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Review Article

Neurological implications of cardiac compromise in COVID-19

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Abstract: Objectives: There is increasing evidence that particularly in patients with severe SARS-CoV-2 infection (COVID-19) the heart can be primarily or secondarily compromised. Neurological disease as a complication of SARS-CoV-2 associated cardiac disease is conceivable. This review aims at summarising and discussing previous and recent advances in the clinical presentation, pathophysiology, diagnosis, treatment, and outcome of cardiac complications and its implications on the brain of SARS-CoV-2 infected patients. Method: Literature review using appropriate search terms and applying inclusion and exclusion criteria. Results: Cardiac complications in SARS-CoV-2 infected patients not only include myocardial injury, myocarditis, Takotsubo cardiomyopathy (TTS), coagulation abnormalities, heart failure, cardiac arrest, arrhythmias, acute myocardial infarction, or cardiogenic shock, but a number of other more rarely occurring cardiac abnormalities. Additionally considered should be endocarditis due to superinfection, viral or bacterial pericarditis, aortic dissection, pulmonary embolism from the right atrium, ventricle or outflow tract, and cardiac autonomic denervation. Cardiac damage due to side effects from the anti-COVID medication should not be neglected. Several of these conditions may be complicated by ischemic stroke, intracerebral bleeding, or dissection of cerebral arteries. Conclusion: The heart can be definitively affected in severe SARS-CoV-2 infection. Heart disease in COVID-19 may be complicated by stroke, intracerebral bleeding, or dissection of cerebral arteries. Treatment of SARS-CoV-2 associated cardiac disease is not at variance from that of cardiac disease without this infection.

Keywords: SARS-CoV-2, COVID-19, myocardium, cardiac, myocarditis, endocarditis

Introduction

Since the outbreak of the SARS-CoV-2 pandemic evidence accumulates that not only the broncho-pulmonary system is affected (COVID-19) but that COVID-19 can become a multisystem disease, predominantly affecting the central and peripheral nervous system (CNS, PNS), the eyes, the intestines, the kidneys, and the heart [1]. Cardiac involvement in COVID-19 is increasingly recognised and has a strong impact on the outcome of COVID-19 patients. COVID-19 patients with concomitant cardiac disease have a worse prognosis than COVID-19 patients without cardiac involvement. Management of patients with severe COVID-19 not only requires infectiologists, pulmologists, cardiologists, and intensive care doctors but all specialists, including neurologists [2]. So far, neurological complications of cardiac involvement in COVID-19 have not been systematically investigated. This review aims for the first time at summarising and discussing previous and recent advances concerning the clinical presentation, pathophysiology, diagnosis, treatment, and outcome of cardiac complications and its implications on the brain of SARS-CoV-2 infected patients.

Methods

A literature review in PubMed using the search terms "cardiac", "cardiologic", "myocardium", "pericardium", "endocardium", "coronary arteries", "myocarditis", "ischemic heart disease", "endocarditis", "pericarditis", "Takotsubo", "arrhythmias", "heart failure", "systolic dysfunction", "cardiomyopathy", "aortic dissection", and "ischemic stroke", "intracerebral bleeding", and "epilepsy" together with "SARS-CoV-2", "COVID-19", and "coronavirus" was conducted. Additionally, reference lists were checked for

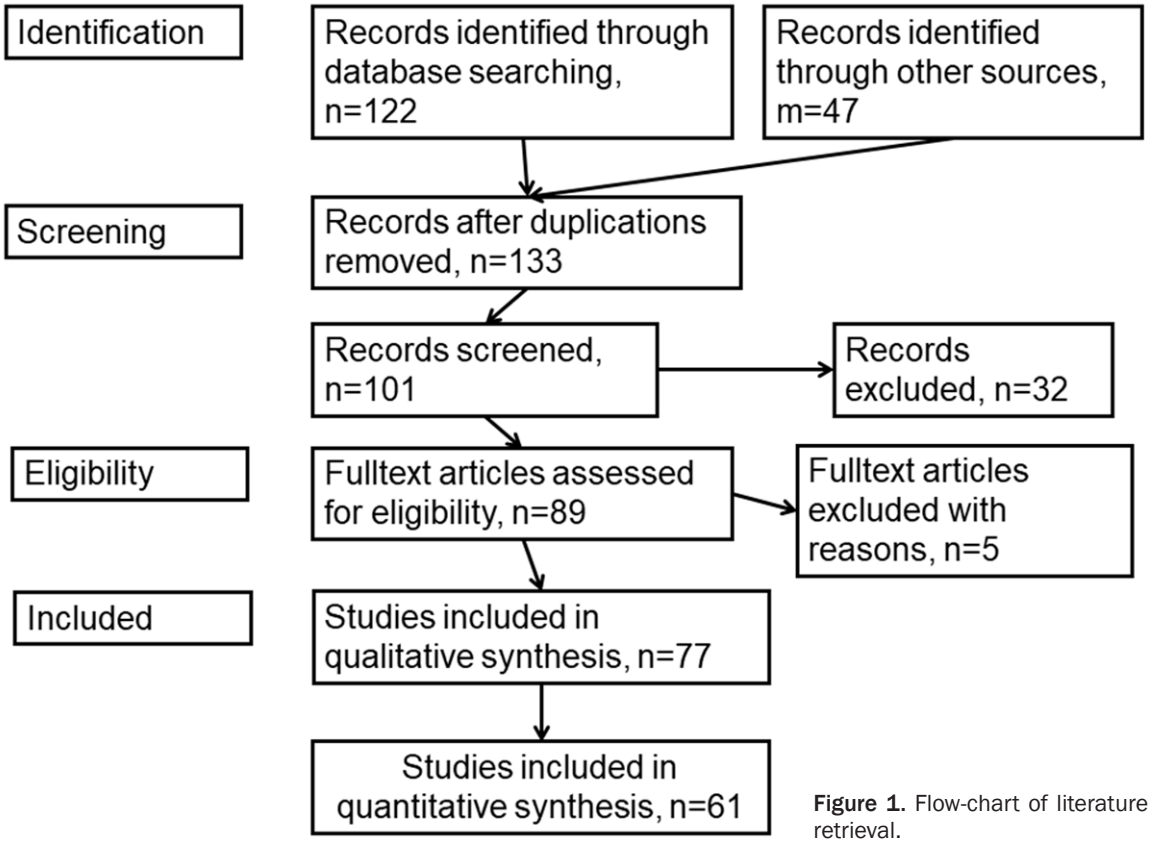

Figure 1. Flow-chart of literature retrieval.

further articles meeting the search criteria. Included were all articles reporting COVID-19 patients with cardiac involvement with secondary neurological compromise. Excluded were articles not meeting the search criteria and written in languages other than English, French, Spanish, Italian, or German.

Results

The process of literature search is outlined in **Figure 1**. There are several cardiac conditions associated with SARS-CoV-2. Some of them have been more frequently described than others. These conditions can be classified according to pathophysiological aspects and are discussed below according to their frequency of occurrence.

Pathophysiology of SARS-CoV-2 associated cardiac injury

The pathophysiology underlying cardiac involvement in COVID-19 is broad. Direct injury by the virus may lead to myocarditis, pericarditis, or vasculitis [3]. Hypoxia due to COVID-19 pneumonia may be complicated by myocardial infarction. Down-regulation of ACE_2-receptors results in elevation of angiotensin-II and thus plaque rupture. Since angiotensin-II induces apoptosis of macrophages, formation of vulnerable plaques may ensue [4]. Thus, SARS-CoV-2 associated myocardial infarction may not only result from global hypoxia or vasculitis, but also from plaque rupture. Thrombus formation due to hypercoagulability and embolism to the coronary arteries may be another mechanism of SARS-CoV-2 associated myocardial infarction. The immune reaction towards the virus (cytokine storm) may result in extensive increase of pro-inflammatory cytokines. Thus, heart failure may not only result from vasculitis or myocardial infarction but also from the immune reaction. The viral infection may lead to stress, which may trigger Takotsubo syndrome (TTS) or arrhythmias. Arrhythmias may also result from vasculitis, myocarditis, endocarditis, TTS, or heart failure [3].

Myocardial injury/infarction and coronary heart disease

Since endothelial cells abundantly express ACE_2 receptors and since SARS-CoV-2 attaches

Table 1. Cardiac diseases associated with SARS-CoV-2

	Cardiac disease	Neurologic compromise	Reference
Myocardium	MCI	ischemic stroke	[54]
	Myocarditis	embolic stroke	[55]
	TTS	embolic stroke	[56]
Conduction system	Arrhythmias	embolic stroke	[57]
Coagulation system	Coagulopathy	embolic stroke	[58]
Endocardium	Endocarditis	embolic stroke	[59]
Pericardium	Pericarditis	ischemic stroke	[60]
Aorta	Aortic dissection	ischemic stroke	[61]

AB: antibiotics, AC: anticoagulation, MCI: myocardial infarction, PE: pulmonary embolism, Takotsubo syndrome.

to ACE_2 receptors for cell invasion, it is conceivable that endothelial cells are predominantly damaged by SARS-CoV-2. Such damage may result in endothelitis, plaque formation, thrombus formation, or abnormal reaction of the vascular smooth muscle cells (VSMCs). Other mechanism of SARS-CoV-2 associated myocardial infarction include plaque rupture due angiotensin-II elevation, down-regulation of ACE_2-receptors, global hypoxia due to COVID-19 pneumonia, or cardio-embolism from intracardiac thrombus formation. Acute coronary thrombosis has been recently reported in a 53 yo male with COVID-19 who presented with myocardial infarction, ventricular fibrillation, cardiac arrest, and profound hypokaliemia, successfully undergoing percutaneous coronary stenting [5]. Non-ST-segment elevation myocardial infarction (NSTEMI) in another 53 yo COVID-19 patient was attributed to systemic inflammatory syndrome and occurred during mechanical ventilation for SARS-CoV-2 pneumonia [6]. Multisite arterial thrombosis, including the right coronary artery, has been reported in an 83 yo female with COVID-19 [7]. Acute coronary artery thrombosis may remain asymptomatic in some COVID-19 patients [8]. Even myocardial infarction without occlusion of a coronary artery has been reported in COVID-19 patients [9]. Several other patients with SARS-CoV-2 associated NSTEMI or STEMI have been published. Since myocardial infarction can be complicated by arrhythmias and heart failure, these patients carry an increased risk of developing cardio-embolism and cerebral ischemia (**Table 1**). There are even reports about an increase in the frequency of simultaneous myocardial infarction and ischemic stroke in COVID-19 patients [10].

There are several original studies and review articles using the term "myocardial injury". This term refers to conditions in COVID-19 patients which go along with elevation of myocardial biomarkers (e.g. creatine-kinase, MB fraction, troponin, proBNP) but without evidence for coronary heart disease or myocardial infarction on ECG, echocardiography, or coronary angiography. Myocardial injury of unknown etiology has been first reported in 5/41 COVID-19 patients originating from Wuhan [3]. Myocardial injury is reported to occur in 7-20% of patients with COVID-19 [11, 12]. Mortality of COVID-19 patients with myocardial injury is significantly increased compared to COVID-19 patients without myocardial injury [12]. There are also indications that patients having received a coronary stent prior to the pandemic carry an increased risk of experiencing stent thrombosis when infected with SARS-CoV-2 [13]. Myocardial injury may additionally result from global hypoxia, spasms of coronary arteries, myocarditis, vasculitis, or stress.

Myocarditis

A number of reports indicate that SARS-CoV-2 can trigger myocarditis, resulting in acute myocardial injury in patients with severe COVID-19 [14]. Myocarditis may go along with normal (case-2 [14]) or reduced systolic function (case-1 [14]). Patho-physiologically, myocarditis may be due to infection with the virus [15] or secondary due to the immunologic reaction against the virus [14]. SARS-CoV-2 associated myocarditis can be associated with intra-ventricular thrombus formation [16]. Under heparin such a thrombus may completely resolve within weeks [16] but thrombus formation may also precipitate embolism. SARS-CoV-2 associated myocarditis has been reported in association with pericarditis [15]. Pericarditis may be the prominent feature of myo-pericarditis and may be complicated by tamponade [15]. In one of these cases, pericardial effusion was positive for SARS-CoV-2 RNA [15]. In a post-mortem endomyocardial biopsy of a patient with myocarditis, interstitial, mononuclear inflammatory infiltrates have been found [17]. In another patient undergoing endo-myocardial biopsy intra vitam diffuse infiltration with T-lymphocytes (CD3+ >/

mm^2) together with interstitial edema has been observed [18]. The SARS-CoV-2 genome was not detected in the myocardium in this patient [18]. Cardiac MRI with contrast medium may show gadolinium enhancement. In a 35 yo female with systemic sclerosis biventricular mechanical circulatory support by utilisation of biventricular impella support during two weeks after onset of systolic dysfunction caused by COVID-19 myocarditis led to complete recovery of the hemodynamic compromise [19]. Myocarditis complicated by systolic dysfunction, arrhythmias, endocarditis, or pericarditis with tamponade and hemodynamic compromise, can be complicated by thrombus formation and the risk of ischemic stroke (**Table 1**).

Takotsubo cardiomyopathy (TTS)

TTS is defined as transient and reversible hypokinesia/dyskinesia/akinesia of the left ventricular myocardium triggered by stress and leading to systolic dysfunction. In one third of the cases each, TTS is triggered by emotional or physical stress. In the remaining third the trigger of TTS remains elusive. Stress causes release of catecholamines and thus overstimulation of adrenergic myocardial receptors. In a recent review of 38 patients with SARS-CoV-2 associated TTS covering appropriate articles published as per the end of September 2020, TTS developed after onset of the viral infection in 17 patients and during the infection in two patients [20]. Fifteen patients developed the classical type, two the mid-ventricular type of TTS, and two patients the basal type. Treatment for TTS was quite variable but most patients received beta-blockers, diuretics, heparin, or acetyl-salicylic acid [20]. One patient each required oral anticoagulation and pericardio-centesis because of immune-mediated pericarditis. Thirteen patients recovered completely, one patient improved, and four died [20]. Since this review several other cases with SARS-CoV-2 associated TTS have been reported. Recent considerations implicate that sepsis, hypoxemia, coronary artery disease, and myocarditis may be also implicated in the pathophysiology of SARS-CoV-2 associated TTS [21]. In a recent review of 27 patients with SARS-CoV-2 associated TTS, mean age was 57 y, the interval between onset of TTS and diagnosis was 6.5 d, the median left ventricular ejection fraction was 36%, troponin was elevated in 26 patients, 54.5% developed cardiac complications such as acute heart failure, atrial fibrillation, supraventricular tachycardia, or cardiogenic shock, three patients required extra-corporal membrane oxygenation (ECMO), and 15% of the patients died [22]. COVID-19 patients who developed TTS had a higher mortality rate particularly if they developed cardiogenic shock [22]. As TTS can be complicated by heart failure, arrhythmias, thrombus formation, or shock, cardio-embolism including the brain may ensue (**Table 1**).

Arrhythmias

Arrhythmias are a common cardiac complication of COVID-19 patients. Arrhythmias may remain asymptomatic or may manifest as palpitations, heart racing, precordial pressure, presyncope, syncope, or sudden death. The most common arrhythmia in COVID-19 is sinus tachycardia. More rarely reported were supra-ventricular tachycardia, including atrial fibrillation or flutter, ventricular arrhythmias such as ventricular tachycardia, ventricular fibrillation, Torsades des pointes, or bradycardias [23]. Also interval changes, axis change, ST-segment changes, and T-wave changes have been reported [23]. Arrhythmias may not only originate from stress, but also from global hypoxia, myocardial infarction, vasculitis, myocarditis, endocarditis, TTS, or heart failure. In a study of 138 hospitalised COVID-19 patients from Wuhan, arrhythmias were reported in 23 patients [24]. In a study of 108 COVID-19 patients, 18% had QTc prolongation, 17% had sinus tachycardia, 5% AV-block-I, 1.8% ventricular tachycardia or ventricular fibrillation, and 0.9% sinus bradycardia [25]. Cardiac injury was found in 26% of these patients, acute coronary syndrome in 2.7%, and probable myocarditis in 2.8% [25]. In a study of 38 COVID-19 patients, one third had ST- and T-wave changes, and 19% had sinus tachycardia [26]. Single patients have been reported with sinus node dysfunction [27]. Arrhythmias manifesting clinically as palpitations may be even the initial manifestation of COVID-19 [28]. A shortcoming of several studies reporting arrhythmias is that the type of arrhythmias was not specified. Particularly atrial fibrillation may be complicated by embolic stroke (**Table 1**).

Coagulopathy

Coagulopathy in COVID-19 more frequently manifests as hyper-coagulability than as hypo-

coagulability. Hyper-coagulability can lead to intra-cardiac thrombus formation in the right or left chambers. Thrombus formation within the right atrium, right ventricle, or right outflow tract can lead to consecutive pulmonary embolism, which has been occasionally reported as complication of COVID-19 [29]. Pulmonary emboli may not only originate from the right heart but also from the veins of the legs, abdomen, thorax, or the pulmonary arteries. In case of a patent foramen ovale (PFO), emboli of the right atrium may transmigrate to the left atrium and consecutively to the brain, leading to embolic stroke (**Table 1**). In case of thrombus formation due to hyper-coagulability within the left chambers, cardio-embolism to the brain, coronary arteries, or peripheral arteries may ensue. In a 63 yo male with COVID-19, thrombosis of the distal aorta has been reported [30]. The patient profited from therapeutic low dose heparin over 6 weeks [30]. The prevalence of venous thrombosis increases with the severity of COVID-19 [31]. Abnormal thrombocytes, which also express ACE_2-receptors, may contribute to the propensity of thrombosis in COVID-19 patients.

Endocarditis

Another cardiac complication of COVID-19 is endocarditis. Endocarditis in SARS-CoV-2 infected patients is usually not due to a direct viral attack against the endocardium by the virus but rather due to superinfection with bacterial agents prone to cause endocarditis. There are several reports about bacterial endocarditis due to superinfection following the viral infection [32-34]. Concerning the pathophysiology, there is ample evidence that the viral infection weakens the humoral and cellular immune system consequently leading to superinfections with bacteria, fungi, helminths, or protozoa. In addition to infectious agents, endocarditis in SARS-CoV-2 infected patients can be due to thrombus formation [35]. Endocarditis in SARS-CoV-2 infected patients can be additionally due to immune-suppression by steroids, frequently given in the post-viremic phase of the infection [36]. Whether COVID-19 patients with prosthetic valves are prone to acquire bacterial endocarditis is currently unsolved but given the fact that only few cases have been reported [37], it is quite likely that this subgroup does not carry an increased risk of acquiring bacterial endocarditis during a SARS-CoV-2 infection. Infectious endocarditis in COVID-19 can be complicated by septic embolism [32]. Neurological complications of endocarditis include thrombus formation and thus cardio-embolic stroke (**Table 1**).

Pericarditis

Another potential cardiac complication of COVID-19 is pericarditis. Pericarditis has been repeatedly reported in SARS-CoV-2 infected patients [38]. Pericarditis may occur in the absence of concomitant myocarditis, usually classified as viral pericarditis, and may resolve spontaneously or upon application of the standard anti-COVID-19 treatment [38]. In some patients viral pericarditis may favourably respond to acetyl-salicylic acid and colchicine [39]. SARS-CoV-2 associated pericarditis may go along with normal systolic function [39] or with systolic dysfunction in case of constrictive pericarditis [40]. Pericarditis may be accompanied by myocarditis or may occur without myocardial involvement [41]. Unfortunately, only few patients with SARS-CoV-2 associated pericarditis underwent pericardial puncture and investigation of the effusion for SARS-CoV-2 [15] why confirmation of viral pericarditis, suspected upon the clinical presentation, usually remains unconfirmed. Myocarditis may present with severe left ventricular systolic dysfunction and cardiogenic shock requiring inotropes and mechanical circulatory support. Treatment of pericarditis with non-steroidal anti-inflammatory drugs, colchicine, and corticosteroids has been proven to be safe in COVID-19 patients [14]. Pericarditis may be associated with stroke only if complicated by heart failure or atrial fibrillation (**Table 1**).

Aortic dissection

Another cardiac abnormality rarely reported so far as a complication of COVID-19 is aortic dissection. Aortic dissection has been reported in a patient with William's syndrome (idiopathic hypercalcemia) who got infected and died from the dissection despite acute surgery [42]. In another COVID-19 patient aortic dissection occurred without knowing that the patient was already infected [43]. Aortic dissection can affect the extra- and intra-cerebral arteries and can thus be complicated by occlusion of cerebral arteries and consecutively ischemic stroke.

Aortic dissection has been also found on autopsy in 2 other COVID-19 patients [44].

Autonomic denervation

COVID-19 can be complicated by immune neuropathy, particularly Guillain Barre syndrome (GBS) and its subtypes. GBSs may include affection of the autonomic fibers supplying the heart and may lead to cardiac autonomic denervation. Autonomic neuropathy may be also due to affection of the vagal nerve in the course of isolated cranial neuropathy or due to toxic neuropathy. Autonomic cardiac denervation has been implicated in the development of heart failure, arrhythmias, or TTS [45]. Autonomic neuropathy may not only be associated with PNS disease but also with CNS disease if heart failure, arrhythmias, or TTS are complicated by cardioembolism.

Others

Further cardiac complications of COVID-19 reported in single patients include arterial hypertension [26], increased diameter of the ascending aorta [26], left atrial enlargement [26], isolated diastolic dysfunction [46], arterial hypotension [47], SARS-CoV-2 induced secondary anti-phospholipid syndrome [48], coronary vasospasms [49], pulmonary hypertension [50], heart failure [51], cardiogenic shock [52], or aortitis [53].

Discussion and conclusions

This review shows that SARS-CoV-2 also primarily or secondarily affects the heart, that SARS-CoV-2 associated cardiac disease is broader than usually anticipated, that COVID-19 patients with cardiac involvement have a worse outcome than COVID-19 patients without cardiac disease, that the risk of cardiac involvement in COVID-19 could be reduced by reducing classical cardio-vascular risk factors, and that multiple mechanisms, such as direct injury by the virus, downregulation of ACE_2-receptors, global hypoxia, the immune response to the virus, or psychological injury are responsible for cardiac damage by the virus. Cardiac involvement in COVID-19 predominantly occurs in patients with severe COVID-19, why these patients should be particularly monitored for cardiac functions and compromise. Additionally, cardiac damage from side effects of anti-COVID-19 drugs should be considered in patients with severe COVID-19 and in case of cardiac damage without an obvious explanation. In COVID-19 patients with newly developing cardiac disease, SARS-CoV-2 should be considered as the cause of cardiac compromise and appropriate cardiologic work-up should be initiated.

Due to the strong heart-brain relationship, secondary affection of the brain should be considered particularly in patients with severe COVID-19. Since acute cerebral compromise in intubated, relaxed, and sedated patients can be easily missed, neurological complications often become evident not before extubation and discontinuation of mechanical ventilation. Since it is not justifiable to monitor all intubated COVID-19 patients by electroencephalography, cerebral imaging, and nerve conduction studies, treating physicians must be alert for any tiny neurological alteration and patients with abnormal neurological exam during ventilation or after extubation should immediately undergo neurological work-up.

In conclusion, the spectrum of cardiac disease associated with a SARS-CoV-2 infection is broader than anticipated. Cardiac disease in COVID-19 patients may be due to a direct attack of the virus or secondary due to immunosuppression and the cytokine storm, favouring superinfections, thrombus formation, due to coagulopathy, and due to cardiac toxicity of anti-COVID-19 drugs. Treatment of cardiac disease in COVID-19 is not at variance from cardiac disease in the absence of a SARS-CoV-2 infection. Various cardiac abnormalities may overlap which should be considered in the therapeutic management.

Disclosure of conflict of interest

None.

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References

[1] Mokhtari T, Hassani F, Ghaffari N, Ebrahimi B, Yarahmadi A and Hassanzadeh G. COVID-19

and multiorgan failure: a narrative review on potential mechanisms. J Mol Histol 2020; 51: 613-628.
[2] Spuntarelli V, Luciani M, Bentivegna E, Marini V, Falangone F, Conforti G, Rachele ES and Martelletti P. COVID-19: is it just a lung disease? A case-based review. SN Compr Clin Med 2020; 2: 1401-1406.
[3] Luo J, Zhu X, Jian J, Chen X and Yin K. Cardiovascular disease in patients with COVID-19: evidence from cardiovascular pathology to treatment. Acta Biochim Biophys Sin (Shanghai) 2021; 53: 273-282.
[4] Shu S, Zhang Y, Li W, Wang L, Wu Y, Yuan Z and Zhou J. The role of monocyte chemotactic protein-induced protein 1 (MCPIP1) in angiotensin II-induced macrophage apoptosis and vulnerable plaque formation. Biochem Biophys Res Commun 2019; 515: 378-385.
[5] Lavoie M, Ramirez A and Kunz J. A unique case of COVID-19-related acute coronary thrombosis complicated by severe hypokalemia. Mil Med 2021; 186: e1053-e1057.
[6] Othman F, Abid AR, Alibrahim M, Abdulkarim S, Abdelaty MA, Aboukamar M and Arafah S. Non-ST segment elevation myocardial infarction in a patient with COVID-19. Heart Views 2020; 21: 215-219.
[7] Angelillis M, De Carlo M, Christou A, Marconi M, Mocellin DM, Caravelli P, De Caterina R and Petronio AS. A case report of multisite arterial thrombosis in a patient with coronavirus disease 2019 (COVID-19). Eur Heart J Case Rep 2020; 5: ytaa339.
[8] Bussmann BM, Shabbir A, Warwick A and Orr W. Acute coronary artery thrombosis presenting as asymptomatic ST-elevation myocardial infarction in a patient with COVID-19 pneumonia. BMJ Case Rep 2021; 14: e241856.
[9] Burkert FR, Niederreiter L, Dichtl W, Mayr A, Virgolini I, Klauser A, Weiss G and Bellmann-Weiler R. Case report of a COVID-19-associated myocardial infarction with no obstructive coronary arteries: the mystery of the phantom embolus or local endothelitis. Eur Heart J Case Rep 2021; 5: ytaa521.
[10] Eskandarani R, Sahli S, Sawan S and Alsaeed A. Simultaneous cardio-cerebral infarction in the coronavirus disease pandemic era: a case series. Medicine (Baltimore) 2021; 100: e24496.
[11] Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, Madhur MS, Tomaszewski M, Maffia P, D'Acquisto F, Nicklin SA, Marian AJ, Nosalski R, Murray EC, Guzik B, Berry C, Touyz RM, Kreutz R, Wang DW, Bhella D, Sagliocco O, Crea F, Thomson EC and McInnes IB. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res 2020; 116: 1666-1687.
[12] Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, Huang H, Yang B and Huang C. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020; 5: 802-810.
[13] Elkholy KO, Khizar A, Khan A, Hakobyan N and Sahni S. Subacute stent thrombosis in a patient with COVID-19 despite adherence to antiplatelets. Cureus 2021; 13: e13194.
[14] Shah JZ, Kumar SA and Patel AA. Myocarditis and pericarditis in patients with COVID-19. Heart Views 2020; 21: 209-214.
[15] Sauer F, Dagrenat C, Couppie P, Jochum G and Leddet P. Pericardial effusion in patients with COVID-19: case series. Eur Heart J Case Rep 2020; 4: 1-7.
[16] Cuevas Vilaplana A, Roldán Torres I and Vizuete Del Río J. Myocarditis and in situ thrombosis in the right ventricle in a COVID-19 patient. Hipertens Riesgo Vasc 2021; 38: 148-150.
[17] Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, Tai Y, Bai C, Gao T, Song J, Xia P, Dong J, Zhao J and Wang FS. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020; 8: 420-422.
[18] Sala S, Peretto G, Gramegna M, Palmisano A, Villatore A, Vignale D, De Cobelli F, Tresoldi M, Cappelletti AM, Basso C, Godino C and Esposito A. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. Eur Heart J 2020; 41: 1861-1862.
[19] Ruiz JG, Kandah F, Dhruva P, Ganji M and Goswami R. Case of coronavirus disease 2019 myocarditis managed with biventricular impella support. Cureus 2021; 13: e13197.
[20] Finsterer J and Stöllberger C. SARS-CoV-2 triggered Takotsubo in 38 patients. J Med Virol 2021; 93: 1236-1238.
[21] Szarpak L, Filipiak KJ, Gasecka A, Pruc M, Drozd A and Jaguszewski MJ. Correlation between Takotsubo cardiomyopathy and SARS-CoV-2 infection. Med Hypotheses 2021; 146: 110454.
[22] Sharma K, Desai HD, Patoliya JV, Jadeja DM and Gadhiya D. Takotsubo syndrome a rare entity in COVID-19: a systemic review-focus on biomarkers, imaging, treatment, and outcome. SN Compr Clin Med 2021; 3: 62-72.
[23] Long B, Brady WJ, Bridwell RE, Ramzy M, Montrief T, Singh M and Gottlieb M. Electrocardiographic manifestations of COVID-19. Am J Emerg Med 2021; 41: 96-103.

[24] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X and Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020; 323: 1061-1069.
[25] Kunal S, Sharma SM, Sharma SK, Gautam D, Bhatia H, Mahla H, Sharma S and Bhandari S. Cardiovascular complications and its impact on outcomes in COVID-19. Indian Heart J 2020; 72: 593-598.
[26] Song L, Zhao S, Wang L, Yang K, Xiao W, Clifford SP, Huang J and Chen X. Cardiovascular changes in patients with COVID-19 from Wuhan, China. Front Cardiovasc Med 2020; 7: 150.
[27] Cimino G, Pascariello G, Bernardi N, Calvi E, Arabia G, Salghetti F, Bontempi L, Vizzardi E, Metra M and Curnis A. Sinus node dysfunction in a young patient with COVID-19. JACC Case Rep 2020; 2: 1240-1244.
[28] Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, Xiao W, Wang YN, Zhong MH, Li CH, Li GC and Liu HG. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl) 2020; 133: 1025-1031.
[29] Sulemane S, Baltabaeva A, Barron AJ, Chester R and Rahman-Haley S. Acute pulmonary embolism in conjunction with intramural right ventricular thrombus in a SARS-CoV-2-positive patient. Eur Heart J Cardiovasc Imaging 2020; 21: 1054.
[30] Wickham H, Tam JCH, Chan XHS, George MJ, Levi M and Brown M. Aortic thrombosis in COVID-19. Clin Infect Pract 2021; 9: 100059.
[31] Fujiwara S, Nakajima M, Kaszynski RH, Fukushima K, Tanaka M, Yajima K, Kobayashi T, Sekiya N, Yamamoto Y, Miwa M, Ishihata A, Yamauchi Y, Yamamoto K, Goto H and Imamura A. Prevalence of thromboembolic events and status of prophylactic anticoagulant therapy in hospitalized patients with COVID-19 in Japan. J Infect Chemother 2021; 27: 869-875.
[32] Dias CN, Brasil Gadelha Farias LA and Moreira Barreto Cavalcante FJ. Septic embolism in a patient with infective endocarditis and COVID-19. Am J Trop Med Hyg 2020; 103: 2160-2161.
[33] Toth E, Dancy L, Amin-Youssef G, Papachristidis A and Dworakowski R. Collateral implications of the COVID-19 pandemic: belated presentation of infective endocarditis in a young patient. Eur Heart J 2020; 41: 4365.
[34] Amir M, Djaharuddin I, Sudharsono A and Ramadany S. COVID-19 concomitant with infective endocarditis: a case report and review of management. Int J Infect Dis 2020; 98: 109-112.
[35] Balata D, Mellergård J, Ekqvist D, Baranowski J, Garcia IA, Volosyraki M and Broqvist M. Nonbacterial thrombotic endocarditis: a presentation of COVID-19. Eur J Case Rep Intern Med 2020; 7: 001811.
[36] Regazzoni V, Loffi M, Garini A and Danzi GB. Glucocorticoid-induced bacterial endocarditis in COVID-19 pneumonia - something to be concerned about? Circ J 2020; 84: 1887.
[37] Hussain A, Roberts N and Oo A. Prosthetic aortic valve endocarditis complicated by COVID-19 and hemorrhage. J Card Surg 2020; 35: 1348-1350.
[38] Patel VD, Patel KH, Lakhani DA, Desai R, Mehta D, Mody P and Pruthi S. Acute pericarditis in a patient with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection: a case report and review of the literature on SARS-CoV-2 cardiological manifestations. AME Case Rep 2021; 5: 6.
[39] Thrupthi K, Ganti A, Acherjee T, Mehmood MA and Vakde T. A rare case of acute pericarditis due to SARS-CoV-2 managed with aspirin and colchicine. Cureus 2021; 13: e12534.
[40] SeyedAlinaghi S, Ghadimi M, Gharabaghi MA and Ghiasvand F. Constrictive pericarditis associated with coronavirus disease 2019 (COVID-19): a case report. Infect Disord Drug Targets 2021; 21: e160921188928.
[41] Chikhireva LN, Chikhirev OA, Pikin DA, Bychkova OP, Cherkashov AM and Belenkov YN. Myopericaditis as a late manifestation of the probable COVID-19. Kardiologiia 2020; 60: 27-32.
[42] Mamishi S, Navaeian A and Shabanian R. Acute aortic dissection in a patient with Williams syndrome infected by COVID-19. Cardiol Young 2021; 31: 132-134.
[43] Fukuhara S, Rosati CM and El-Dalati S. Acute type A aortic dissection during the COVID-19 outbreak. Ann Thorac Surg 2020; 110: e405-e407.
[44] Hanley B, Naresh KN, Roufosse C, Nicholson AG, Weir J, Cooke GS, Thursz M, Manousou P, Corbett R, Goldin R, Al-Sarraj S, Abdolrasouli A, Swann OC, Baillon L, Penn R, Barclay WS, Viola P and Osborn M. Histopathological findings and viral tropism in UK patients with severe fatal COVID-19: a post-mortem study. Lancet Microbe 2020; 1: e245-e253.
[45] Acanfora D, Casucci G, Ciccone MM, Scicchitano P, Lonobile T, Chiariello L, Maestri R, Pedone C, Provitera V, Nolano M and Antonelli Incalzi R. Pathological evidence of adrenergic cardiac denervation in a patient with congestive heart failure. Cardiovasc Pathol 2018; 36: 20-21.
[46] Standl E and Schnell O. Heart failure outcomes and Covid-19. Diabetes Res Clin Pract 2021; 175: 108794.

[47] Chen Q, Xu L, Dai Y, Ling Y, Mao J, Qian J, Zhu W, Di W and Ge J. Cardiovascular manifestations in severe and critical patients with COVID-19. Clin Cardiol 2020; 43: 796-802.
[48] Bamgboje A, Hong J, Mushiyev S and Pekler G. A 61-year-old man with SARS-CoV-2 infection and venous thrombosis presenting with painful swelling and gangrene of the lower limb consistent with phlegmasia cerulea dolens. Am J Case Rep 2020; 21: e928342.
[49] Rivero F, Antuña P, Cuesta J and Alfonso F. Severe coronary spasm in a COVID-19 patient. Catheter Cardiovasc Interv 2021; 97: E670-E672.
[50] Khaund Borkotoky R, Banerjee Barua P, Paul SP and Heaton PA. COVID-19-related potential multisystem inflammatory syndrome in childhood in a neonate presenting as persistent pulmonary hypertension of the newborn. Pediatr Infect Dis J 2021; 40: e162-e164.
[51] Umbrajkar S, Stankowski RV, Rezkalla S and Kloner RA. Cardiovascular health and disease in the context of COVID-19. Cardiol Res 2021; 12: 67-79.
[52] Kurz DJ and Eberli FR. Cardiovascular aspects of COVID-19. Swiss Med Wkly 2020; 150: w20417.
[53] Dhakal P, Khadka S, Clowes JA and Chakinala RC. Aortitis in COVID-19. IDCases 2021; 24: e01063.
[54] Qureshi AI, Baskett WI, Huang W, Shyu D, Myers D, Raju M, Lobanova I, Suri MFK, Naqvi SH, French BR, Siddiq F, Gomez CR and Shyu CR. Acute ischemic stroke and COVID-19: an analysis of 27,676 patients. Stroke 2021; 52: 905-912.
[55] Ford JS, Holmes JF and Jones RF. Cardioembolic stroke in a patient with coronavirus disease of 2019 (COVID-19) myocarditis: a case report. Clin Pract Cases Emerg Med 2020; 4: 332-335.
[56] Jain SS, Liu Q, Raikhelkar J, Fried J, Elias P, Poterucha TJ, DeFilippis EM, Rosenblum H, Wang EY, Redfors B, Clerkin K, Griffin JM, Wan EY, Abdalla M, Bello NA, Hahn RT, Shimbo D, Weiner SD, Kirtane AJ, Kodali SK, Burkhoff D, Rabbani LE, Schwartz A, Leon MB, Homma S, Di Tullio MR, Sayer G, Uriel N and Anstey DE. Indications for and findings on transthoracic echocardiography in COVID-19. J Am Soc Echocardiogr 2020; 33: 1278-1284.
[57] Tiwari A, Berekashvili K, Vulkanov V, Agarwal S, Khaneja A, Turkel-Parella D, Liff J, Farkas J, Nandakumar T, Zhou T, Frontera J, Kahn DE, Kim S, Humbert KA, Sanger MD, Yaghi S, Lord A, Arcot K and Dmytriw AA. Etiologic subtypes of ischemic stroke in SARS-CoV-2 patients in a cohort of New York City Hospitals. Front Neurol 2020; 11: 1004.
[58] Ranard LS, Engel DJ, Kirtane AJ and Masoumi A. Coronary and cerebral thrombosis in a young patient after mild COVID-19 illness: a case report. Eur Heart J Case Rep 2020; 4: 1-5.
[59] Yang Y, Qidwai U, Burton BJL and Canepa C. Bilateral, vertical supranuclear gaze palsy following unilateral midbrain infarct. BMJ Case Rep 2020; 13: e238422.
[60] Maeshima E, Sakagashira M, Yamada Y, Maeda T, Yukawa S and Maeshima S. A case of malignant rheumatoid arthritis with lupus anticoagulant and cerebral infarction. No To Shinkei 1995; 47: 391-395.
[61] Hu X, Wang Y, Liu J, Qiu X, Liu X, Jiang X, Huang X, Feng X, Zhang Y, Zhang S, Qian H, Liu W, Zhang J, Dong J, Chen J, Xia J, Dong N and Wu L. Early outcomes of Stanford type A aortic dissection under the coronavirus disease 2019 (COVID-19) pandemic: a multicentre study from Hubei province. Interact Cardiovasc Thorac Surg 2020; 31: 834-840.