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Cardiovascular disease and COVID-19: Australian and New Zealand consensus statement

Abstract

Introduction: The coronavirus 2019 disease (COVID-19) pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Pre-existing cardiovascular disease (CVD) increases the morbidity and mortality of COVID-19, and COVID-19 itself causes serious cardiac sequelae. Strategies to minimise the risk of viral transmission to health care workers and uninfected cardiac patients while prioritising high quality cardiac care are urgently needed. We conducted a rapid literature appraisal and review of key documents identified by the Cardiac Society of Australia and New Zealand Board and Council members, the Australian and New Zealand Society of Cardiac and Thoracic Surgeons, and key cardiology, surgical and public health opinion leaders.

Main recommendations: Common acute cardiac manifestations of COVID-19 include left ventricular dysfunction, heart failure, arrhythmias and acute coronary syndromes. The presence of underlying CVD confers a five- to tenfold higher case fatality rate with COVID-19 disease. Special precautions are needed to avoid viral transmission to this population at risk. Adaptive health care delivery models and resource allocation are required throughout the health care system to address this need.

Changes in management as a result of this statement: Cardiovascular health services and cardiovascular health care providers need to recognise the increased risk of COVID-19 among CVD patients, upskill in the management of COVID-19 cardiac manifestations, and reorganise and innovate in service delivery models to meet demands. This consensus statement, endorsed by the Cardiac Society of Australia and New Zealand, the Australian and New Zealand Society of Cardiac and Thoracic Surgeons, the National Heart Foundation of Australia and the High Blood Pressure Research Council of Australia summarises important issues and proposes practical approaches to cardiovascular health care delivery to patients with and without SARS-CoV-2 infection.

On 11 March 2020, the World Health Organization declared coronavirus disease 2019 (COVID-19) a pandemic. The presence of underlying cardiovascular disease (CVD) confers the highest mortality with COVID-19. Thus, patients with CVD must be considered a particularly at-risk population.¹⁻⁵ Community transmission, patient-to-patient transmission and health care worker infection with severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) are overwhelming health services worldwide.⁴⁻⁶ High quality cardiac care must minimise risk of viral transmission to patients and health care workers. It should adapt resources in the context of reduced access to hospital beds and personal protective equipment (PPE). This consensus statement reviews and summarises data on SARS-CoV-2 infection in pre-existing CVD and acute cardiovascular manifestations of COVID-19, and makes recommendations for cardiac service provision during the pandemic.

Development process for the recommendations

A group of CVD experts, drawn from the Cardiac Society of Australia and New Zealand (CSANZ), the Australian and New Zealand Society of Cardiac and Thoracic Surgeons, the National Heart Foundation of Australia and the High Blood Pressure Research Council of Australia, convened in March 2020. Key opinion leaders in cardiology, cardiothoracic surgery and public health with broad geographic representation were consulted. We searched major databases (EMBASE, MEDLINE and PubMed) to identify relevant systematic reviews, randomised controlled trials and clinical case series in English from January 2020 to 25 March 2020. As the majority of studies relating to COVID-19 and CVD at the time of writing were observational in nature, results must be interpreted with caution. Given data limitations, consensus documents produced by international cardiology societies from December 2019 to March 2020 were reviewed.⁷⁻⁹ Experts from key areas (electrophysiology and pacing, interventional cardiology, imaging, cardiothoracic surgery, nursing, hypertension, prevention and rural) generated key recommendations from their respective councils and groups. In addition, social networking platforms (eg, WhatsApp) involving CSANZ board members, cardiology heads of department and key opinion leaders were used to identify relevant resources, guidance documents and protocols. An online living document was shared to facilitate wide input. The full draft underwent peer review by the listed authors as well as external experts in each subspecialty field of cardiology before agreement and acceptance of the final document.

Pre-existing cardiovascular disease and COVID-19

Patients with COVID-19 and pre-existing CVD are at increased risk of severe disease and death.¹⁻⁵ A meta-analysis of eight studies and over 46 000 patients in China reported that hypertension, diabetes and CVD were the most common comorbidities.⁵ Baseline CVD conferred the highest odds of any comorbidity for developing severe versus mild COVID-19 (odds ratio [OR], 3.42; 95% CI, 1.88–6.22). Hypertension (OR, 2.36; 95% CI, 1.46–3.83) and respiratory disease (OR, 2.46; 95% CI, 1.76–3.44) also increased the risk of severe COVID-19,⁵ while smoking did not.¹⁰ Patients with pre-existing CVD had high case fatality rates; five times that of the overall COVID-19 infected population (Box 1).⁴ In Italy, the case fatality rate has been the highest reported worldwide at 12.8%, with a corresponding high prevalence of baseline CVD in fatal cases.¹¹

Pre-existing CVD confers an increased risk of death with COVID-19; health services and patients should therefore take additional precautions.

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers

As SARS-CoV-2 enters cells by binding to human angiotensin-converting enzyme 2 (ACE2) receptors found in the lungs and heart,¹² activation of the renin-angiotensin system may contribute to the increased susceptibility to infection in patients with pre-existing CVD.¹³ It has been suggested that angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARBs) may increase the risk of SARS-CoV-2 infection or worsen the outcome,¹⁴ as treatment with ACE-I or ARBs can increase the expression and activity of ACE2 in some animal models.¹⁵ However, there is no clinical evidence substantiating an adverse effect of ACE-I or ARBs on COVID-19 outcomes. Conversely, there is evidence for protective effects from mouse models,¹⁶ and recombinant ACE2 and the ARB losartan are currently being tested in the United States as potential COVID-19 therapies.¹⁷ An Italian case-control study revealed that while ACE-I or ARB use was more frequent among COVID-19 patients owing to higher CVD prevalence, they did not influence COVID-19 severity.¹⁸

Given the well established beneficial effects of ACE-I and ARBs, we, along with numerous national and international societies, strongly recommend that these medications be continued.¹⁹⁻²¹

Acute cardiac injury and COVID-19

Acute cardiac injury in COVID-19 manifests as left ventricular dysfunction, heart failure, ventricular arrhythmias, electrocardiogram (ECG) changes, and elevated B-type natriuretic peptide and troponin levels.^{2,22-24} In the first 41 confirmed Chinese COVID-19 cases, acute cardiac injury defined as elevated cardiac biomarkers with ECG changes and left ventricular dysfunction was seen in 12% of patients.² A later study found acute cardiac injury in 19.7% of participants,²⁴ while a US study of 21 intensive care unit (ICU) patients described cardiomyopathy in 33%.²² Acute cardiac injury was independently associated with mortality in hospitalised patients with COVID-19 in China.²⁴

Pathophysiological theories for cardiac injury include direct infection of the myocardium with SARS-CoV-2, myocardial inflammation, Takotsubo syndrome and overwhelming multi-organ sepsis. While direct viral spread via ACE2 receptors in the myocardium has been postulated, a histopathological study of COVID-19-associated cardiomyopathy did not find direct SARS-CoV-2 infection.²⁵ Myocardial inflammatory infiltrates were instead seen.²⁶ For patients with left ventricular dysfunction, ACE-I, ARBs and β -blockers are indicated as the proposed pathophysiology of renin-angiotensin system imbalance with COVID-19 points to their potential therapeutic roles. However, much more study is needed to define the underlying pathophysiology and optimal

treatment.

Elevated troponin levels and myocardial infarction

Troponin and other cardiac enzymes are commonly elevated in COVID-19.^{2,3,5,22,26} Troponin elevation is a prognostic marker and may reflect myocarditis or myocardial infarction (MI).²⁷ The diagnostic implications are unclear as it can be associated with non-coronary conditions including acute respiratory infections²⁸ and type 2 MI.²⁹ Myocardial injury in COVID-19 patients can manifest with ST elevation in the absence of obstructive coronary artery disease. Many pathophysiological mechanisms have been proposed for COVID-19-related myocardial injury, including myocarditis, microvascular injury or obstruction, endothelial dysfunction and acute plaque rupture. In addition, a prothrombotic state has been commonly described with prominent elevations of D-dimer and fibrin/fibrinogen degradation products.³⁰⁻³²

In the setting of acute COVID-19 illness and suspected non-ST elevation (NSTEMI), patients who are haemodynamically stable without ongoing ischaemia may be best managed conservatively, with invasive procedures deferred until after recovery.

Cardiovascular implications of novel therapies

Numerous clinical trials assessing treatment for COVID-19 are being conducted. Chloroquine, hydroxychloroquine, azithromycin and ritonavir–lopinavir are under investigation, alone or in combination. These medications can cause cardiac toxicity, specifically QTc prolongation and torsades de pointes, especially in patients with hepatic or renal dysfunction.³³

Off-label prescribing of hydroxychloroquine has been reported and health professionals should be alert to cardiac toxicity in the community.

Recommendations for cardiovascular health care services

Safety is of paramount importance to limit COVID-19 exposure in high risk cardiology patients and our workforce. All patients need to be risk assessed for COVID-19 status to guide appropriate infection control measures (Box 2). All health services need to review elective procedures in order to increase hospital capacity and conserve valuable PPE. Alternative health care for patients at risk of COVID-19 that avoids exposure within the hospital system requires multidisciplinary assessment. Cardiac procedures that require long stays in hospital or the ICU should be carefully considered, owing to their impact on bed availability. An adaptable threshold for acute cardiology admissions and cardiac monitoring is needed. Stable angina, troponin-negative chest pain, non-life-threatening arrhythmias or cardiac diagnoses without clinical instability may be managed in an outpatient setting. Rapid discharge strategies should be instituted, including same-day discharge for elective percutaneous coronary intervention (PCI), and next-day discharge

for NSTEMI following revascularisation. As some elective procedures or hospital admissions cannot be safely postponed, nuanced clinical judgement is required.

Key considerations in the management of acute MI and coronary angiography

A critical concern during the COVID-19 pandemic is use of the cardiac catheterisation laboratory (Box 3). Bringing a COVID-19-positive patient to the cardiac catheterisation laboratory exposes staff to the risk of infection, and prevents post-procedure laboratory use pending a terminal clean. Delays are to be expected with primary PCI to allow for COVID-19 assessment and infection control measures. ST elevation MI (STEMI) protocols from China and the US during the COVID-19 pandemic have been published.^{23,29} The Sichuan Provincial People's Hospital proposed fibrinolytic therapy for all STEMI, with suspension of their primary PCI service.²⁹ This lysis protocol relied on rapid nucleic acid testing, which may be limited by individual hospital availability and policy. The US Cardiology Society recommended primary PCI continuation with appropriate PPE, and lysis for select cases.²³ In Australia, each health care service will be different, but it is important that a local protocol is developed and adapted (Box 4), with CSANZ guidance available.³⁴ Training in PPE, sourcing fibrinolytic medications and updating lysis protocols are critical. As COVID-19 is associated with STEMI mimickers (ST elevation without obstructive coronary artery disease due to microvascular thrombosis or myocarditis), use of lysis may confer risk without benefit in some cases, exacerbated by COVID-associated coagulation abnormalities.^{17,30} Bedside echocardiography to ascertain regional wall abnormalities and computed tomography coronary angiography to limit cardiac catheterisation laboratory staff exposure could all be considered.

Reliance on the presence of an elevated troponin level to indicate NSTEMI in COVID-19 patients will be misleading. Greater emphasis should be given to high risk clinical features such as recurrent chest pain, dynamic ischaemic ECG changes, heart failure, haemodynamic instability, major arrhythmias and regional wall motion abnormalities. It is reasonable to defer invasive investigations in stable COVID-19-positive patients without high risk features.

Regional and remote cardiovascular services

In Australia, established pre-hospital lysis programs currently exist, with cardiologist-led 24/7 ECG-reading service and pre-hospital/small hospital lysis for STEMI where PCI access is limited. Patients are then transferred to a PCI-capable hospital. These transfers will require additional screening for COVID-19. A greater level of cardiologist-led telehealth support for regional and rural centres will be needed. Centralised ECG-reading services are well placed to coordinate transfer logistics with linked calls between cardiologists and state retrieval, emergency and ICU consultants, balancing patient needs with staff safety and resource utilisation. It is important to continue to provide STEMI services for non-COVID-19 rural and regional patients already at a disadvantage in terms

of cardiovascular outcomes, while balancing the enormous resourcing demands that COVID-19 places on health care systems.

Cardiothoracic surgery considerations

On 25 March 2020, the Australian government suspended non-urgent surgery (<https://www.pm.gov.au/media/elective-surgery#:~:text=The%20National%20Cabinet%20is%20acting,will%20continue%20until%20further%20notice>). This suspension was lifted on 27 April 2020, with non-urgent surgery allowed, at a reduced capacity (<https://www.health.gov.au/news/australian-health-protection-principal-committee-ahppc-statement-on-restoration-of-elective-surgery-and-hospital-activity>). However patients with symptomatic disease will continue to present to hospital and require inpatient cardiac surgery. Cardiac surgical cases are likely to take longer during the COVID-19 pandemic owing to infection control measures, and access to ICU may at times be limited. The multidisciplinary heart team will need to consider and adjust thresholds for management of coronary artery disease in the event of increased hospital COVID-19 case load. The same applies to surgical aortic valve replacement or transcatheter aortic valve implantation for severe symptomatic aortic valve stenosis. The inherent risk of the untreated cardiovascular condition will need to be weighed against the risk of nosocomial infection during hospitalisation and the implications for ventilator use, bed stay and recovery time. Establishing or re-establishing cardiac surgical ICU programs with outcomes measures equivalent to those of the general ICU³⁵ could be considered in the future if needed, to free up precious general ICU resources.

Key considerations in imaging and stress testing

During the COVID-19 pandemic, elective cardiac investigations will need to be prioritised, based on short term management change versus risk of deferment until the pandemic passes. Certain cardiac investigations such as stress testing and transoesophageal echocardiography pose significant viral transmission risk. Exercise stress testing can result in droplet spread, whereas pharmacological testing that obviates the need for exercise or a technician in close proximity may be relatively safer.³⁶ Transoesophageal echocardiography involves instrumentation of the oropharynx, known to harbour the virus with high risk of aerosol transmission,³⁷ and should be undertaken only if transthoracic echocardiography cannot be performed, or after exclusion of COVID-19. If transoesophageal echocardiography is performed in a patient with COVID-19, it should be occur in a negative pressure room or with patient intubation with appropriate PPE. General considerations for transthoracic and transoesophageal echocardiography for patients with suspected or confirmed COVID-19 are summarised in Box 5.

Acute cardiac care and cardiopulmonary resuscitation

In COVID-19 cases with concomitant heart failure and hypoxaemia, non-invasive ventilation such as continuous positive airway pressure and bilevel positive airway

pressure is aerosol generating and not recommended.^{37,38} High flow nasal oxygen can be used within single rooms or shared COVID-19 ward spaces with strict attention to staff safety and the lowest flow necessary to maintain oxygen saturation $\geq 92\%$. Cardiopulmonary resuscitation is another important consideration, currently under review by the Australian National COVID-19 Taskforce. Defibrillation is not aerosol generating but all other resuscitative procedures are, and PPE is therefore recommended.³⁹ Ways to reduce COVID-19 transmission during cardiopulmonary resuscitation include covering the patient's mouth and nose with a mask, towel or plastic cover, and using mechanical compression devices. Discussion of goals of care remains important in both the inpatient and community setting. Management of hypoxaemia and cardiac arrest in patients with suspected or confirmed COVID-19 is summarised in Box 6.

Key considerations in electrophysiology and pacing services

The COVID-19 pandemic poses particular challenges in cardiac arrhythmia management, as patients require outpatient clinic review, ambulatory monitoring, electrophysiological interventions, implantation and follow-up of cardiac implanted electronic devices (Box 7). A team-based approach is advised, with teleconferences at weekly intervals to ensure maintenance of appropriateness criteria, urgency, and alignment of practices with the local outbreak response.

Considerations for outpatient cardiology care and use of telehealth

Strategies to minimise COVID-19 exposure in cardiovascular outpatient clinics must be adopted, including government recommendations for physical distancing. Serious consideration should be given to using telehealth for all outpatient consultations. For in-person consultations, verbal and temperature screening and social distancing are required. Administrative teams should be supported in their ability to maintain physical distancing to reduce their own exposure. Nurse-led clinics and cardiac rehabilitation programs will need to adapt by using telehealth or digital health platforms. Patients can be monitored and supported at home remotely, ensuring adequate medication supply, using a set of scales and blood pressure machines to titrate medications. Online support can enable patients to continue cardiac rehabilitation during home isolation.

Considerations for primary care and cardiovascular disease in the community

The importance of maintaining contact with patients by primary care physicians is highlighted by trends showing an unintended consequence of COVID-19 is less frequent primary care and delayed hospital presentations. The National Heart Foundation has released public health messages emphasising the importance of medication continuation and staying connected to treating doctors, and that it is both safe and beneficial to present to hospital if required.⁴⁰

Health care workers

There is a considerable risk of SARS-CoV-2 infection among health care workers.^{4,6} Health care services need to ensure adequate protection with appropriate PPE in the care

of COVID-19 patients. This includes fitted respirator masks (N95, FFP2 or equivalent) for any aerosol-generating procedures, and training in correct PPE use. Services may need to adapt to health care worker shortages and leave due to illness or quarantine. Cardiology trainees may also be affected by re-allocation within the hospital. The decision to move to a weekly rotation of staggered cardiology teams (relevant for clinicians, surgeons, sonographers and STEMI on-call teams) may limit infection of all staff if case numbers rise. Links to relevant documents and important websites are provided in the Supporting Information.

Conclusion

The COVID-19 pandemic is constantly evolving, and we must both prepare for and adapt to this global health care crisis. Cardiology services and providers need to develop and refine COVID-19 strategies according to the level of community infection and in accordance with both local hospital and governmental policy.

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[Boxes]

1 Case fatality rates of patients with COVID-19 with selected comorbidities*

Condition	Case fatality rate
Cardiovascular disease	10.5%
Diabetes	7.3%
Chronic respiratory disease	6.3%
Hypertension	6.0%
Cancer	5.6%
No comorbidities	0.9%

* Data from 44 672 confirmed COVID-19 cases from mainland China with an overall case fatality rate of 2.3% (1023 deaths).⁴

2 Assessment of patient risk for COVID-19

Clinical and radiological risk factors:*

- fever > 37.5°C (patients may have no or low grade fever on presentation)
- cough, shortness of breath or sore throat
- any influenza-like symptoms in a health care worker
- contact with a confirmed COVID-19 contact in the past 14 days
- arrival from overseas in the past 14 days
- lymphocyte count < $1.5 \times 10^9/L$
- bi-basal ground glass appearance (computed tomography) or bi-basal pneumonia (chest x-ray)

* Note: These risk factors may change; check the Australian Government Department of Health website at <https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert> for updates.

3 General considerations for catheterisation laboratory use during the COVID-19 pandemic

- Determine patient's COVID-19 status (see Box 2):
 - when available, consider rapid point-of-care testing; if unable to obtain history (eg, intubated patient), consider the patient to be at risk
- For all confirmed or suspected COVID-19 cases:
 - patients: surgical/medical mask if not intubated
 - all catheterisation laboratory staff: personal protective equipment including aerosol protection (N95 mask), given risk of emergent intubation/cardiopulmonary

resuscitation/vomiting in ST elevation myocardial infarction (aerosol-generating procedures)

- Patients approaching or requiring intubation should receive this before transfer to cardiac catheterisation laboratory, as intubation/suction/active cardiopulmonary resuscitation all increase aerosolisation of respiratory secretions
- Designate “dirty” COVID-19 catheterisation laboratories within each institution that are cleared of non-essential equipment and stock to facilitate cleaning. Consider dedicated laboratory stock for COVID-19 patients
- Limit the number of staff in the cardiac catheterisation laboratory to essential personnel (eg, cardiologist, scrub assistant, scout nurse)
- Minimise or abolish staff movements in and out of the laboratory during the case
- Institute a dedicated “clean” nurse role outside the laboratory to allow for passing equipment and medication, coordinate destination teams for transfer, and facilitate correct use of personal protective equipment
- A terminal clean following the procedure is required, with potential for delays in subsequent cases

4 General principles to consider for management of ST elevation myocardial infarction (STEMI) during the COVID-19 pandemic

[zam_mja20.00403_gr]

CTCA = computed tomography coronary angiography; PCI = percutaneous coronary intervention; PPCI = primary PCI; PPE = personal protective equipment. Note: At any stage in this pathway either PPCI or thrombolysis could be considered.

5 General considerations for transthoracic and transoesophageal echocardiography for patients with suspected or confirmed COVID-19

- Personal protective equipment for health care providers and assistants performing the test
- Shorten study duration to reduce face-to-face contact; eg, limiting transthoracic echocardiography to 15 minutes
- Dedicated COVID-19 machine and equipment
- Perform test in patient's room; do not bring patient to the cardiology department
- Plastic disposable covers for the machine and equipment, removed inside the room on completion, followed by complete clean of equipment with alcohol
- Consider hand-held or portable echocardiography if available
- Transoesophageal echocardiography has high risk for respiratory transmission and should be performed only if result will change treatment, in negative pressure room or designated theatre space
- Exercise electrocardiography and exercise stress echocardiography have high respiratory transmission risk and suspension of these services should be carefully considered

6 Management of hypoxaemia and cardiac arrest in patients with suspected or confirmed COVID-19

- Continuous positive airway pressure and bilevel positive airway pressure are aerosol generating and should be avoided
- High flow nasal oxygen can be used in single rooms or shared COVID-19 ward spaces with appropriate staff protection
- For resuscitation:
 - cover the patient's mouth and nose (mask, towel or other cover)
 - early defibrillation is life saving and not considered aerosol generating
 - chest compressions, assisted ventilation and advanced airway manoeuvres are considered aerosol generating (weak level of evidence)³⁹ and personal protective equipment should be worn
 - use mechanical compression devices if available
- Consider and document advance care directives

7 General considerations for electrophysiology and pacing during the COVID-19 pandemic

- For cardiac implanted electronic device follow-up:
 - avoid in-person clinics, hospitals and office visits
 - use remote monitoring/telehealth

- ▶ for major problems (eg, lead/battery or device therapies in defibrillator patients), consider risks of delayed visit versus risk of COVID-19 exposure
- Requests for urgent cardiac implanted electronic device interrogation by wards and emergency departments:
 - ▶ use remote monitoring and/or manual transmissions
 - ▶ face-to-face interrogation requires use of personal protective equipment and minimal number of technicians with wireless technology if possible
- Defer elective electrophysiology procedures for 1–3 months until personal protective equipment stocks are sufficient
- Urgent procedures to be continued: pacemaker for atrioventricular block and asystolic pauses; generator change for pacing dependent patients; secondary prevention defibrillators; catheter ablation in selective patients with ventricular tachycardia storm; lead extraction as determined by specialist centres
- Avoid ambulatory monitoring due to low yield; consider mail-out mobile electrocardiogram monitors