Review

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Effect of coronavirus infection on the human heart: A scoping review

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Abstract

Background: The global coronavirus disease 2019 pandemic has highlighted the importance of understanding the cardiovascular implications of coronavirus infections, with more severe disease in those with cardiovascular co-morbidities, and resulting cardiac manifestations such as myocardial injury, arrhythmias, and heart failure.

Design: A systematic review of the current knowledge on the effects of coronavirus infection on the cardiovascular system in humans was performed and results were summarized.

Methods: Databases such as MEDLINE, EMBASE, CENTRAL, Scopus, Web of Science, ClinicalTrials.gov, Chinese Knowledge Resource Integrated Database and Chinese Clinical Trial Registry were searched on 20 March 2020.

Results: In total, 135 studies were included, involving severe acute respiratory syndrome, Middle East respiratory syndrome, coronavirus disease 2019 and other coronaviruses. Most were case reports, case series and cohort studies of poor to fair quality. In post-mortem examinations of subjects who died from infection, around half had virus identified in heart tissues in severe acute respiratory syndrome, but none in Middle East respiratory syndrome and coronavirus disease 2019. Cardiac manifestations reported include tachycardia, bradycardia, arrhythmias, and myocardial injury, secondary to both systemic infection and treatment. Cardiac injury and arrhythmias are more prevalent in coronavirus disease 2019, and elevated cardiac markers are associated with intensive care unit admission and death. In severe acute respiratory syndrome, Middle East respiratory syndrome, and coronavirus disease 2019, comorbidities such as hypertension, diabetes mellitus, and heart disease are associated with intensive care unit admission, mechanical ventilation, and mortality. There were cases of misdiagnosis due to overlapping presentations of cardiovascular diseases and coronavirus infections, leading to hospital spread and delayed management of life-threatening conditions.

Conclusion: This review highlighted the ways in which coronaviruses affect cardiovascular function and interacts with pre-existing cardiovascular diseases.

Keywords

Coronavirus, cardiovascular system, heart, coronavirus disease 2019, severe acute respiratory syndrome, Middle East respiratory syndrome, common cold

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Introduction

The recent global pandemic of coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus (SARS-CoV-2), has drawn international attention to coronaviral infections and highlights the importance of increasing the understanding of this pathogen. Coronaviruses are enveloped single-stranded RNA viruses that consist of four main subgroups, namely alpha, beta, gamma, and delta. They often cause infections in mammals and birds, and in humans they commonly cause respiratory infections such as the common cold, but rarely more

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severe presentations can occur. For example, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) are caused by betacoronaviruses SARS-CoV and MERS-CoV, respectively. Although mainly affecting the lungs, these infections can have multisystemic consequences, including the gastrointestinal tract and the heart.[1] Other coronaviruses that affect humans include alphacoronaviruses human coronavirus (HCoV)-229E and HCoV-NL63, as well as betacoronaviruses HCoV-OC43 and HCoV-HKU1.[2]

COVID-19 has been observed to lead to cardiac manifestations such as arrhythmias, myocardial injury, and heart failure.[3] Furthermore, patients with cardiovascular comorbid conditions have an elevated mortality rate, particularly those with cardiovascular diseases.[4] It is therefore clinically important to understand the cardiac implications of coronavirus infections. In this scoping review, we aim to summarize current knowledge on the effect of coronavirus infections on the human heart and cardiovascular system, through a systematic search of available literature.

Methods

Comprehensive literature searches of MEDLINE, EMBASE, Cochrane Library and CENTRAL, Scopus, Web of Science and ClinicalTrials.gov were performed on the 20 March 2020 with search terms "coronavirus" and "heart or cardi*". The Chinese databases Chinese Knowledge Resource Integrated Database (CNKI) and Chinese Clinical Trial Registry were also searched on 20 March 2020. Additional studies were identified from reference scanning of included studies. Inclusion criteria were (a) a research study or systematic review performed on human participants, (b) with reported coronavirus infection and cardiovascular effects or co-morbidities. Coronavirus infection was defined as infection with any virus from the *Coronaviridae* family, including the coronavirus OC43, 229E, NL-63, HKU1, SARS, MERS, and COVID-19. Studies were excluded if (a) they were animal or in vitro studies or (b) data could not be reliably extracted. There were no limitations on the publication type, language, or publication date.

Two bilingual researchers (JSYH and CHS) with over 10 years of education in Chinese independently screened and assessed all identified titles, abstracts, and full texts in both Chinese and English. Corresponding authors were contacted for articles which had no available full text or missing data.

Data extraction was performed independently by two researchers (JSYH and CHS) and any discrepancies were resolved through discussion. A standardized data extraction form was used, and data collected included study type, publication date and country, population characteristics, setting, virus type, sample size, and results extracted. The quality of included studies was assessed using validated protocols, for example the Cochrane Risk of Bias Tool for randomized controlled trials,[5] the Newcastle/Ottawa scale for case series, cohort studies, or case-control studies,[6] the AMSTER (A MeaSurement Tool to Assess systematic Reviews) Tool for systematic reviews[7] and credibility assessment tool for genetic associations.[8]

Studies were grouped by the types of effects they demonstrated and their characteristics such as setting, population, study design, and outcomes, and were summarized in narrative review and table of results.

Results

The primary search identified 1289 articles after removal of duplicates and 19 were identified from review of reference lists in these studies. In total, 135 studies met the inclusion criteria and were included in this scoping review (Figure 1). The quality of included studies was assessed and is presented in Supplementary Material Table 1. Based on the results reported in these studies, they were grouped into four main themes: (a) coronaviruses causing direct damage to the heart; (b) clinical cardiovascular manifestations of coronaviral infections or treatment; (c) effects of cardiac comorbidities on susceptibility and prognosis of coronavirus infection; and (d) missed diagnosis of coronavirus infection due to associated cardiac co-morbidities (Figure 2).

Coronaviruses causing direct damage to the heart

A systematic search of literature found 19 articles on 211 patients that studied the micro- and macro-histological changes caused by coronaviruses in the heart from tissue examination (Supplementary Material Table 2).[9–26] A majority of studies were case reports and case studies with resulting poor quality due to their retrospective nature, lack of representativeness and control population. Thirteen studies were from Asia on SARS, two studies were on MERS from the Middle East, one on COVID-19 in China and one on NL-63 from USA. All were autopsy or post-mortem studies, therefore only cases with the most severe disease manifestation were represented.

Of the 19 studies included, nine positively detected the virus in heart tissues.[14,15,23] All positive results were seen in SARS patients only. One case series with six patients focused on the conductive dysfunction caused by SARS detected SARS-CoV by *in situ* hybridization in the conductive system of the heart, which correlated to four patients having elevated cardiac markers and five with dysrhythmias.[16] Of the six studies that failed

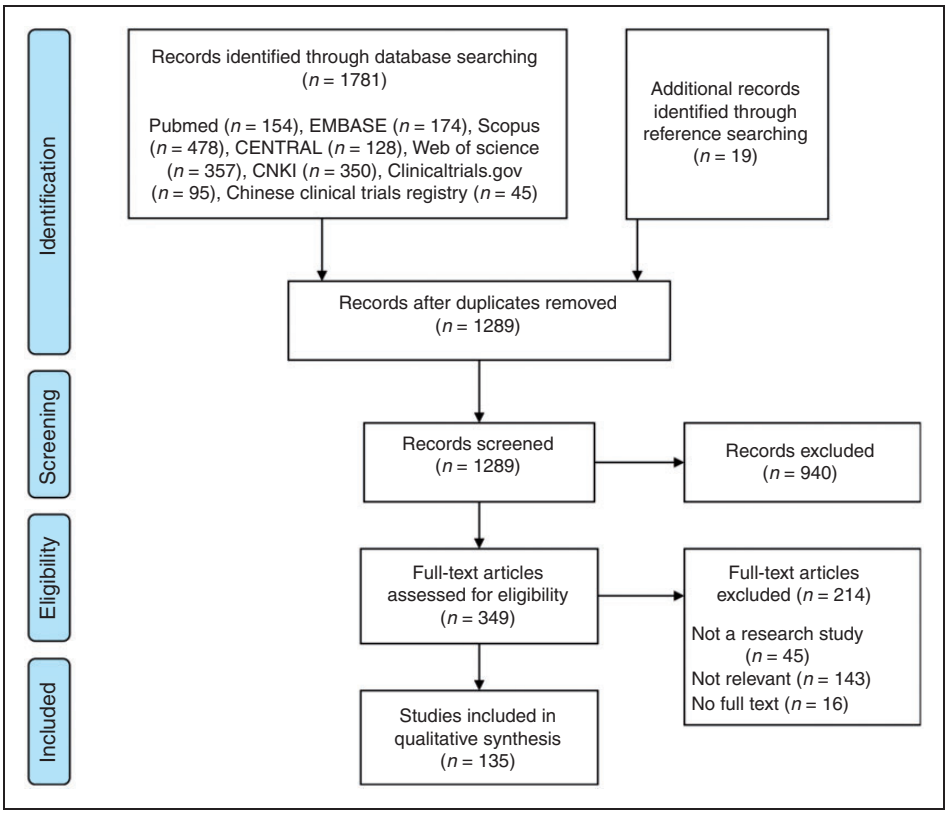

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for the systematic search and review.
CNKI: Chinese Knowledge Resource Integrated Database.

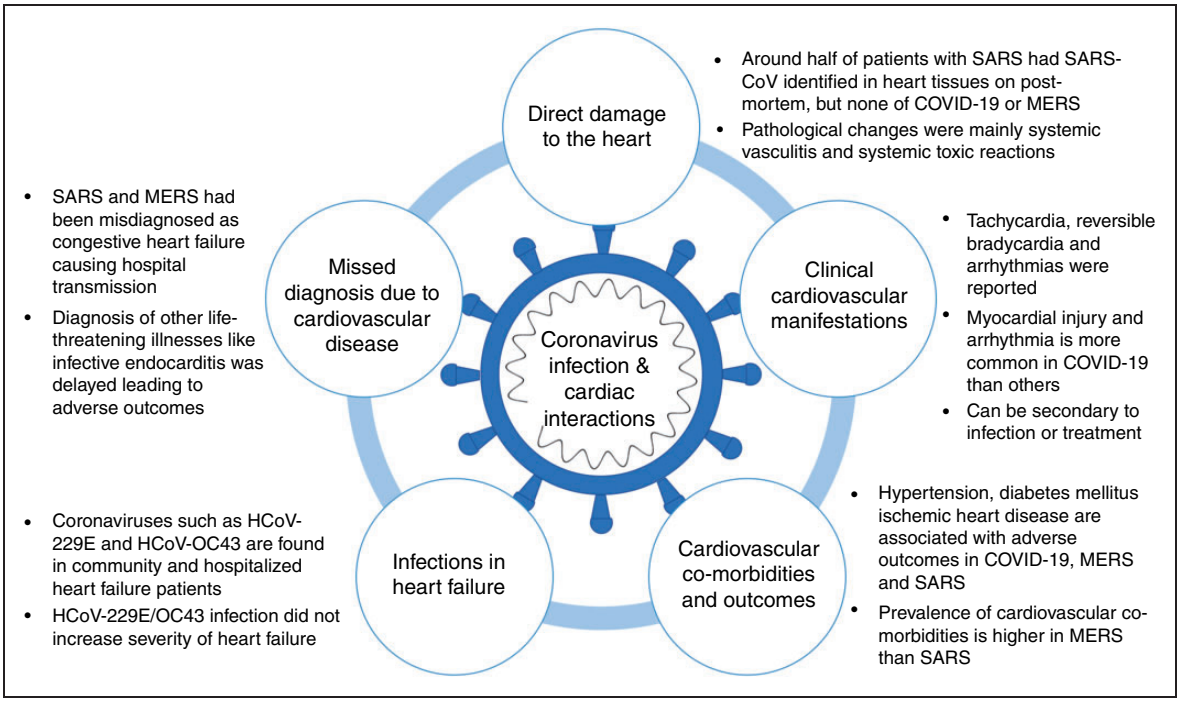

Figure 2. Summary diagram of the main findings for each of the themes presented in this review. COVID-19: coronavirus disease 2019; HCoV: human coronavirus; MERS: Middle East respiratory syndrome; SARS: severe acute respiratory syndrome.

to detect coronavirus in heart tissues, two investigated MERS, two SARS, one COVID-19 and one HCoV-229E/OC43, while the other four studies did not report whether this was sought for.

Studies on SARS found that the pathological changes to the heart were mainly systemic vasculitis and systemic toxic reactions. Changes observed on pathological examination include myocardial edema, endothelial swelling and junctional widening, and infiltration of mononuclear and lymphocytic cells. Myocarditis was not observed on histopathological examination except for mild cases in one case series.[16] Interestingly, one SARS patient had systemic infarcts with widespread intravascular fibrin thrombi and others showed pulmonary thromboemboli, intravascular microemboli and systemic infarction.[23] It is unknown if this was due to multiorgan dysfunction and acute respiratory distress syndrome or viral-associated damage. One case report of MERS found that on histopathology, the heart was unremarkable with no significant inflammatory infiltrate.[13] Similarly, the heart tissue of a patient who died from COVID-19 showed minor interstitial mononuclear inflammatory infiltrates, but no other substantial damage in the heart tissue.[26]

Clinical cardiovascular manifestations of coronavirus infections or treatment

Although most commonly causing respiratory diseases, coronaviral infections may lead to a variety of clinical cardiovascular manifestations, as reported in 69 studies involving 49,156 patients (Supplementary Material Table 3), with one study having 36,408 subjects.[1,2,11,16,23,25,27–89] Few studies were designed to investigate cardiovascular outcomes as the primary aim, therefore results must be interpreted with high risk of reporting and information bias. Of the 69 studies, 22 were performed on HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-NH, HCoV-HKU1, and non-specified coronaviruses. Eleven studies investigated MERS-CoV, 19 were on SARS-CoV and 17 were on COVID-19.

Studies on SARS found that acutely, some patients presented with tachycardia, bradycardia, and electrocardiogram (ECG) changes such as ST and T wave changes.[30,34,37] At six-weeks post-recovery, a retrospective cohort study found that 28 out of 62 patients (45%) had palpitations, and 18% of these patients had sinus tachycardia on ECG.[35] Another article reported that 87 patients (71.9%) had tachycardia which persisted in 47 (38.8%) of the cohort even when fever had resolved.[37] In MERS, tachycardia was found to be an initial sign in two-thirds of patients.[52]

Bradycardia was reported in five studies on SARS,[30,31,37,61] particularly in association with ribavirin treatment.[1] This bradycardia was often transient and would resolve with a decrease in ribavirin dose and recovery from infection. This ribavirin-associated bradycardia was also seen in MERS patients, with prevalence of 88–100% of those on the medication.[54] Severe bradycardia requiring temporary pacemaker insertion was reported in 15% (11 out of 70) of MERS cases.[47] Similarly to SARS and MERS, other coronaviruses that often cause the common cold were found to be associated with bradycardia in four studies, particularly in neonates in conjunction with apneic episodes.[28,38,39,64]

In COVID-19, the rate of cardiac arrhythmias was reported to be 4.5% by a meta-analysis of three studies involving 314 patients,[77] up to 16.7% in a cohort of 138 patients.[89] However, data on the specific type of arrhythmias have yet been published. In non-COVID-19 infections, other cardiac arrhythmias occurred very rarely. Two cases with SARS were reported to have new atrial fibrillation.[30,37] An infant infected with HCoV-NL63 had chaotic atrial tachycardia on ECG, and presented with cardiogenic shock, dilated cardiomyopathy, and impaired left ventricular systolic function.[43]

Reports on myocardial injury caused by SARS are contradictory, with a few studies reporting increased cardiac markers,[16,30] while others did not.[34,37] In MERS, results were similarly mixed.[41,51] Myocardial injury was also similar in patients treated with ribavirin versus those who were not.[64] In contrast, cardiac damage may be a more prominent part of disease process in COVID-19, and may be associated with more adverse outcomes. Fourteen studies reported elevated cardiac markers such as cardiac troponin I (cTnI) or creatine kinase-myocardial band (CK-MB) in 4–12% of cases but increasing to up to 31% of intensive care unit (ICU) patients and 28–46% in those who died.[72–75,78–81,84–89] In total, 7.2% developed myocardial injury and 16.7% had cardiac arrhythmias, increasing to 22.2% and 44.4% in the ICU respectively.[89] A meta-analysis of four studies from China, on 341 patients, found that cTnI is significantly higher in patients with severe disease.[84] However, focusing on 112 COVID-19 patients with cardiovascular disease, no difference was observed in cTnI, brain natriuretic peptide, or CK-MB between those with critical disease and those without.[83]

Rarely, coronavirus infections were associated with myocarditis and pericarditis. One MERS patient who had elevated troponin I and pro-BNP was found to have myocarditis on cardiac magnetic resonance imaging, leading to acute onset heart failure and significant left ventricular impairment, which remained unchanged after 3 months.[51] Two studies also reported pericarditis and pericardial effusion associated with

MERS-CoV.[51,57] Cases of myocarditis were reported in COVID-19, and a large cohort study on 150 patients reported 7% of 68 patients died of fulminant myocarditis diagnosed based on clinical data and circulatory failure.[85] A case report found myocarditis in a 37-year-old male, who had cardiomegaly, ST-elevation on ECG, elevated troponin T, CK-MB, and BNP, as well as systolic dysfunction on echocardiogram.[78] One case of pericardial effusion in COVID-19 was found on computed tomography (CT).[76] Two cases of myocarditis, pericarditis, and pericardial effusion were also reported in HCoV-OC43 and HCoV-NL63 infection.[27,42]

On echocardiogram, cardiac dysfunction caused by SARS was uncommon. One study which compared acute versus 30-day echocardiogram found subclinical diastolic dysfunction acutely which resolved, but no change in systolic function.[25] Lower left ventricular ejection fraction (LVEF) and impaired myocardial performance was, however, associated with more severe disease represented by mechanical ventilation. A few cases reported mild global dyskinesia with mild LVEF decrease which resolved on follow-up.[37] Cardiomegaly was also observed in 10% of cases in one retrospective cohort study, which was transient and not associated with heart failure.[37] Two retrospective cohort studies also reported deaths from myocardial infarction.[23,71] One patient with MERS had non-ST-elevation myocardial infarction but no acute vessel closure on coronary angiogram. He was diagnosed with MERS-CoV vasculopathy, and eventually succumbed to a subsequent ischemic brainstem stroke.[90] A retrospective cohort study of 112 COVID-19 patients observed that three patients died of acute myocardial infarction (17.7% of deaths), and two (11.8%) died of heart failure.[83] Angiotensin receptor blocker (ARB) or angiotensin-converting enzyme inhibitor (ACEi) use was similar between survivors and non-survivors. Cases of antiphospholipid syndrome, procoagulant changes, and myocardial calcification were also reported in association with coronavirus infections.[40,55]

Two studies investigated the long-term consequences of SARS, more than 10 years after recovery.[56,60] They found that patients had residual cardiopulmonary functional abnormalities, such as right heart failure. They also tended to have hyperlipidemia with increased triglycerides and very-low-density lipoprotein (VLDL) cholesterol, and abnormal glucose metabolism. This may be caused by the high-dose corticosteroids used to treat SARS, causing long-term metabolic side effects.[91]

Effects of cardiac comorbidities on susceptibility and prognosis of infection

Among 61 included studies on 57,798 subjects that reported cardiovascular comorbidities and outcomes, three were systematic reviews and meta-analyses, 35 were cohort studies (six were prospective and 28 were retrospective), three case-control studies, 17 case series, two case reports and one genetic network-based analysis (Supplementary Material Table 4).[1,23,48,49,52,57,60,63,71–73,75,79–83,85,87,89,92–132] In general, these studies were of fair to good quality.

In SARS, the overall prevalence of diabetes mellitus was 3–24%, chronic heart disease was 3–10%, chronic renal disease was 2–6%, and hypertension was 19%.[1,60,63,92] Patients with MERS had higher rates of comorbidities, reporting rates of up to 68% diabetes mellitus, 59% with hypertension, 28–68% chronic heart disease, and 49% chronic renal disease.[92] This may in part account for the lower death rate of 10% in SARS[1,133] compared with 35% in MERS.[92,99,107,134]

Regarding cardiovascular comorbidities, 25 studies found an association with poorer outcomes,[1,49,60,71,93,94,99,101,102,104–107,109,115] while seven did not.[52,63,100,108] Cardiovascular disease and diabetes mellitus were reported to be higher in MERS than H1N1 influenza in a systematic review of 38 studies.[102] In MERS, mortality had been associated with increasing number of co-morbidities,[49,99,101,106] diabetes mellitus,[101,104,106,107] ischemic heart disease,[101,107] heart failure,[106,107] hypertension.[44,106] Similarly, studies on SARS found that comorbidities such as diabetes mellitus[1,60,71] and heart disease[1,71] were associated with poor outcomes defined as mechanical ventilation, ICU admission or death.

Cardiovascular comorbidity is associated with poorer outcomes in COVID-19 in 11 studies (49,059 patients; one study had 44,672)[72,75,80,83,85,87,89,117,119,125,126] but not in three studies (185 patients).[73,79,124] Among 17 studies reporting prevalence figures, hypertension was seen in 9–31% of patients, diabetes in 4–14%, and coronary artery disease (CAD) in 2–40%. In those with severe, critical disease or death, 15–58% had hypertension, 11–42% had diabetes, and 9–25% had CAD. A meta-analysis of six studies found a risk ratio for ICU admission of 2.03 for hypertension, 3.30 for cardio-cerebrovascular disease, 2.21 for diabetes.[75] The case fatality rate (CFR) calculated from 44,672 confirmed cases from China found an elevated rate of 10.5% for cardiovascular disease, 7.3% for diabetes, and 6.0% for hypertension, higher than the 2.3% overall.[126]

Five cohort studies in other coronavirus infections found that children with heart disease and cardiovascular comorbidities were associated with higher risk of acquiring HCoV infections,[93,94] respiratory support requirement and pediatric ICU admission.[105] In a cohort of community patients with congestive heart failure (CHF) or chronic obstructive pulmonary disease (COPD), nine (7%) patients were found to be

infected with coronavirus, and the incidence of infection was significantly higher in CHF than COPD.[127] In those with acute decompensated CHF, 13% of patients had respiratory viral infection, 12% of whom had human coronavirus infection.[128] These patients did not have more severe disease or any specific clinical manifestation. Coronavirus infection may be present but not common in patients with CHF, but the consequence of such infection is uncertain. It has been suggested that coronavirus infections may cause acute decompensation of heart failure but needs to be tested in larger prospective studies.

Missed diagnosis associated with cardiovascular co-morbidities

The literature search found nine case reports and case series on 14 patients that reported difficulty in diagnosing and management of patients with coronavirus infection and significant cardiovascular co-morbidities[68,135–142] (Supplementary Material Table 5). The quality of studies was poor due to studies having a high risk of selection bias, low representativeness, and lack of control population.

Infection with severe coronaviruses SARS-CoV or MERS-CoV was initially misdiagnosed in six studies.[68,135,136,138,139,141] In patients with a background of CHF or ischemic heart disease, four articles reported misdiagnosis of SARS or MERS as CHF, where pulmonary edema confounded radiological changes of a respiratory infection.[135,136,138,141] Patients with comorbidities also presented atypically, with no fever or no chest signs, therefore delaying appropriate tests and infection control measures causing nosocomial transmission in the hospital.

Conversely, suspicion of coronavirus infection may in fact negatively impact diagnosis and treatment of other illnesses. In France, a patient with risk factors of infective endocarditis and travel history to the Middle East resulted in a delay of 12 h in diagnosis of infective endocarditis.[137] Due to infectious hazards in sending blood cultures prior to exclusion of MERS, the patient had delayed antibiotic treatment and died. A pregnant patient was diagnosed with coronaviral infection based on positive respiratory polymerase chain reaction (PCR) and was initially managed supportively with no antibiotics.[140] However, she deteriorated and cultures on the fifth day grew *Haemophilus parainfluenzae*, and mitral valve vegetations were found on transesophageal echocardiography. A third case with CAD and diabetes was initially diagnosed as severe pneumonia due to MERS and heart failure, but cultures grew *Candida* and he died due to lack of treatment. Therefore, in an outbreak of serious coronavirus infection, misdiagnosis can occur in both directions with severe consequences.

Discussion

The new COVID-19 caused by SARS-CoV-2 resembles other betacoronavirus infections such as SARS and MERS in many aspects, and their characteristics are compared in Table 1. Severe coronavirus infections such as SARS often demonstrate multi-organ involvement as observed from the autopsy studies, which has implications on the clinical manifestation, transmission, and prognosis of the disease. Infection triggers a systemic inflammatory response that may affect the heart, and observation of viral particles in the heart suggests possible viral spread. Both SARS-CoV and SARS-CoV-2 interact with host cells via the angiotensin-converting enzyme 2 (ACE2) receptor, and 6.5% of myocardial cells are found to express this.[143] Animal studies and studies on diabetes and hypertension found that ACE2 levels are increased in those treated with ACEi/ARB.[144] It has been proposed that this upregulation of ACE2 facilitates SARS-CoV-2 entry into target cells. On the other hand, upregulation of soluble ACE2 reduce binding of SARS-CoV-2 to membranous ACE2 and reduce angiotensin II activity, thus protect against vasoconstriction and inflammatory oxidative damage.[145,146] Current European and American guidelines recommend continuation of ACEi/ARB therapy in COVID-19 patients due to lack of strong evidence for benefit or harm.[147,148] Limited evidence from one study showed no differences in adverse outcomes with use of these medications,[83] and ongoing randomized controlled trials on losartan (NCT04311177) may further reveal the interaction of ACE2 and SARS-CoV-2 infection. Only a proportion of patients who died from coronavirus infections demonstrated positive viral detection in heart tissues by PCR in SARS but none have been observed in COVID-19 so far, further questioning the function of ACE2 expressed in the heart during SARS-CoV-2 infection.

The cardiovascular manifestations of coronavirus infection are varied. Early identification of cardiac involvement requires investigation of cardiac symptoms such as chest pain, shortness of breath, and palpitations by ECG and cardiac markers. COVID-19 may lead to cardiac damage and arrhythmias in some patients, although information on the specific arrhythmias is limited and further characterization is needed. Patients with more severe disease have higher CK-MB and troponin I, therefore testing of cardiac markers may be useful in risk stratification clinically. Furthermore, reports of death due to myocardial infarction suggests as possible association with SARS,

Table 1. Comparison of severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and coronavirus disease 2019 (COVID-19).

	SARS	MERS	COVID-19 (until 24 March 2020)
Viral pathogen and receptor	SARS-CoV, ACE2 receptor	MERS-CoV, DPP4 receptor	SARS-CoV-2, ACE2 receptor
Case numbers	8096[a]	2494[b]	372,757[c]
Median age	41.3	52.8	47[d]
Mortality rate (%)	9.6	34.4	4.4
Viral isolation from heart	Positive in some patients	Not seen	Not seen
Cardiovascular comorbidities			
Hypertension (%)	19	59	9–31
Diabetes mellitus (%)	3–24	68	4–14
CAD (%)	3–10	28–68	2–40
Cardiac manifestation	Tachycardia, bradycardia, cardiac injury, heart failure	Tachycardia, bradycardia, myocarditis	Cardiac injury, arrhythmia, myocarditis, heart failure

ACE2: angiotensin-converting enzyme 2; CAD: coronary artery disease; DPP4: dipeptidyl peptidase-4.
[a]World Health Organisation (WHO). Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003 (2020). Available from: https://www.who.int/csr/sars/country/table2004_04_21/en/.
[b]WHO. Middle East respiratory syndrome coronavirus (MERS-CoV) (2020). Available from: https://www.who.int/emergencies/mers-cov/en/.
[c]WHO. Coronavirus disease 2019 (COVID-19)
Situation Report – 64 (2020). Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200324-sitrep-64-covid-19.pdf?sfvrsn=703b2c40_2.
[d]Guan W-J, Ni Z-Y, Hu Y, et al.[125]

MERS, and COVID-19 infection. The systemic inflammatory environment may lead to pro-coagulant changes and increase risk of plaque rupture, as observed in influenza.[149] Prevention of infection in vulnerable populations, for example by vaccines currently in development (NCT04299724, NCT04313127), may prevent severe cardiovascular consequences. Myocarditis in COVID-19 is rare, but may account for raised troponin and new cardiac arrhythmias in some patients. Given the likely cardiac involvement of COVID-19, targeted studies on cardiovascular outcomes are needed to further characterize and investigate the diagnosis, prognosis, and management of cardiovascular manifestations.

Cardiovascular comorbidity was shown to be associated with more severe coronavirus disease such as mechanical ventilation, ICU admission and mortality in SARS, MERS, and COVID-19. Therefore, it is important to closely monitor patients with underlying cardiovascular diseases identified on comprehensive past medical history taking. Infection with coronavirus may also increase severity of underlying cardiac conditions such as CHF and ischemic heart disease. Patients with severe disease are also older, which may confound results but hypertension, diabetes and CAD remain associated with mortality on multivariate analysis in one study with 475 patients.[119] Prevention and effective control of chronic cardiovascular disease may play an important role in improving the outcome of coronavirus infections in the population.

Cardiovascular diseases can present similarly to acute respiratory infections with coronaviruses. In patients presenting with heart failure symptoms, a high index of suspicion is needed to initiate appropriate testing and infection control measures. While coronavirus remains a diagnostic possibility, clinicians should be cognizant that there is still a need to evaluate other time-critical life-threatening conditions such as infective endocarditis. Appropriate treatment should still be instituted while awaiting test results for COVID-19. When managing acute coronary events in COVID-19 patients, guidance from the American College of Cardiology states that balance between staff exposure and patient benefit must be made, with the use of personal protective equipment and avoidance of positive-pressure catheterization laboratories.[150]

Limitations of this systematic review include the poor quality of many studies included on the Newcastle/Ottawa Scale due to them being case reports and case series with high risk of bias. The population sizes in these studies were also small, therefore the incidence and prevalence of various characteristics and outcomes were difficult to estimate, with some reporting contrasting findings. On the other hand, this review included studies published in a language other than English, particularly searching for studies on Chinese databases. This is especially relevant to performing a comprehensive search of literature on SARS and COVID-19, with a substantial number of cases in China.

In conclusion, cardiac manifestations can occur in coronavirus infections, and patients with cardiovascular comorbidities have poorer outcomes when infected. Although managing patients during a major outbreak

is a challenging task, ongoing research sheds light on strategies to combat the coronavirus, including promising trials of anti-viral medications and vaccine development.

Author contribution

JSYH, PAT, AFWH, MYYC, and CHS contributed to the conception or design of the work. JSYH and CHS contributed to the acquisition, analysis, or interpretation of data for the work. JSYH, PAT, and CHS drafted the manuscript. JSYH, PAT, AFWH, MYYC, and CHS critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of conflicting interests

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