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CASE REPORT

Cardiac damage in an adolescent patient with COVID-19: a case report

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ABSTRACT

COVID-19 has been found to affect the cardiovascular system leading to myocardial damage. A study of 41 patients in Wuhan, China, found that 12% of COVID-19 patients experienced virus-related acute cardiac damage. Subsequent bigger Chinese studies also found acute cardiac damage in 7.2% to 27.8% of hospitalized patients. As a chronic sequela, this condition may result in cardiomyopathy. We report a case of an adolescent COVID-19 survivor with dilated cardiomyopathy with no underlying heart disease. A male patient aged 16 years old was admitted to our outpatient clinic with the primary symptom of exhaustion and had recovered from mild to moderate COVID-19 one month prior to the visit. No previous history of heart disease was documented. Physical examination showed no abnormalities. Laboratory results revealed substantially elevated NT-proBNP (7705 pg/mL) and D-dimer (1850 ng/mL). ECG presented normal sinus rhythm with poor R wave progression. Echocardiography revealed all chamber dilatation, eccentric left ventricular hypertrophy, global hypokinetic, moderate mitral regurgitation, and reduced ejection fraction (22%). We diagnosed the patient with new-onset dilated cardiomyopathy and began treatment with candesartan, bisoprolol, furosemide, spironolactone, rivaroxaban, and trimetazidine. The recovery was steady at three-month follow-up visit. The emergence of new-onset cardiomyopathy in this previously healthy adolescent raises the possibility of COVID-19 acting as the sole cause of myocardial injury in the absence of underlying heart disease. To avoid further complications, comprehensive evaluation and effective therapy should be implemented during hospitalization and post-discharge. Additional tests such as cardiac magnetic resonance imaging and endomyocardial biopsies should be performed to support final proof.

Keyword: cardiomyopathy, COVID-19, ejection fraction, myocardial injury, NT-proBNP

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an ongoing pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) which started in Wuhan, China.[1] The virus keeps spreading globally and as of 20 March 2022, the number of confirmed cases and deaths has reached 468 million and 6 million, respectively.[2] In Indonesia alone, 5 million cases have been reported since 6 March 2020 with 26.3 new cases per 100,000 which made it the second country with the highest numbers of new cases in the South-East Asia Region.[2-4]

COVID-19 commonly manifests as fever, fatigue, cough, dyspnea, and neurological symptoms such as anosmia or hyposmia and dysgeusia.[5] In a substantial minority of COVID-19 patients, cardiovascular manifestations have also been described.[66] A study of 41 patients in Wuhan, China, found that 12% of COVID-19 patients experienced virus-related acute cardiac damage, which is marked by increasing serum levels of cardiac biomarkers (e.g. troponin I) to above the 99th percentile upper reference limit, or new abnormalities in electrocardiography (ECG) or echocardiography findings.[1] Subsequent, more extensive Chinese studies found acute cardiac damage in 7.2% to 27.8% of hospitalized patients.[7-9]

After surviving the acute phase of infection, these patients may develop varying degrees of chronic cardiomyopathy. According to a recent recommendation, pre-existing cardiovascular diseases may increase morbidity and mortality in COVID-19 patients, and COVID-19 may induce substantial cardiac sequelae.[10] Cardiomyopathies, which are caused by heart muscle involvement, are one of the leading reasons for sudden adolescent mortality and heart failure.[11] Here we present a case of a previously healthy adolescent who developed clinically suspected myocarditis with new-onset dilated cardiomyopathy (DCM) as a sequela of infection with SARS-CoV-2.

CASE PRESENTATION

A 16-year-old male was admitted to the cardiology outpatient clinic of the Gatot Soebroto Army Hospital in Jakarta with the main symptom of exhaustion. One month before the visit, the patient had recently recovered from mild to moderate COVID-19. No history of cardiovascular disease was documented.

Physical examination showed no abnormalities, blood pressure 112/82 mmHg, respiratory rate 20 breaths per minute, heart rate 90 beats per minute, and body temperature 36°C. Jugular vein distention and pitting edema are negative. Neither heart murmur nor Gallop was heard on auscultation.

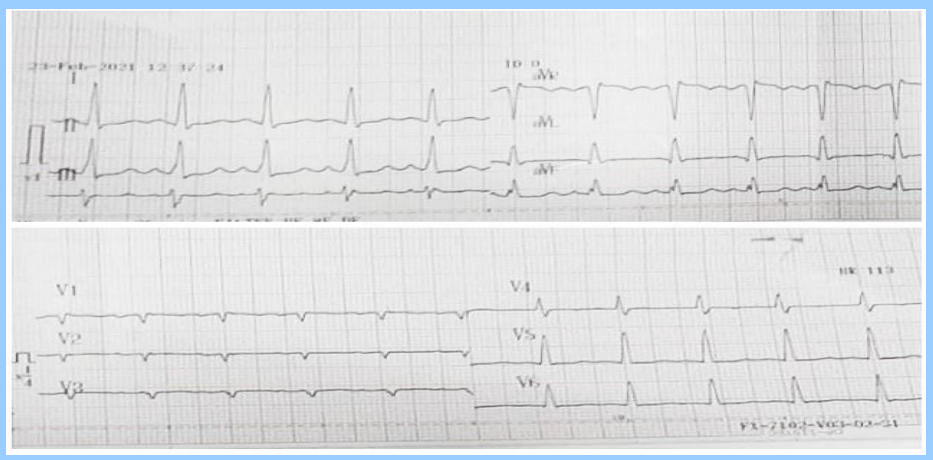

Fig. 1. ECG on first visit. Poor R wave progression is marked on V1–V3.

Laboratory results revealed substantially elevated NT-proBNP (7705 pg/mL) and D-dimer (1850 ng/mL). ECG presented normal sinus rhythm with poor R wave progression (fig. 1). Bedside echocardiography revealed all chamber dilatation, eccentric left ventricular hypertrophy, global hypokinetic, moderate mitral regurgitation and reduced ejection fraction (22.9%) (fig. 2).

We diagnosed the patient with new-onset dilated cardiomyopathy as a COVID-19 sequela, and we began treatment with Candesartan 8mg once daily), Bisoprolol 2.5mg once daily, Furosemide 20mg once daily, Spironolactone 5mg once daily, Rivaroxaban 20mg once daily, and Trimetazidine 80mg once daily.

After three months, the patient's recovery was stable, and the physical assessment was within normal limits. Laboratory findings showed reduction of NT-proBNP (3587 pg/mL) and D-dimer (961 ng/mL).

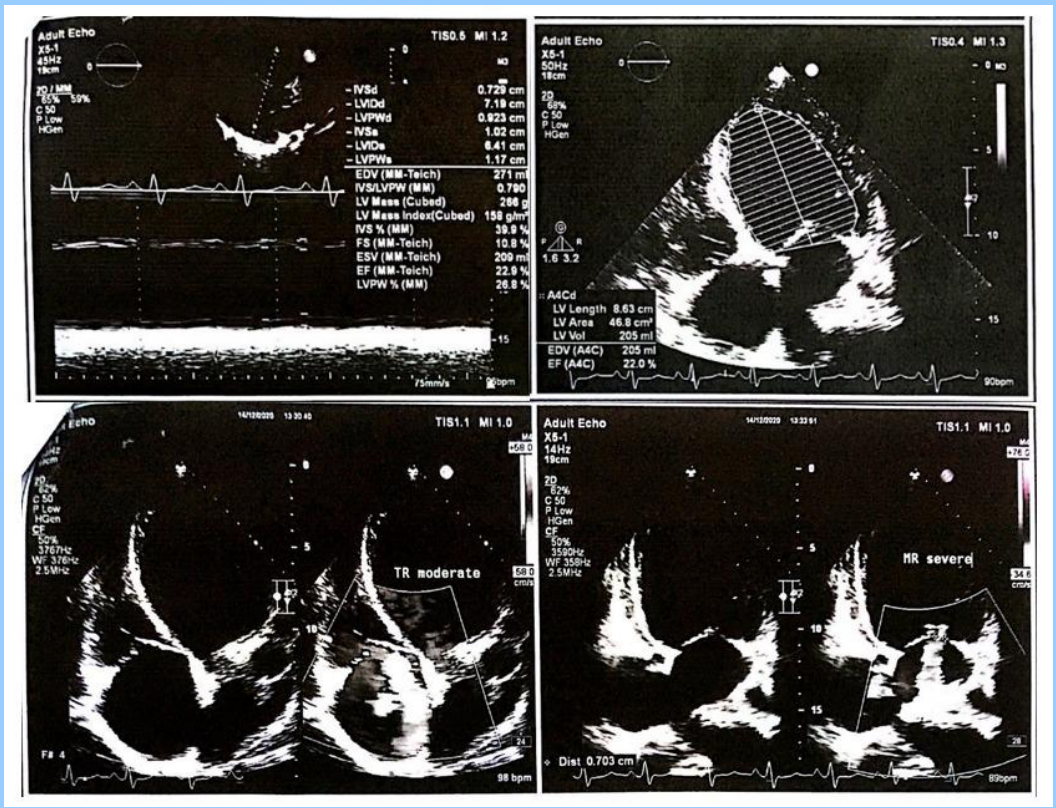

Fig. 2. Echocardiography findings

DISCUSSION

Several cardiac manifestations are involved in COVID-19, including acute myocardial infarction, acute heart failure, arrhythmias, myocarditis, and cardiogenic shock (fig. 3).[12] Myocardial injury, defined by elevated troponin levels, is a prevalent complication in COVID-19 hospitalized patients.[10] A change in cardiac biomarkers, ECG, or echocardiogram relative to the patient's previous condition is another criterion of cardiac damage. In a 416-patient cohort study, cardiac injury was found in 19.7% of hospitalized patients.[9]

COVID-19 has various possible mechanisms of cardiac damage leading to cardiomyopathy. For starters, the latter phase of COVID-19 is associated with a significant systemic inflammatory response, the cytokines released during this phase are potential to cause cardiomyocyte dysfunction and cardiac depression. SARS-CoV-2 can also infect the heart directly, causing immune cell

recruitment and myocarditis. Third, SARS-CoV-2 infection may affect the microvasculature due to its influence on ACE2. This might result in microvascular dysfunction and tissue ischemia, leading to cardiac dysfunction and/or arrhythmias. All of the aforementioned processes may result in varying degrees of cardiac fibrosis once the illnesses have subsided and may eventually result in cardiomyopathy sequelae.[14]

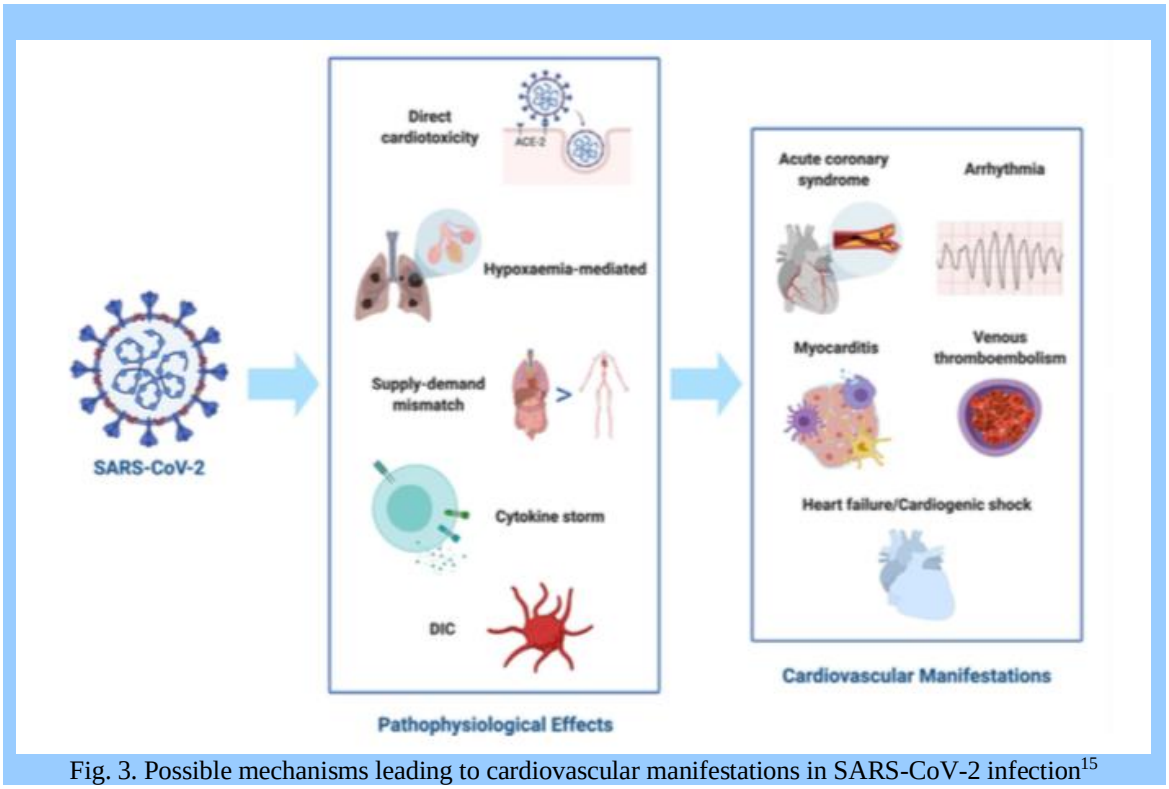

Fig. 3. Possible mechanisms leading to cardiovascular manifestations in SARS-CoV-2 infection[15]

Our patient had a COVID-19 infection one month prior to presentation without previous history of heart disease. After completing the history and physical examination, additional cardiac assessments, such as ECG would be required. ECG abnormalities such as ST elevation or depression, PVCs, and low voltage in the limb lead may occur in certain COVID-19 patients. Although there are no particular ECG changes for patients with COVID-19, combining the data with other examinations and testing is feasible.[16] Dilated cardiomyopathy (DCM) is distinguished by the enlargement and dilatation of one or both ventricles, and decreased contractility (with an LVEF of 40%).[17] The use of echocardiography in the diagnosis of DCM is critical. Left ventricular (LV) dilatation and systolic dysfunction with impaired global contractility and normal LV wall thickness, as well as LV diastolic dysfunction with elevated LV filling pressure, are echocardiographic characteristics of DCM. Atrial dilation, RV dysfunction, LV dyssynchrony, functional tricuspid and mitral regurgitation, and secondary pulmonary hypertension are also prevalent.[18] Echocardiography on our patient revealed all chamber dilatation, eccentric LV hypertrophy, global hypokinetic, moderate mitral regurgitation, and reduced ejection fraction (22.9%).

Some biomarkers elevate in a patient with COVID-19 suggesting cardiovascular conditions, including B-type natriuretic peptide (BNP)/N-terminal pro B-type

natriuretic peptide (NT-proBNP) and D-dimer. BNP/NT-proBNP levels are often elevated in patients suffering from severe inflammation and/or respiratory diseases. As quantitative markers of hemodynamic myocardial stress and heart failure, BNP/NT-proBNP concentrations in a patient with COVID-19 should be viewed as the combination of the presence/extent of pre-existing cardiac illness and/or the acute hemodynamic stress caused by COVID-19. D-dimer is produced by division of fibrin monomers and signals the presence of thrombin production or a non-specific acute-phase response to infection or inflammation. Elevated levels of D-dimer have been linked to poor outcomes.[19]

Other modalities in assessing cardiac complication due to COVID-19 include endomyocardial biopsy, cardiac catheterization, and/or cardiac magnetic resonance, if necessary.[16]

Treatments for COVID-19 have been discussed extensively in many reviews, some of them are still under investigation. However, consideration of potential therapies to support the cardiovascular system cannot be neglected. Before entering the cell, SARS-CoV-2 binds to the angiotensin-converting enzyme 2 (ACE2) receptor (fig. 4).[20]

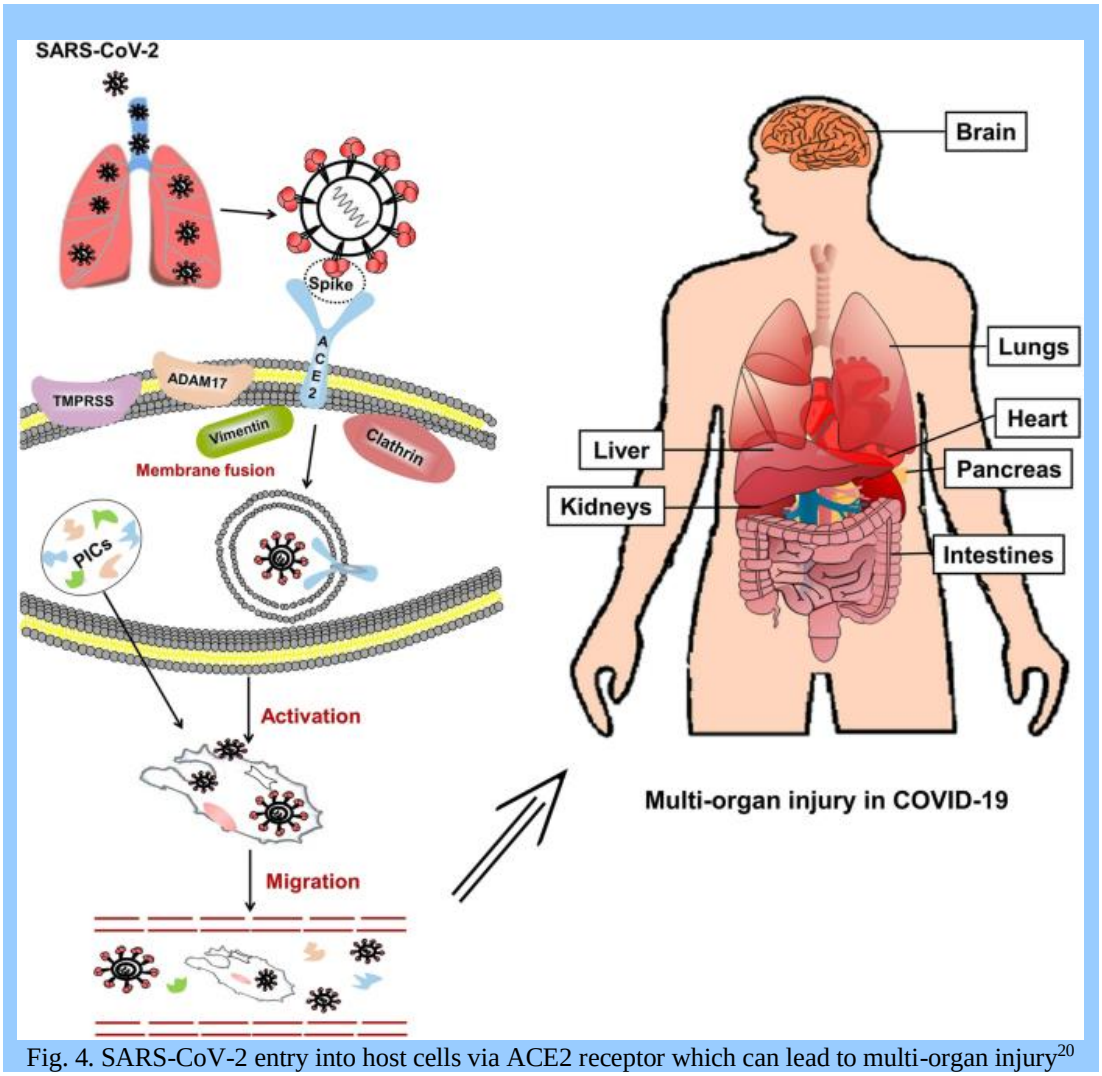

Fig. 4. SARS-CoV-2 entry into host cells via ACE2 receptor which can lead to multi-organ injury[20]

On the other hand, renin-angiotensin-aldosterone system (RAAS) inhibitors may boost ACE2 production. It is debatable whether increased ACE2 expression makes

people at risk of SARS-CoV-2 infection or provides cardioprotection. Yang *et al*. in a single-center, retrospective study of 126 COVID-19 patients with hypertension, found that those receiving ARBs/ACE inhibitors showed significantly lower concentrations of high-sensitivity C-reactive protein (hs-CRP) and procalcitonin (PCT) compared to non-ARB/ACE inhibitors.[21] Findings from an observational multicenter study in Italy and meta-analysis of 19 studies concluded that the use of ARB/ACE inhibitor was not correlated with severity or in-hospital mortality in COVID-19 patients.[22] Despite the uncertainties around the overall impact of RAAS inhibitors (ACEI and ARB medication) in COVID-19, numerous specialty societies now suggest that RAAS inhibitors be maintained in otherwise stable patients. Hence, we prescribe Candesartan for this patient.[15]

According to recent studies, COVID-19 is linked to a higher risk of arterial, venous and microvascular thromboembolic disease, including disseminated intravascular coagulation (DIC). Thus, anticoagulation should be assessed in all patients admitted with COVID-19.[23] A retrospective study of 449 patients with severe COVID-19 found no difference in 28-day mortality between those who received heparin for 7 days or longer and those who didn't. But in subgroups of patients with sepsis-induced coagulopathy (SIC) score ≥4 or D-dimer >6-fold of upper normal limit, 28-day mortality of the heparin users was lower compared to the non-users.[24] The MICHELLE trial found that Rivaroxaban 10mg daily, given to COVID-19 patients after hospital discharge, improved clinical outcomes compared to the patients with no anticoagulation.[25] In this case, we prescribed Rivaroxaban as we expect to improve the patient's clinical outcomes, reducing thrombotic events.

The risk of plaque rupture and thrombus formation is increasing in patients with severe viral infections. This condition can be accompanied by decreased oxygen delivery to the myocardium and vasoconstriction, thus increasing the oxygen demand.[15] Trimetazidine (TMZ) is an agent to treat angina that blocks thiolase II in order to inhibit the β-oxidation of fatty acids and increases glucose oxidation. TMZ enhances cellular hemostasis and prevents intracellular reduction of adenosine triphosphate (ATP), it is also effective against injury caused by ischemic-reperfusion and cardiac fibrosis.[26] Therefore, we considered the use of TMZ in this patient.

CONCLUSION

In conclusion, cardiac damage and CMPSs are common in COVID-19 patients, including worsening an underlying CMP or the appearance of new CPMs. Furthermore, they are linked to increased mortality and morbidity in these patients. As a result, underlying cardiovascular comorbidities should be included in COVID-19 diagnostic tools. In examining these patients, history, signs, and symptoms of cardiac damage should be evaluated. To avoid further COVID-19 complications, comprehensive assessment and effective therapy should be implemented during hospitalization and post-discharge to avoid further COVID-19 complications.

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DECLARATION OF INTERESTS

The authors declare that they have no conflict of interest.

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REFERENCES

1. 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;395:497–506. https://doi.org/10.1016/s01406736(20)30183-5

2. World Health Organization. COVID-19 weekly epidemiological update [update 22 March 2022; cite 22 March 2022]. Available from https://www.who.int/docs/default-source/coronaviruse/situation-reports/20220322_weekly_epi_update_84.pdf?sfvrsn=9ec904fc_4&download=true

3. Tosepu R, Effendy DS, Ahmad LOAI. The first confirmed cases of COVID-19 in Indonesian citizens. Public Health of Indonesia. 2020;6(2):70–71. https://doi.org/10.36685/phi.v6i2337

4. Indonesian Ministry of Health. COVID-19 situation in Indonesia [update 22 March 2022; cite 22 March 2022]. Available from https://covid19.go.id/artikel/2022/03/22/situasi-covid-19-di-indonesia-pdate-22-maret-2022

5. Mesquita RR, Junior LCFS, Santana FMS, Oliveira TF, Alcantara RC, Arnozo GM, *et al*. Clinical manifestations of COVID-19 in the general population: systematic review. Wien Klin Wochenschr. 2021;133:377–382. https://doi.org/10.1007/s00508-020-01760-4

6. Hendren NS, Drazner MH, Bozkurt B, Cooper LT. Description and proposed management of the acute COVID-19 cardiovascular syndrome. Circulation. 2020;141(23):1903–1914. https://doi.org/10.1161/circulationaha120.047349

7. 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;323(11):1061–1069. https://doi.org/10.1001/jama.2020.1585

8. 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;5(7):802–810. https://doi.org/10.1001/jamacardio.2020.0950

9. Guo T, Fan Y, Chen M, Wu X, Zhang L, He Tao, *et al*. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):811–818. https://doi.org/10.1001/jamacardio.2020.1017

10. Zaman S, MacIsaac AI, Jennings GLR, Schlaich MP, Inglis SC, Arnold R, *et al*. Cardiovascular disease and COVID-19: Australian and New Zealand consensus statement. Med J of Australia. 2020;213(4):182–187. https://doi.org/10.5694/mja2.50714

11. Limongelli G, Crotti L. COVID-19 pandemia and inherited cardiomyopathies and channelopathies: a short term and long term perspective. Orphanet J Rare Dis. 2020;15(157). https://doi.org/10.1186/s13023-020-01444-2

12. Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E, *et* al. The variety of cardiovascular presentations of COVID-19. Circulation. 2020;141:1930–1936. https://doi.org/10.1161/CIRCULATIONAHA.120.047164

13. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, *et al*. Cardiovascular considerations ro patients, health care workers, and health

systems during the COVID-19 pandemic. J Am College Cardiol. 2020;75:2352–2371. https://doi.org/10.1016/j.jacc.2020.03.031

14. Schilling JD, Ravichandran AK, Mandras SA. Management of the hospitalized COVID-19 patient with acute cardiomyopathy or heart failure [update 16 April 2020; cite 23 March 2022]. Available from https://www.acc.org/latest-in-cardiology/articles/2020/04/16/14/42/management-of-the-hospitalized-covid-19-coronavirus-2019-patient-with-acute-cardiomyopathy-or-heart-failure

15. Kang Y, Chen T, Mui D, Ferrari V, Jagasia D, Scherrer-Crosbie M, *et al*. Cardiovascular manifestations and treatment considerations in COVID- 19. Heart. 2020;106:1132–1141. http://dx.doi.org/10.1136/heartjnl-2020-317056

16. Sukmawan R. Cardiomyopathy in COVID-19 survivors: mechanism, management, and prevention. Indonesian J Cardiol. 2020;41:120–124. https://doi.org/10.30701/ijc.1012

17. Herman DS, Lam L, Taylor MR, Wang L, Teekakirikul P, Christodoulou D, *et al*. Truncations of titin causing dilated cardiomyopathy. N Engl J Med. 2012;366:619–628. https://doi.org/10.1056/nejmoa1110186

18. Pinamonti B, Abate E, de Luca A, Finocchiaro G, Korcova R. Role of cardiac imaging: echocardiography. In: Sinagra G, Merlo M, Pinamonti B, Eds. Dilated cardiomyopathy: from genetics to clinical management. Cham (CH): Springer, 2019. https://doi.org/10.1007/978-3-030-13864-6_7

19. European Society of Cardiology. European Society of Cardiology guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 1–epidemiology, pathophysiology, and diagnosis. Eur Heart J. 2022;43:1033–1058. https://doi.org/10.1093/eurheartj/ehab696

20. Ni W, Yang X, Yang D, Bao J, Li R, Xiao Y, *et al*. Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. Crit Care. 2020;24(422). https://doi.org/10.1186/s13054-020-03120-0

21. Yang G, Tan Z, Zhou L, Yang M, Peng L, Liu J, *et al*. Effects of angiotensin II receptor blockers and ACE (angiotensin-converting enzyme) inhibitors on virus infection, inflammatory status, and clinical outcomes in patients with COVID-19 and hypertension: a single-center retrospective study. Hypertension. 2020;76(1):51–58. https://doi.org/10.1161/hypertensionaha.120.15143

22. COVID-19 RISk and Treatments (CORIST) Collaboration. RAAS inhibitors are not associated with mortality in COVID-19 patients: findings from an observational multicenter study in Italy and a meta-analysis of 19 studies. Vascul Pharmacol. 2020;135:106805. https://doi.org/10.1016/j.vph.2020.106805

23. European Society of Cardiology. ESC guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 2–care pathways, treatment, and follow-up. Eur Heart J. 2022;43:1059–1103.

https://doi.org/10.1093/eurheartj/ehab697

24. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020;18:1094–1099. https://doi.org/10.1111/jth.14817

25. Ramacciotti E, Agati LB, Calderaro D, Aguiar VCR, Spyropoulos AC, de Oliveira CCC, *et al*. Rivaroxaban versus no anticoagulation for post-discharge thromboprophylaxis after hospitalisation for COVID-19 (MICHELLE): an open-label, multicentre, randomised, controlled trial. Lancet. 2022;399:50–59. https://doi.org/10.1016/s0140-6736(21)02392-8

26. Al-kuraishy HM, Al-Gareeb AI, Welson NN, Batiha GES. Trimetazidine and COVID-19-induced acute cardiac injury: a missed key. Int J Clin Pharm. 2022;44:832–833. https://doi.org/10.1007/s11096-022-01408-5