practice, which limitations of the review should be considered?
- Which cardiovascular complications have the highest rate of hospital readmission?
- What advice can be given to patients about the range of cardiovascular complications that occur in people with suspected or confirmed COVID-19?

## Declaration

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