Cardiac complications of COVID-19 infection

Sharan Randhawa, Ammar J Alsamarrai, Simon Lee, Jithendra B Somaratne

ABSTRACT

Since the start of the COVID-19 pandemic, studies emerged reporting the occurrence of cardiovascular complications in patients affected by SARS-CoV-2. Initial data were likely skewed by higher risk populations and those with severe disease. Recent, larger studies have corroborated this association and provide estimates for risk of cardiovascular complications. Patients affected by COVID-19 are at increased risk of myocardial infarction, myocarditis, venous thromboembolism, arrhythmias, and exacerbation of heart failure. Furthermore, a subset of patients who recover from the acute illness have persistent symptoms, a condition termed "long COVID", and management of these symptoms is challenging. Clinicians treating patients affected by COVID-19 should remain vigilant for cardiac complications during the acute illness, particularly in high-risk populations.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in late 2019 and heralded the coronavirus disease 2019 (COVID-19) pandemic. As of November 2022, there have been over 638 million reported cases of COVID-19 infection and 6.6 million fatalities worldwide.[1] New Zealand's initial years of the pandemic were characterised by a low prevalence of COVID-19 compared to other developed nations, but the country has since witnessed discrete periods of widespread community transmission, the most recent of which was the February 2022 Omicron variant outbreak. As of November 2022, there have been almost two million recorded cases of COVID-19 infection in New Zealand, representing approximately 40% of the total population, of which there were 2,212 deaths.[2]

Ever since the first global outbreak in the early months of 2020, emerging data suggested that affected patients were at increased risk of cardiovascular morbidity and mortality, particularly those with underlying risk factors or established cardiovascular disease. Furthermore, observational studies reported on the development of *de novo* cardiac pathology in otherwise healthy individuals. The long-term complications of COVID-19 infection are unknown, but evidence suggests that some patients have persistent symptoms after recovery from the index infection, which has been termed "long COVID".

As New Zealand healthcare professionals continue to face surges in infection rates of COVID-19 in the community, we present a review of the current research into the cardiac complications of COVID-19 infection (see Table 1) and recommendations as to their management.

Mechanisms of cardiac injury

Multiple potential mechanisms have been proposed to explain the acute cardiac complications of COVID-19. These include direct invasion into myocardial tissue via transmission through angiotensin converting enzyme II receptors with activation of the inflammatory pathways and cytokine activation, destabilisation of existing coronary plaques by means of inflammatory cell activation, increasing the mismatch between myocardial oxygen demand and supply due to infection, endothelial and microvascular injury, platelet activation and thrombus formation.[3–5]

Severe COVID-19 infection and mortality in patients with established cardiovascular disease

Early in the pandemic, observational studies reported an increased risk of severe COVID-19 infection and mortality in patients with established cardiovascular disease or those with risk factors. These early data were summarised by Bae et al. in their systematic review and meta-analysis of 51 studies up to June 2020,[6] which included 48,317 adult patients with confirmed COVID-19 infection. Hypertension was present in 26%, and these patients were at significantly higher risk of severe COVID-19 infection (odds ratio [OR] 2.42) and death (OR 2.60). Similarly, diabetes was present in 15% and these patients had higher risk of severe COVID-19 (OR 2.47) and death (OR 2.11). Overall, cardiovascular disease, although not defined, was present in 8%, and of note, pooled analysis showed a significantly higher risk of severe COVID-19 infection (OR 3.15) and death (OR 3.23). Findings

Table 1: Summary of study findings—COVID-19 related cardiac complications.

Cardiovascular complications	Countries	COVID-19 positive cases	Type of study	Main findings
Myocardial infarction				
Katsoularis et al. (2021)	Sweden	86,742	Nationwide database	- 2.5x increased risk of MI in the 2 weeks after COVID-19 infection.
Modin et al. (2020)	Denmark	5,119	Nationwide database	- 5.9x increased risk of MI in the 2 weeks after COVID-19 infection.
Zuin et al. (2023)	USA	1,245,157	Systematic review and meta-analysis	- MI occurs in 0.5% of COVID-19 recovered patients. - 93% higher risk acute MI in COVID-19 recovered patients (8.5 months follow-up).
Rodriguez-Leor et al. (2021)	Spain	91	Nationwide database	- 9% of STEMI patients had COVID-19. - Higher risk of HF, cardiogenic shock, stent thrombosis, and mortality in COVID-19 patients.
Garcia et al. (2021)	USA	230	Multicentre registry	- Higher rate of cardiogenic shock and less PCI in COVID-19 STEMI patients. - COVID-19 patients more likely to have no culprit lesion and be medically managed.
Gharibzadeh et al. (2021)	Brazil, USA, UK, Spain, Italy	447	Systematic review and meta-analysis	- 25% mortality in COVID-19 STEMI patients. - Cardiogenic shock in 18%, cardiac arrest in 3–28% - COVID-19 infection independent risk factor for mortality in STEMI patients.
Myocardial injury and myocarditis				
Biasco et al. (2021)	Switzerland	452	Multicentre prospective cohort	- Myocardial injury in 48% of COVID-19 patients (c.f. 65% influenza patients). - COVID-19 patients have 3.5x higher 28-day mortality compared to influenza patients.
Puntmann et al. (2020)	Germany	100	Prospective cohort	- Cardiac MRI evidence of cardiac involvement in 78% - Persistent myocardial inflammation in 60% of COVID-19 recovered patients.
CAPACITY-COVID-19 and LEOSS Study Group (2022)	18 countries	16,511	Multinational observational	- Myocarditis in 0.2% of COVID-19 patients.
Daniels et al. (2021)	USA	1,597	Multicentre observational	- Myocarditis in 2.3% (most subclinical). - Cardiac MRI increased detection of myocarditis by 7.4x.

Table 1 (continued): Summary of study findings—COVID-19 related cardiac complications.

Cardiovascular complications	Countries	COVID-19 positive cases	Type of study	Main findings
Arrhythmia				
Coromilas et al. (2021)	12 countries	4,526	International multicentre observational	- Tachyarrhythmia in 18% of COVID-19 patients (80% atrial, 20% ventricular). - Bradyarrhythmia in 22%. - High mortality in patients with arrhythmia (49% any arrhythmia; 62% for ventricular arrythmia).
Venous thromboembolism				
Knight et al. (2022)	England and Wales	1,367,059	Nationwide cohort	- Increased risk of DVT (12x) and PE (39x) in the first week after diagnosis with COVID-19. - Risk decreases over time.
Nasrullah et al. (2022)	USA	1,659,040	Nationwide database	- Hospitalised patients with COVID-19 and PE had higher need for mechanical ventilation and higher in-hospital mortality.
Heart failure				
CAPACITY-COVID-19 and LEOSS Study Group (2022)	18 countries	16,511	Multinational observational	- *de novo* HF in 0.6%. - HF associated with in-hospital mortality (RR 1.6).
Rey et al. (2020)	Spain	3,080	Single-centre prospective	- Acute HF in 2.5%, most *de novo*. - Pre-existing HF strongest risk factor for developing HF with COVID-19. - COVID-19 patients with HF had >2x mortality rate (26%) compared to those without HF.
Petrili et al. (2020)	USA	5,279	Single-centre prospective	- HF strongly associated with hospital admission (OR 4.4) and critical illness (OR 1.9).

Table 1 (continued): Summary of study findings—COVID-19 related cardiac complications.

Cardiovascular complications	Countries	COVID-19 positive cases	Type of study	Main findings
Long COVID				
Subramanian et al. (2022)	UK	486,149	National database	- Female gender, ethnic minority and socioeconomic deprivation associated with risk of long COVID. - COPD (HR 1.55), smoking (HR 1.12) and obesity (HR 1.1) were also risk factors. - Most common cardiorespiratory symptoms were shortness of breath at rest and chest pain.
Roca-Fernandez et al. (2022)	UK	534 with long COVID-19	Multicentre prospective	- 19% had abnormal baseline cardiac MRI, most with normal cardiac biomarkers. - Cardiac symptoms not predictive of cardiac impairment on MRI. - Persistent cardiac impairment in 58% of those with follow up data at 12 months.

Abbreviations: COPD = chronic obstructive pulmonary disease; DVT = deep vein thrombosis; HF = heart failure; MI = myocardial infarction; MRI = magnetic resonance imaging; OR = odds ratio; PCI = percutaneous coronary intervention; PE = pulmonary embolus; STEMI = ST-elevation myocardial infarction.

from these studies shaped public health messaging early in the pandemic to suggest that patients with cardiac co-morbidities were at higher risk of adverse outcomes from COVID-19 infection. However, this notion has been subsequently challenged.

Investigators from two large registries (CAPACITY-COVID registry and LEOSS Study Group), which included 16,511 patients across 18 countries, assessed the association between different subtypes of cardiovascular disease (arrhythmia, conduction disease, atrial fibrillation [AF], coronary artery disease, heart failure [HF] and valvular disease) and in-hospital mortality in patients hospitalised with COVID-19. After multivariable analysis, only HF (New York Heart Association class III or IV) was found to confer a significantly higher risk of in-hospital mortality (relative risk 1.41).[7] This association between pre-existing HF and in-hospital mortality was also reported by Bhatt et al., who found that approximately 25% of patients with HF died during hospitalisation.[8]

It is unclear why there is a discrepancy between earlier and later data; however, one possible explanation is that limited testing capacity in the early days of the pandemic may have under-estimated the true prevalence of COVID-19, and hence milder cases were not diagnosed and captured in the observational studies.

Myocardial infarction

There is an established link between respiratory infections and the incidence of acute myocardial infarction (AMI). For example, patients who are affected by influenza virus or other respiratory infections have an increased hazard of AMI (OR 2.01). In addition, vaccination against influenza virus has been shown to reduce the incidence of AMI, further supporting the association between these two conditions.[9] From a pathophysiology perspective, this observation can be explained by a number of factors. Respiratory illness can lead to systemic inflammation, prothrombotic states, myocardial supply–demand mismatch, platelet activation, coronary vasoconstriction and endothelial cell dysfunction. These factors can lead to plaque rupture and thrombosis, with resultant myocardial injury. Therefore, it is not surprising that cohort studies have identified an increased risk of AMI after COVID-19 infection.

A self-controlled case series and cohort study from Sweden examined the temporal association between COVID-19 infection and AMI in 86,742 patients.[10] In the first week after infection, the relative risk of AMI was 8.44, which reduced to 2.56 in the second week and 1.62 for the third and fourth weeks following infection (risk ratios are lower when day 0 was excluded). Similarly, a nationwide, register-based, self-controlled case series from Denmark examined the short-term outcome of 5,119 patients with confirmed COVID-19 infection. It found that the incidence of AMI was five times higher in the first 14 days after diagnosis when compared to a control interval. The increased incidence of AMI remained statistically significant when extended to include cases occurring within 21 and 31 days from the index COVID-19 diagnosis, indicating a sustained period of enhanced risk.[11] Recent data have shown that COVID-19 recovered patients have persistently higher risk of incident myocardial infarction several months following recovery (hazard ratio [HR] 1.93 at a mean follow up of 8.5 months), though the risk reduces with time.[12]

Concurrent COVID-19 infection and myocardial infarction

Given the frequent occurrence of AMI and COVID-19 infection in most populations, it naturally follows that some patients will be affected by both conditions concurrently. This raises the question about the outcome of these patients, taking into account the virulence of SARS-CoV-2.

In a multi-centre observational study across 42 ST-elevation myocardial infarction (STEMI) care networks in Spain, investigators examined the outcome of patients presenting with STEMI during a period where there was COVID-19 community transmission.[13] Of 1,010 consecutive patients, 91 patients (9%) had COVID-19 infection. Patients with concurrent COVID-19 infection and STEMI were more likely to have HF on admission (31.9% vs 18.4%), cardiogenic shock post primary coronary intervention (PCI) (9.9% vs 3.8%), stent thrombosis (3.3% vs 0.8%) and cardiovascular (13.2% vs 5.1%) and all-cause mortality (23.1% vs 5.7%).

Further corroborating these findings is data from the North American COVID-19 STEMI registry,[14] which investigated the outcome of 230 patients with confirmed COVID-19 infection compared to 995 controls. Patients with COVID-19 and STEMI were more likely to present in cardiogenic shock or following cardiac arrest, but were less likely to have primary PCI as compared to age and sex-matched control patients. While door-to-balloon time was longer in those with COVID-19 infection, they were more likely to have no culprit lesions identified on invasive angiography. COVID-19 positive patients had longer intensive care and hospital lengths of stay, and the primary outcome of in-hospital

death, stroke, recurrent MI or unplanned revascularisation occurred in 36%, compared to only 4% in control patients, which was driven primarily by in-hospital mortality.

These above findings are not surprising when considering the observation that COVID-19 positive patients presenting with STEMI have greater infarct size, reduced left ventricular function, greater intracoronary thrombus burden, higher rates of cardiogenic shock, requirement for haemodynamic support and life-threatening arrhythmias.[5] Summarising these studies and others, a meta-analysis by Gharilbzadeh et al. found the pooled prevalence of mortality of COVID-19 patients with STEMI was just over 25%.[4]

Currently, recommended management of patients remains the same regardless of COVID-19 status—invasive coronary angiography and PCI to culprit lesions is considered first line for STEMI management, with fibrinolysis performed in cases where target time cannot be achieved. Thrombus aspiration can be utilised on a case-by-case basis for patients with high intracoronary thrombus burden, and case series have demonstrated the potential use of low-dose rivaroxaban in scenarios where no culprit lesion was found.[15] In patients with non-ST elevation acute coronary syndromes (NSTE-ACS), medical stabilisation and early angiography is recommended in high-risk cases, while non-invasive imaging can be considered in selected intermediate or low risk cases.[16]

Another important factor to consider is the organisation of hospital operations during a pandemic. In an analysis by Sofi et al., it was found that during the first peak of the pandemic, STEMI hospitalisations had reduced in countries with lower hospital bed availability but remained similar to previous levels in countries with greater hospital bed availability.[3] There was no evidence indicating that the stringency of lockdown measures made a difference to STEMI presentations. This pattern has been confirmed in a national New Zealand registry study by Chan et al. and other single centre studies,[17,18] noting that in the absence of widespread community transmission and low hospital occupancy of COVID-19 cases, there was no difference in hospitalisation for STEMI, whereas the rates of NSTE-ACS initially reduced during a national COVID-19 lockdown. As the burden of COVID-19 was low, the reduced hospitalisation for NSTE-ACS was likely in part the result of behavioural changes in response to public health messages, but a genuine reduction in NSTE-ACS was also possible. These epidemiological advantages are no longer applicable to New Zealand's current status.

Myocardial injury and myocarditis

Raised serum cardiac troponin levels are commonly observed in patients with COVID-19 and can reflect myocardial injury.[19] Similar to other viral respiratory infections, a raised troponin level is associated with adverse outcomes and in-hospital mortality in patients with COVID-19.[20] However, the link between troponin elevation and outcome is not uniform. For example, in a study across four Swiss centres, raised troponin levels were more commonly observed among patients hospitalised with influenza than those with COVID-19, yet COVID-19 patients had significantly higher 28-day mortality.[21] The exact cause of raised troponin levels in this setting may not always be clear, but potential causative mechanisms for myocardial injury in patients with COVID-19 have been described. For example, SARS-CoV-2 has been found in endomyocardial biopsies of some patients suspected of having myocarditis.[22] Furthermore, Puntmann et al. found that among patients recently recovered from COVID-19 infection, there was evidence of ongoing myocardial inflammation in about 60% of patients based on cardiac magnetic resonance imaging.[23] Despite these findings, only a small proportion of patients develop clinical pericarditis or myocarditis (0.2% as reported by the CAPACITY-COVID study), indicating that the myocardial inflammation seen on histology or imaging may be asymptomatic. Lastly, other biomarkers such as brain natriuretic peptide are also raised in some patients with COVID-19.[24] All of this underscores the need to investigate the underlying aetiology of raised biomarkers, if clinically appropriate, to guide appropriate treatment.

Routine screening for myocarditis in COVID-19 patients is not generally recommended except for those with supportive clinical features or evidence from clinical examination, electrocardiography or echocardiography. The best estimate for the incidence of myocarditis in patients with COVID-19 comes from a unique study performed by Daniels et al. In their cohort study of 1,597 patients with COVID-19, cardiac evaluation and magnetic resonance imaging was performed, and 37 (2.3%) were diagnosed with myocarditis, but this was subclinical in 28 out of 37 patients,[25] and this raises a question about the relevance of asymptomatic imaging findings. However, the presence of myocardial inflammation likely reflects a more aggressive disease course, which adds to the overall risk and clinical picture of the individual patient.

Arrhythmia

Arrhythmic complications of COVID-19 have been observed in several cohorts. These data are

best summarised in a study by Coromalis et al., who conducted a large retrospective analysis of 4,526 patients with COVID-19, across 12 countries, of whom 827 patients had been affected by incident arrhythmia.[26] It is noteworthy that most of these patients had no prior history of arrhythmia, indicating that this was a *de novo* phenomenon. Of the 827 patients, greater than 80% developed atrial arrhythmias, while the remainder developed ventricular arrhythmias (non-sustained ventricular tachycardia [VT], polymorphic VT/torsade de point, or ventricular fibrillation). Furthermore, 22% also developed bradyarrhythmia, antrio-ventricular (AV) block or ventricular pauses greater than 3 seconds. In this group, 5% underwent permanent pacemaker insertion, suggesting significant or persistent bradyarrhythmic events. Regional variation was noted, for example, patients from Asia had lower rates of incident AF (34% compared to the global incidence of 61%) but higher rates of bradyarrhythmia and AV block (43% compared to global incidence of 22%). Overall, only 51% of patients who developed arrhythmias survived to discharge from hospital, with slightly increased mortality risk for those who developed VT (37% survival to discharge).

Despite these observations, it is difficult to directly attribute incident arrhythmia to COVID-19 infection. In the above study, patients with arrhythmia were older (71 years, compared to mean age of 62.8 for the total cohort). Those patients who developed ventricular arrhythmias also had high rates of hypoxia, metabolic abnormalities, renal failure, and treatment with QT prolonging medications, and there was a subset that were treated with inotropic agents. All of these factors could contribute to a pro-arrhythmic milieu, and it is possible that the observation of *de novo* arrhythmia simply reflects a more aggressive disease course. It remains to be established whether SARS-CoV-2 can directly lead to the development of *de novo* arrhythmia.

The management of arrhythmias in patients with COVID-19 is similar to standard care advice.[16] In all cases, precipitating factors such as electrolyte imbalances should be corrected. For AF, beta-blockers and calcium channel blockers are recommended for rate control in hemodynamically stable patients, while intravenous amiodarone is recommended for patients with hemodynamic instability. Therapeutic anticoagulation is indicated for male patients with a CHA_2DS_2-VASc score >1 or female patients with a score of >2. Transthoracic echocardiography is recommended for assessment cardiac structure and function. For VT, therapeutic options include intravenous beta-blockers, lidocaine, amiodarone, and synchronised direct-current cardioversion. For ventricular fibrillation, asynchronous direct current defibrillation is indicated. Advanced therapies are reserved for patients with refractory ventricular arrhythmias, with options including temporary pacing, intubation, and extra-corporeal membrane oxygenation.

Severe incident bradyarrhythmias should be investigated with echocardiography or cardiac magnetic resonance imaging where appropriate. In patients with hemodynamic instability, chronotropic agents such as intravenous atropine and isoprenaline should be administered. A subset of patients may require temporary or permanent pacemaker implantation, and these are evaluated on an individual patient basis.

Venous thromboembolism (VTE)

COVID-19 has been associated with increased risk of venous and arterial thromboembolic events. The risk of incident events declines with time from the initial COVID-19 diagnosis, though it remains elevated for up to a year. Amongst 1.4 million patients from England and Wales who tested positive for COVID-19, when adjusted for age, sex and region, the HR for developing deep vein thrombosis (DVT) was 12 in the first week after COVID-19 diagnosis, declining to 2.6 at 27–49 weeks. Similar trends were observed for pulmonary embolism (PE) (adjusted HR 39 at 1 week, declining to 2.2 at 27–49 weeks) and arterial thrombosis (HR 27 at 1 week, and 1.9 at 27–49 weeks).[27] This is pertinent because patients with PE have high mortality rates (19%) compared to those with COVID-19 without PE.[28] It has been noted that COVID-19 patients with VTE have fewer classical risk factors, though they still suffer from high mortality rates. Given the propensity of COVID-19 patients to develop PE without DVT, *in situ* clot formation via disruption of the pulmonary circulation (due to endothelial damage, micro-embolism and angiogenesis) have been postulated as mechanisms to explain this difference.[29,30]

Guideline recommendations in hospitalised and critically ill COVID-19 patients suggest low molecular weight heparin as the first line agent for VTE prophylaxis, as per standard prophylaxis dosing.[31] Therapeutic heparinisation (low molecular weight heparin or unfractionated heparin) is recommended for the initial treatment of VTE, while direct oral anticoagulants or warfarin can be used for extended treatment. A minimum of

three months of anticoagulation is suggested for treatment. In patients already on anticoagulation presenting with recurrent VTE, higher dose low molecular weight heparin is recommended. Patients with confirmed PE who have obstructive shock or cardiopulmonary compromise, and who are at low risk for major bleeding, should be treated with thrombolysis. Mechanical thromboprophylaxis should be avoided in critically ill COVID-19 patients.

Heart failure

COVID-19 has been implicated in the development of *de novo* HF and in exacerbation of chronic HF.[32] *De novo* HF appears to be relatively uncommon, with observational studies providing estimates of 1.2%–2.5% of affected patients,[7,33] whereas the total combined incidence of *de novo* and acute decompensation of chronic HF was estimated to be 10% in one study.[34]

More importantly, patients with pre-existing HF represent a particularly high-risk group for adverse outcomes. As mentioned earlier, pre-existing HF is an independent risk factor for developing severe COVID-19 infection.[35] A large review by Bader et al. reported that patients who had HF and septic shock had mortality rates of 70–90%, compared to 20% in those with sepsis but without HF or cardiovascular disease.[32]

For patients with chronic HF, standard guideline recommendations regarding goal-directed medical therapy remain unchanged,[16] and emphasis is placed on preventing COVID-19 infection. This can be achieved with measures such as vaccination and use of telemedicine to reduce physical clinics visits where possible, as well as standard public health measures.

Long COVID

There is emerging evidence that a proportion of patients who develop COVID-19 have persistent symptoms after recovery from the index infection, termed “long COVID”. Numerous risk factors have been described, including female gender, belonging to an ethnic minority, socio-economic deprivation, chronic obstructive pulmonary disease, smoking, obesity and psychiatric conditions.[36] While fatigue appears to be the most common feature, cardiopulmonary symptoms are an important component of this syndrome, and there are wide-ranging estimates of their prevalence.[37] For example, separate cohorts have reported that six months after recovery, chest pain was reported by 5% and palpitations reported by 9% of survivors.[38] Autonomic symptoms are common, and while most patients do not demonstrate abnormal findings during tilt table testing,[39] cardiac symptoms should not be discounted, as imaging studies have provided evidence for cardiac abnormality in this group. For example, in one study of 534 patients who underwent cardiac magnetic resonance imaging at baseline, 6 months and 12 months after the onset of long COVID symptoms, there was evidence of cardiac impairment in approximately 20% of patients (ventricular dilatation or systolic dysfunction, reduced global strain, or elevated native T1 signals).[40] Therefore, the occurrence of cardiovascular symptoms in survivors of COVID-19 should be investigated as per usual standards of practice.

It should be stated that there is a paucity of data about the long-term outcome of COVID-19 survivors who suffer any of the aforementioned complications during the index illness. While it is reasonable to extrapolate treatment strategies from existing guidelines pertaining to each condition, it is not known whether cardiac phenomena observed during acute COVID-19 illness follow the expected natural history. A good example of this is the occurrence of *de novo* AF in patients with acute COVID-19 or similarly any other systemic illness. Clinical experience suggests that many of these patients may not necessarily develop recurrent AF after recovery, which obviates the need for rate, rhythm, and antithrombotic therapy.[41,42]

Conclusion

COVID-19 infection is associated with numerous cardiac complications, and the occurrence of these is often a negative prognostic indicator. Clinicians should be vigilant for the development of adverse cardiac events in hospitalised patients with COVID-19. Long COVID will possibly become an epidemic itself, and further research into its mechanisms and treatment strategies is needed. Vaccination against COVID-19 and public health measures remain key in curbing infection rates, and therefore risks of both short and long-term complications of COVID-19.

COMPETING INTERESTS
The authors report no relationships that could be construed as a conflict of interest.

ACKNOWLEDGEMENT
We would like to thank Charlene Nell, Desktop Support Administrator, for formatting and submitting the manuscript and for excellent secretarial assistance.

AUTHOR INFORMATION
Sharan Randhawa MBChB: House Officer, Te Whatu Ora – Health New Zealand, Counties Manukau, Cardiology Department, Middlemore Hospital, Auckland, New Zealand.
Ammar J Alsamarrai MBChB: Cardiology Registrar, Te Whatu Ora – Health New Zealand, Te Toka Tumai Auckland, Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand.
Simon Lee MBChB: Cardiology Registrar, Te Whatu Ora – Health New Zealand, Counties Manukau, Cardiology Department, Middlemore Hospital, Auckland, New Zealand.
Jithendra B Somaratne MBChB, FRACP, PhD: Cardiologist, Te Whatu Ora – Health New Zealand, Te Toka Tumai Auckland, Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand.

CORRESPONDING AUTHOR
Ammar J Alsamarrai: Cardiology Registrar, Te Whatu Ora – Health New Zealand, Te Toka Tumai Auckland, Green Lane Cardiovascular Service, Auckland City Hospital, Park Road, Grafton, Auckland 1142, New Zealand; Ph: +64 9 307 4949.
E: AmmarAl@adhb.govt.nz

REFERENCES
1. World Health Organisation. WHO Coronavirus (COVID-19) Dashboard. [cited 2022 November 30]. Available from: https://covid19.who.int.
2. New Zealand Ministry of Health – Manatū Hauora. COVID-19: Current cases. [cited 2022 November 30]. Available from: https://www.health.govt.nz/COVID-19-novel-coronavirus/COVID-19-data-and-statistics/COVID-19-current-cases.
3. Sofi F, Dinu M, Reboldi G, et al. Worldwide differences of hospitalization for ST-segment elevation myocardial infarction during COVID-19: A systematic review and meta-analysis. Int J Cardiol. 2022;347:89-96.
4. Gharibzadeh A, Shahsanaei F, Rahimi Petrudi N. Clinical and Cardiovascular Characteristics of Patients Suffering ST-Segment Elevation Myocardial Infarction After Covid-19: A Systematic Review and Meta-Analysis. Curr Probl Cardiol. 2021:101045.
5. Toscano O, Cosentino N, Campodonico J, Bartorelli AL, Marenzi G. Acute Myocardial Infarction During the COVID-19 Pandemic: An Update on Clinical Characteristics and Outcomes. Front Cardiovasc Med. 2021;8:648290.
6. Bae S, Kim SR, Kim MN, Shim WJ, Park SM. Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis. Heart. 2021;107:373-80.
7. Consortium C-CC, Group LS. Clinical presentation, disease course, and outcome of COVID-19 in hospitalized patients with and without pre-existing cardiac disease: a cohort study across 18 countries. Eur Heart J. 2022;43:1104-20.
8. Bhatt AS, Jering KS, Vaduganathan M, et al. Clinical Outcomes in Patients With Heart Failure Hospitalized With COVID-19. JACC Heart Fail. 2021;9:65-73.
9. Barnes M, Heywood AE, Mahimbo A, Rahman B, Newall AT, Macintyre CR. Acute myocardial infarction and influenza: a meta-analysis of case-control studies. Heart. 2015;101:1738-47.
10. Katsoularis I, Fonseca-Rodriguez O, Farrington P, Lindmark K, Fors Connolly AM. Risk of acute myocardial infarction and ischaemic stroke following COVID-19 in Sweden: a self-controlled case series and matched cohort study. Lancet. 2021;398:599-607.
11. Modin D, Claggett B, Sindet-Pedersen C, et al. Acute COVID-19 and the Incidence of Ischemic Stroke and Acute Myocardial Infarction. Circulation. 2020;142:2080-2.
12. Zuin M, Rigatelli G, Battisti V, Costola G, Roncon L, Bilato C. Increased risk of acute myocardial infarction after COVID-19 recovery: A systematic review and meta-analysis. Int J Cardiol. 2023;372:138-43.
13. Rodriguez-Leor O, Cid Alvarez AB, Perez de Prado A, et al. In-hospital outcomes of COVID-19 ST-elevation myocardial infarction patients. EuroIntervention. 2021;16:1426-33.
14. Garcia S, Dehghani P, Grines C, et al. Initial Findings From the North American COVID-19 Myocardial Infarction Registry. J Am Coll Cardiol. 2021;77:1994-2003.
15. Kelham M, Choudry FA, Hamshere S, et al. Therapeutic Implications of COVID-19 for the Interventional Cardiologist. J Cardiovasc Pharmacol Ther. 2021;26:203-16.
16. Task Force for the management of C-otESoC. 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;43:1059-103.
17. Chan DZ, Stewart RA, Kerr AJ, et al. The impact of a national COVID-19 lockdown on acute coronary syndrome hospitalisations in New Zealand (ANZACS-QI 55). Lancet Reg Health West Pac. 2020;5:100056.
18. Elliott JM, Crozier IG. Decreases in cardiac catheter laboratory workload during the COVID-19 level 4 lockdown in New Zealand. Intern Med J. 2020;50:1000-3.
19. Bhatia KS, Sritharan HP, Chia J, et al. Cardiac Complications in Patients Hospitalised With COVID-19 in Australia. Heart Lung Circ. 2021;30:1834-40.
20. Crudo VL, Ahmed AI, Cowan EL, Shah DJ, Al-Mallah MH, Malahfji M. Acute and Subclinical Myocardial Injury in COVID-19. Methodist Debakey Cardiovasc J. 2021;17:22-30.
21. Biasco L, Klersy C, Beretta GS, et al. Comparative frequency and prognostic impact of myocardial injury in hospitalized patients with COVID-19 and Influenza. Eur Heart J Open. 2021;1:oeab025.
22. Escher F, Pietsch H, Aleshcheva G, et al. Detection of viral SARS-CoV-2 genomes and histopathological changes in endomyocardial biopsies. ESC Heart Fail. 2020;7:2440-7.
23. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020;5:1265-73.
24. Changal K, Veria S, Mack S, et al. Myocardial injury in hospitalized COVID-19 patients: a retrospective study, systematic review, and meta-analysis. BMC Cardiovasc Disord. 2021;21:626.
25. Daniels CJ, Rajpal S, Greenshields JT, et al. Prevalence of Clinical and Subclinical Myocarditis in Competitive Athletes With Recent SARS-CoV-2 Infection: Results From the Big Ten COVID-19 Cardiac Registry. JAMA Cardiol. 2021;6:1078-87.
26. Coromilas EJ, Kochav S, Goldenthal I, et al. Worldwide Survey of COVID-19-Associated Arrhythmias. Circ Arrhythm Electrophysiol. 2021;14:e009458.
27. Knight R, Walker V, Ip S, et al. Association of COVID-19 With Major Arterial and Venous Thrombotic Diseases: A Population-Wide Cohort Study of 48 Million Adults in England and Wales. Circulation. 2022;146:892-906.
28. Nasrullah A, Gangu K, Shumway NB, et al. COVID-19 and Pulmonary Embolism Outcomes among Hospitalized Patients in the United States: A Propensity-Matched Analysis of National Inpatient Sample. Vaccines (Basel). 2022;10.
29. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med. 2020;383:120-8.
30. Tufano A, Rendina D, Abate V, et al. Venous Thromboembolism in COVID-19 Compared to Non-COVID-19 Cohorts: A Systematic Review with Meta-Analysis. J Clin Med.2021; 10.
31. Moores LK, Tritschler T, Brosnahan S, et al. Prevention, Diagnosis, and Treatment of VTE in Patients With Coronavirus Disease 2019: CHEST Guideline and Expert Panel Report. Chest. 2020;158:1143-63.
32. Bader F, Manla Y, Atallah B, Starling RC. Heart failure and COVID-19. Heart Fail Rev. 2021;26:1-10.
33. Rey JR, Caro-Codon J, Rosillo SO, et al. Heart failure in COVID-19 patients: prevalence, incidence and prognostic implications. Eur J Heart Fail. 2020;22:2205-15.
34. Vakili K, Fathi M, Pezeshgi A, et al. Critical complications of COVID-19: A descriptive meta-analysis study. Rev Cardiovasc Med. 2020;21:433-42.
35. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ. 2020;369:m1966.
36. Subramanian A, Nirantharakumar K, Hughes S, et al. Symptoms and risk factors for long COVID in non-hospitalized adults. Nat Med. 2022;28:1706-14.
37. Munro DAaM. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK. 2022.
38. Satterfield BA, Bhatt DL, Gersh BJ. Cardiac involvement in the long-term implications of COVID-19. Nat Rev Cardiol. 2022;19:332-41.
39. Shouman K, Vanichkachorn G, Cheshire WP, et al. Autonomic dysfunction following COVID-19 infection: an early experience. Clin Auton Res. 2021;31:385-94.
40. Roca-Fernandez A, Wamil M, Telford A, et al. Cardiac impairment in Long Covid 1-year post SARS-CoV-2 infection. European Heart Journal. 2022; 43.
41. Mitrani RD, Dabas N, Goldberger JJ. COVID-19 cardiac injury: Implications for long-term surveillance and outcomes in survivors. Heart Rhythm. 2020;17:1984-90.
42. Siripanthong B, Asatryan B, Hanff TC, et al. The Pathogenesis and Long-Term Consequences of COVID-19 Cardiac Injury. JACC Basic Transl Sci. 2022;7:294-308.